Open Forum Infectious Diseases

MAJOR ARTICLE

Truth in DAIR: Duration of Therapy and the Use of Quinolone/Rifampin-Based Regimens After Debridement and Implant Retention for Periprosthetic Joint Infections

Don Bambino Geno Tai,[1] Elie F. Berbari,[1] Gina A. Suh,[1] Brian D. Lahr,[2] Matthew P. Abdel,[3] and Aaron J. Tande[1]

[1]Division of Public Health, Infectious Diseases and Occupational Medicine, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA, [2]Department of Quantitative Health Sciences, Mayo Clinic, Rochester, Minnesota, USA, and [3]Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota, USA

Background. The optimal duration of antibiotic therapy after debridement and implant retention (DAIR) for periprosthetic joint infections (PJIs) is debated. Furthermore, the best antibiotic regimens for staphylococcal PJI are also unclear. In this study, we evaluated the impact of antibiotic therapy duration on the risk of failure. We assessed the utility of rifampin-based regimens for staphylococcal PJI managed with DAIR.

Methods. We performed a retrospective cohort study of patients 18 years and older diagnosed with hip and knee PJI who underwent DAIR between January 1, 2008 and 31 December 31, 2018 at Mayo Clinic, USA. The outcome was failure of DAIR. For statistical analysis, joint-stratified Cox regression models adjusted for age, sinus tract, symptom duration, and primary/revision arthroplasty were performed.

Results. We examined 247 cases of PJI with a median follow-up of 4.4 years (interquartile range [IQR], 2.3–7) after DAIR. The estimated 5-year cumulative incidence of failure was 28.1% ($n = 65$). There was no association between the duration of intravenous (IV) antibiotics (median 42 days; IQR, 38–42) and treatment failure ($P = .119$). A shorter duration of subsequent oral antibiotic therapy was associated with a higher risk of failure ($P = .005$; eg, 90-day vs 1-year duration; hazard ratio [HR], 3.50; 95% confidence interval [CI], 1.48–8.25). For staphylococcal knee PJI, both the use and longer duration of a rifampin-based regimen were associated with a lower risk of failure (both $P = .025$). There was no significant association between fluoroquinolone (FQ) use and failure (HR, 0.62; 95% CI, .31–1.24; $P = .172$).

Conclusions. The duration of initial IV antibiotic therapy did not correlate with treatment failure in this cohort of patients. Rifampin use is recommended for staphylococcal knee PJI. There was no apparent benefit of FQ use in staphylococcal PJI.

Keywords. prosthetic joint infection; quinolone; rifampin; treatment duration.

Total joint arthroplasty is among the most commonly performed surgical procedures in the United States. In the United States, primary total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) are projected to grow to more than 2 million procedures performed annually by 2030 [1]. It is unfortunate that periprosthetic joint infections (PJIs) complicate 0.5%–2% of primary THAs and TKAs [2]. Despite advances in infection control and surgical technique, PJI still has significant morbidity and economic burden [3, 4]. Debridement, antibiotics, and implant retention (DAIR) is one of the least invasive surgical management strategies for PJI. The surgical procedure involves excision of infected skin margins and sinus tracts, if present, radical synovectomy, thorough lavage, and exchange of modular components such as a polyethylene liner [5, 6]. Patients are commonly managed with a course of intravenous (IV) antibiotic therapy to be followed by a prolonged oral regimen.

Optimal regimens and duration of antimicrobial therapy in patients managed with DAIR are not fully elucidated. Published studies show conflicting results, with some showing incremental benefit with indefinite chronic suppression whereas others support shorter durations of less than 1 year [7–10]. Guidelines from the Infectious Diseases Society of America (IDSA) recommend a range of 2 to 6 weeks of initial IV antibiotics, whereas the International Consensus Meeting (ICM) guidelines on PJI suggest that 6 weeks is sufficient [11, 12]. The choice and route of antibiotics have garnered significant interest. The ICM guidelines do not specify the route of antibiotics, whereas trials, including the Oral versus Intravenous Antibiotics for Bone and Joint Infection (OVIVA) trial, show that early transition to oral antibiotics is noninferior to a full

Received 17 December 2021; editorial decision 18 July 2022; accepted 21 July 2022; published online 25 July 2022

Correspondence: Aaron J. Tande, MD, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 (tande.aaron@mayo.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofac363

course of IV antibiotics [13, 14]. For the most common type of PJI, staphylococcal infections, the role of rifampin and its companion antibiotics is contested [15]. An old randomized trial shows the superiority of rifampin with ciprofloxacin for staphylococcal PJI compared with ciprofloxacin alone, but a more recent trial did not show the same benefit [16, 17]. Observational studies also show conflicting results [18, 19].

This study aimed to identify the optimal duration of antibiotics in DAIR. To that end, we evaluated the risk of failure of DAIR concerning the duration of IV and oral antibiotics. For staphylococcal PJI, we also evaluated the risk of failure using rifampin and companion antibiotics. More specifically, we assessed the effect of the duration of rifampin use by joint on risk of failure.

METHODS

We performed a retrospective cohort study of patients 18 years and older diagnosed with PJI of the hip or knee and who underwent DAIR between January 1, 2008 and December 31, 2018 at a quaternary academic medical center. We queried our institution's Total Joint Registry (TJR) and its accompanying PJI database for an initial list of patients. The TJR and PJI database collected information on all cases of PJI diagnosed in our institution regardless of where the index arthroplasty was performed [20]. Patients who met the criteria for PJI and underwent DAIR for the first time in our institution were included. We excluded patients who were not managed with DAIR (eg, 1-stage or 2-stage exchange arthroplasty), underwent DAIR in another facility, did not consent to research, or died within the same admission. We reviewed the electronic medical record of all patients that met our inclusion criteria. Patients were followed from the debridement date until they met our definition of failure or the identified last visit in the electronic medical record. Study data were collected and managed using REDCap electronic data capture tool [21].

Definitions

We defined PJI as the presence of (1) 2 positive periprosthetic specimens with at least 1 matching organism, (2) a sinus tract, or (3) 3 of the following 5 criteria: elevated serum erythrocyte sedimentation rate/C-reactive protein, synovial fluid white blood cell count, synovial polymorphonuclear percentage, acute inflammation on histopathology, 1 positive periprosthetic culture [22, 23]. See Supplementary Table 1 for cutoff values used. Failure of DAIR was defined if any one of the following was present on follow-up: (1) recurrence of PJI as defined, (2) unplanned reoperation (DAIR, implant resection, amputation) secondary to infection, or (3) infection-related death. Clinical factors such as age, comorbidities, duration of symptoms, and orthopedic and infection history were assessed at the time of debridement. A staphylococcal PJI was defined as isolating at least 1 *Staphylococcus* species in cultures and was deemed clinically significant by treating physicians.

Antimicrobial Therapy

Orthopedic infectious diseases specialists selected the antibiotic regimens based on microorganism identified, susceptibility data, clinical scenario, contraindications, and drug-drug interactions. The duration of therapy was computed from the date of surgery to the date of stoppage. The antibiotic strategy was aligned with the IDSA guidelines [11]. Duration of IV and oral antibiotics were computed separately. If multiple changes were made during the oral antibiotic phase, the antibiotic used for the majority (>50%) of the time was listed.

Statistical Analysis

Treatment failure rates were estimated over time based on the cumulative incidence function to account for the competing risk of death from unrelated causes. Follow-up time was described by Kaplan-Meier quartile estimates. Extended Cox proportional hazard regression models with time-dependent variables were used to relate dynamic treatment measures with the risk of treatment failure. The duration of treatment was the primary independent variable, and a separate model was fit for each type of therapy: IV, oral (limited to cases free of failure at 60-day follow-up); and rifampin (for staphylococcal PJI). Each time-dependent duration variable was updated during follow-up to reflect the cumulative number of days on treatment; this was achieved by coding 0 for the days before therapy and then incrementally adding 1 for each additional day treated. Time-dependent variables indicating the use of treatment were also created for rifampin and FQ. To control for potential confounding, the models included 4 baseline covariates chosen a priori based on clinical relevance: age, presence of sinus tract, duration of symptoms, and primary or revision arthroplasty [12].

Specific models for the use or duration of rifampin were extended with treatment-by-joint interactions to allow for differential treatment effects for knees and hips. Because data were analyzed at the joint level and some patients contributed more than 1 observation, the White [24] cluster sandwich estimator was used to correct model estimates for correlated responses from the same patient. Treatment duration was modeled as a continuous, nonlinear variable using a restricted cubic spline function. The partial effects were plotted to depict the association between duration and the hazard of failure. The *P* value reported from the model is a test of nonflatness and represents the overall effect across the entire range of durations, whereas hazard ratios (HRs) were used to compare 2 specific values of the continuous function. Therefore, due to possible nonlinearity in the duration effect, the overall test of association may be significant even when the 95% confidence interval (CI) for the HR includes 1.0. All analyses were performed with

R statistical software (version 3.6.2; R Foundation for Statistical Computing, Vienna, Austria).

Patient Consent

This study was deemed exempt by the Mayo Clinic Institutional Review Board. Consent process was in compliance with the Minnesota Research Authorization law.

RESULTS

Baseline Characteristics

There were 1439 PJI cases identified during the study period. Of those, 247 cases of PJI in 237 patients were managed with DAIR. Most cases involved males (54.3%) with a median age of 70 years (interquartile range [IQR], 60–78). The most common comorbidity was diabetes mellitus (25.9%, $n = 64$) (Table 1). Twenty-five percent of cases had a history of revision arthroplasty due to infection ($n = 62$). The median duration of symptoms was 7 days (IQR, 3–19). Sinus tract was present in 12.1% ($n = 30$). The majority were monomicrobial infections (72.9%, $n = 180$), 19% were polymicrobial ($n = 47$), and 8.1% were culture-negative ($n = 20$). Overall, 23.3% had an associated bloodstream infection ($n = 57$). The most common causative microorganism was *Staphylococcus aureus* complex (35.6%, $n = 88$), followed by coagulase-negative staphylococci (23.4%, $n = 58$). Gram-negative bacteria were involved in 29 cases (11.7%). See Supplementary Table 2 for the full list of organisms isolated.

Table 1. Baseline Clinical Characteristics of Cases

Clinical Characteristics	Total ($N = 247$)
Age in years, median (IQR)	70 (60–78)
Male sex, *n* (%)	134 (54.3)
Race, White, *n* (%)[a]	242 (98.8)
Body mass index in kg/m^2, median (IQR)[a]	32.0 (27.7–38.6)
Diabetes mellitus, *n* (%)	64 (25.9)
Congestive heart failure, *n* (%)	38 (15.4)
Chronic obstructive pulmonary disorder, *n* (%)	36 (14.6)
Rheumatoid arthritis, *n* (%)	31 (12.6)
Immunocompromised, *n* (%)	14 (5.7)
Chronic kidney disease, *n* (%)	11 (4.5)
Liver cirrhosis, *n* (%)	8 (3.2)
Active tobacco use, *n* (%)	22 (8.9)
Alcohol use disorder, *n* (%)	5 (2.0)
Primary arthroplasty, *n* (%)	125 (50.6)
Revision arthroplasty, *n* (%)	122 (49.4)
Due to infection	62 (25.1)
Due to aseptic reasons	60 (24.3)
Joint Type	
Total hip arthroplasty, *n* (%)	87 (35.2)
Hip hemiarthroplasty, *n* (%)	11 (4.5)
Total knee arthroplasty, *n* (%)	147 (59.5)
Unicompartmental knee arthroplasty, *n* (%)	2 (0.8)
Cemented arthroplasty, *n* (%)	172 (69.6)
C-reactive protein in mg/L, median (IQR)[b]	101.2 (41.3–196.1)

Abbreviations: IQR, interquartile range.

[a] $n = 245$ (99.2%) with available information.

[b] $n = 214$ (86.6%) with available information.

Management of Infection

All procedures were performed through open debridement. Modular components were exchanged in 59.1% ($n = 146$) of cases. Intravenous antibiotic therapy was used to treat all but 2 cases for a median duration of 42 days (IQR, 38–42). The most commonly used IV antibiotics were beta-lactams (66.8%, $n = 165$) followed by vancomycin (32.4%, $n = 80$). Note that 9.3% were concurrently treated with a second IV antibiotic ($n = 23$), most often due to polymicrobial infection. Oral antibiotics were prescribed after IV antibiotics in 227 cases (91.9%) for a median duration of 2.1 years (IQR, 0.9–4.1), 26 of whom had oral antibiotics discontinued after a median of 1.4 years (IQR, 0.7–2.4) due to various reasons (ie, patient preference, provider recommendation, adverse events). The remaining patients were still on oral antibiotics until the end of follow-up.

Outcomes and Duration of Therapy

Failure of therapy occurred in 65 cases over a median follow-up of 4.4 years (IQR, 2.3–7.0), with a 5-year cumulative failure rate of 28.1% (35.9% in knee cases and 16.2% in hip cases) (Figure 1). Thirty-six failures occurred in the first year (55.4%), including 13 while receiving IV antibiotics. When the duration of IV antibiotics was modeled as a continuous

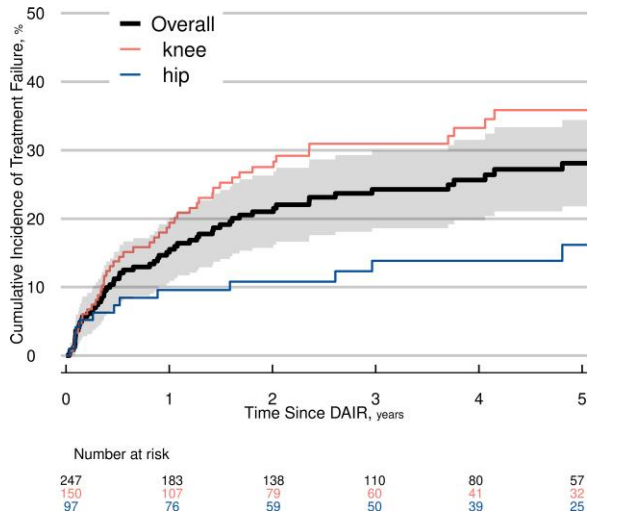

Figure 1. Cumulative incidence of treatment failure. The thick black curve depicts the overall rate of treatment failure over time, as estimated by the cumulative incidence function after accounting for the competing risk of death from unrelated causes. The shaded region represents the 95% confidence band. Joint-specific cumulative incidence curves begin to diverge at approximately 3 months, after which time failure is proportionately less for hip periprosthetic joint infection (PJI) than for knee PJI. DAIR, debridement, antibiotics, and implant retention.

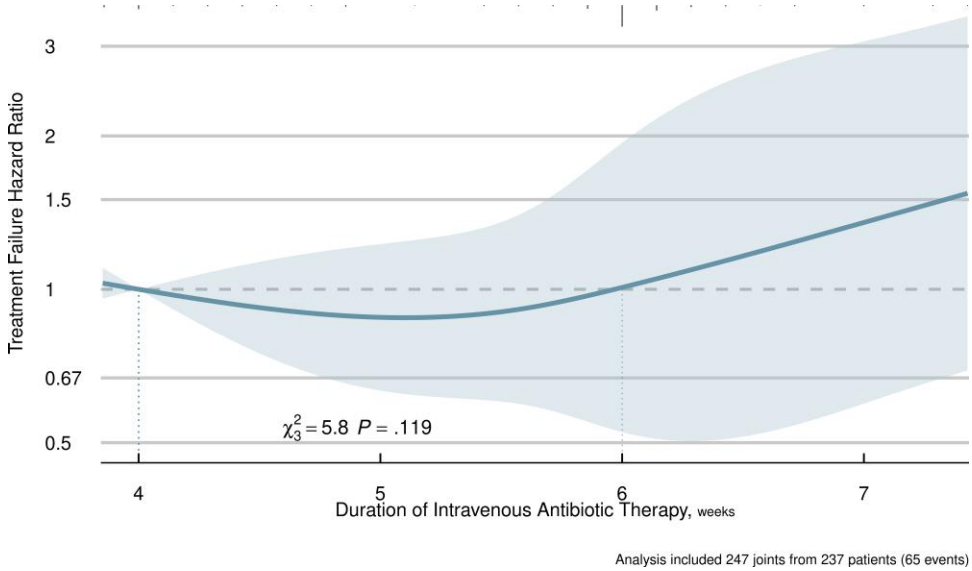

Figure 2. Estimated relationship between duration of intravenous antibiotic therapy and failure. The curve displays the hazard ratio for failure comparing any given value of intravenous antibiotic duration on the x-axis with the reference value, as computed from the adjusted analysis after accounting for 4 relevant covariates in a time-dependent Cox model. Shaded areas represent 95% confidence intervals. Dotted vertical lines are used to denote the reference value of 4 weeks and the primary comparison value of 6 weeks, which are shown to have similar hazard. The tick marks displayed at the top of the plot represent the data distribution, with the height of the lines proportional to the number of patients treated for that value of duration.

variable adjusting for possible confounding factors, we did not find a significant association between duration and treatment failure ($P = .119$) (Figure 2). Specifically, when comparing 4 weeks versus 6 weeks in the continuous function, we did not see a difference in outcomes (HR, 1.01; 95% CI, .52–1.94).

Of the 26 cases in which oral antibiotics were stopped during follow-up, 5 subsequently failed (median time from surgery to failure was 2.0 years [range, 0.8–6.0] and 4.0 months [range, 1.8–24.0] after cessation). An additional 46 cases failed over time while on oral antibiotics (median time to failure on oral antibiotics was 12.3 months [range, 1.5–72.8]). In the adjusted Cox analysis restricted to cases free of failure at 60-day follow-up (thereby removing those who failed early on before receiving oral antibiotics), a shorter duration of oral antibiotic duration was associated with an increased risk of failure ($P = .005$). However, the increased hazard appeared to be driven by data early in the treatment course (eg, 90-day vs 1-year duration; HR, 3.50; 95% CI, 1.48–8.25), because no detectable differences in risk were observed over longer durations (eg, comparison of 5-year vs 1-year duration; HR, 1.43; 95% CI, .29–6.98). Supplementary Figure 1 illustrates the relation between the duration of oral antibiotics with the risk of failure.

Antibiotics for Staphylococcal Periprosthetic Joint Infection

Staphylococcal PJI comprised 60.7% of all cases ($n = 150$). There were 135 cases (90.0%) that succeeded past the IV antibiotic phase (median duration of 42 days [IQR, 39–42]) and were prescribed oral antibiotics. Of these, FQ were used in 31.1% (42 of 135) with a median duration of 102 days (IQR, 42–156) before failing or being switched to another class of oral antibiotics. Of the 42 staphylococcal PJI cases treated with FQ, 38 were also given rifampin. The remaining 93 cases were treated with non-FQ, most commonly tetracyclines ($n = 46$) followed by beta-lactams ($n = 39$) and trimethoprim/sulfamethoxazole ($n = 13$). Note that 6 cases were concomitantly treated with 2 non-FQ antibiotics. In the adjusted analysis, there was no significant association between FQ use and failure (HR, 0.62; 95% CI, .31–1.24; $P = .172$).

Of the 150 cases with staphylococcal PJI, 103 (68.7%) received a rifampin-based regimen for a median duration of 95 days (IQR, 51.5–180.5). In the adjusted Cox analysis, the use of rifampin showed a protective effect overall ($P = .025$), with a lower risk of failure in treating knee PJI (HR, 0.40; 95% CI, .20–.79; $P = .008$) but no significant effect for hip PJIs (HR, 1.47; 95% CI, .35–6.15; $P = .597$). A longer duration of rifampin was also associated with a significantly lower risk of failure overall ($P = .025$) (Figure 3). Specifically, for knee PJI, there was a significant benefit from a longer duration of rifampin ($P = .025$), with the specific comparison of 6- versus 3-month duration trending toward significance (HR, 0.58; 95% CI, .28–1.20). See Table 2 for a summary of the results.

DISCUSSION

The optimal antimicrobial strategy in patients managed with DAIR is unknown, with wide variations in practice worldwide. Establishing the optimal antimicrobial strategy will undoubtedly improve the success rates of DAIR and reduce the misuse of

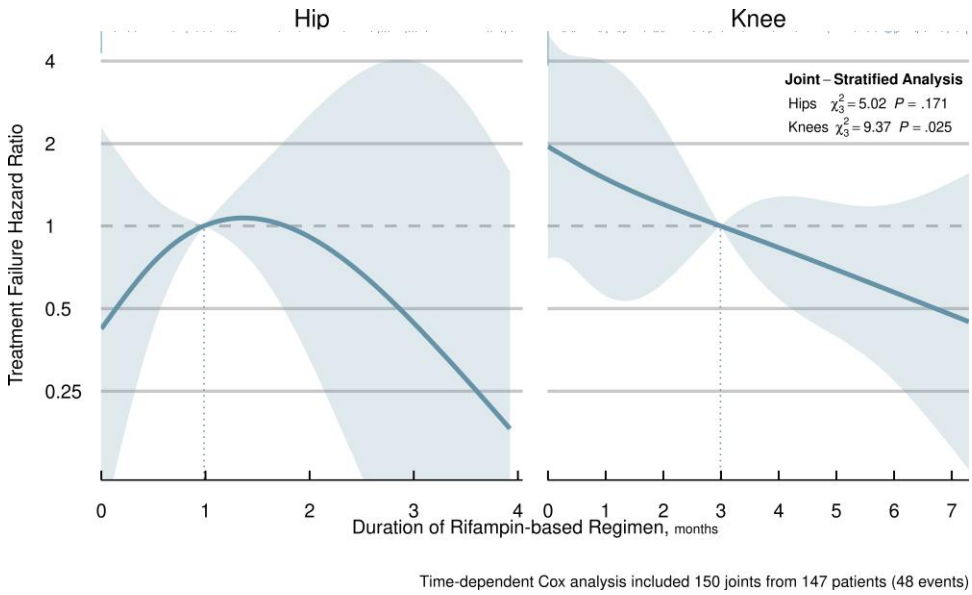

Figure 3. Estimated relationship between rifampin duration and failure for knee- and hip-specific staphylococcal periprosthetic joint infection (PJI). The curves display the hazard ratios for failure comparing any given value of rifampin duration on the x-axis with the reference value, as computed from the joint-stratified analysis after adjusting for 4 relevant covariates in a time-dependent Cox model. Shaded areas represent 95% confidence intervals. For reference levels, which are denoted by the dotted vertical lines, we used a rifampin duration of 1 month for hip PJI and 3 months for knee PJI. The tick marks displayed at the top of each panel represent the data distribution, with the height of the lines proportional to the number of patients treated for that value of duration.

antibiotics. In this retrospective cohort study, we looked at outcomes of patients with PJI managed with DAIR concerning the duration of treatment. We also investigated the antibiotic regimens for staphylococcal PJI.

Table 2. Association of Time-Dependent Treatment Measures with Failure of DAIR[a]

Variable	Joints (Patients)	Events	Contrast	Adjusted HR (95% CI)	*P* Value
Total cohort Intravenous antibiotic duration	247 (237)	65	6 w: 4 w	1.01 (0.52-1.94)	.119
Cases failure-free at day 60 Oral antibiotic duration	223 (213)	51	90d:1y 5y: 1y	3.50 (1.48-8.25) 1.43 (0.29-6.98)	.005
Staphylococcal PJI cases FQ use	150 (147)	48	Yes: No	0.62 (0.31–1.24)	.172
Rifampin use					
Knee	90 (87)	38	Yes: No	0.40 (0.20–0.79)	.008
Hip	60 (60)	10	Yes: No	1.47 (0.35–6.15)	.597
Rifampin duration					
Knee	90 (87)	38	6 m: 3 m	0.58 (0.28–1.20)	.025
Hip	60 (60)	10	3 m: 1 m	0.45 (0.05–4.01)	.171

Abbreviations: FQ, fluoroquinolone; HR, hazard ratio; CI, confidence interval; d, days; m, months; w, weeks; y, year/s.

[a]To assess association with treatment failure, each treatment measure was analyzed separately as a time-dependent covariate in a Cox model among individuals eligible to receive that treatment. Duration was modeled with a restricted cubic spline to relax linearity assumptions; hazard ratios were computed based on prespecified (arbitrary) time points for comparison, whereas *P* values represent the overall effect across the entire range of durations. Due to possible nonlinearity, the overall test of association may be significant even when the CI does not exclude HR = 1.

Statistical analysis of the duration of IV antibiotics revealed no overall association with the risk of treatment failure. Our analysis did not suggest any thresholds for which dichotomizing duration into 2 groups would have yielded significant differences in risk. Note that only a small number of patients in our cohort were treated with IV antibiotics for less than 4 weeks. Thus, we cannot definitively conclude whether a 2-week or even 2-week duration of IV antibiotics is as effective as 6 weeks. Nevertheless, this finding was consistent with randomized controlled trials showing that early switching to oral therapy was noninferior to completing the entire course with IV antibiotics [13, 14]. We observed an increased risk of failure associated with a shorter duration of oral antibiotics. This finding is consistent with the findings of the DATIPO trial that showed that a 6-week course of antibiotic therapy was inferior to 12 weeks of antibiotics for DAIR [25]. However, the vast majority of our cohort were treated with indefinite suppression, which precludes us from drawing conclusions on the optimal duration of oral antibiotics.

For staphylococcal PJI, most studies and guidelines support the use of rifampin-combination therapy [11, 26]. This study confirms the findings of Beldman et al [26], showing that there are outcome benefits to using a rifampin-based regimen, particularly with knee PJIs. This study is congruent with existing literature that endorses using a longer duration of rifampin and its association with improved outcomes, particularly for knee PJIs [18, 27, 28]. Our modeling further showed a modest but nonsignificant reduction in risk for the 6-month duration of

therapy compared with 3 months for knee PJIs. We did not see a significant treatment benefit of rifampin with hip PJI. However, this might be due to the smaller sample size and fewer observed events in this subgroup.

Some studies showed that non-FQ regimens portend a higher risk of failure [12, 26]. However, this study did not detect a significant difference in outcomes between a rifampin-based regimen containing FQ versus non-FQ. This finding is significant because many patients may not tolerate a prolonged course of FQ and discontinuation is necessary for up to 36% of patients [29]. There are considerable differences in definitions and methods among the studies assessing these antibiotic strategies for staphylococcal PJI; thus, head-to-head comparisons are challenging.

The limitations of this study include the possibility of confounding. Although efforts were made to adjust for key risk factors of failure, the sample size and number of events limited our ability to adjust for all known risk factors. There is potential bias from confounding by indication, because there might be comorbidities that increase the risk of failure and are also a contraindication to rifampin and FQ. The antimicrobial treatment strategy for each case was not standardized, leading to heterogeneity in our patient population. Our definition of antibiotics did not evaluate short-term exposures to different antibiotics due to modifications in treatment by the managing physicians. Furthermore, the study's retrospective nature limits our ability to ensure adherence to oral antibiotics. Randomized, adequately powered trials on patients with a defined surgical strategy that reflects the reality of clinical practice are required to the question on the duration of antibiotics past 12 weeks.

CONCLUSIONS

In conclusion, among patients with PJI managed with DAIR, the duration of initial IV antibiotics did not correlate with treatment failure. For staphylococcal PJI, the use of rifampin is associated with a reduced risk for failure of DAIR, whereas there was no apparent benefit of FQ.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

We thank Paula Clausen, Youlonda Loechler, and Brenda Dylla for invaluable contributions to this study.

Disclaimer. The contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

Financial support. This project was partly funded by Grant Number UL1 TR002377 from the National Center for Advancing Translational Sciences.

Potential conflicts of interest. M. P. A. reports royalties from Stryker and is on the American Academy of Orthopaedic Surgeons (AAOS) Board of Directors. E. F. B. and A. J. T. reports honorary from Uptodate.com, unrelated to this work. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Sloan M, Premkumar A, Sheth NP. Projected volume of primary total joint arthroplasty in the U.S., 2014 to 2030. J Bone Joint Surg Am **2018**; 100: 1455–60.
2. Ahmed SS, Haddad FS. Prosthetic joint infection. Bone Joint Res **2019**; 8:570–2.
3. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty **2012**; 27:61–5.e1.
4. Kurtz SM, Lau EC, Son M-S, Chang ET, Zimmerli W, Parvizi J. Are we winning or losing the battle with periprosthetic joint infection: trends in periprosthetic joint infection and mortality risk for the Medicare population. J Arthroplasty **2018**; 33: 3238–45.
5. Qasim SN, Swann A, Ashford R. The DAIR (debridement, antibiotics and implant retention) procedure for infected total knee replacement—a literature review. SICOT J **2017**; 3:2.
6. Choo KJ, Austin M, Parvizi J. Irrigation and debridement, modular exchange, and implant retention for acute periprosthetic infection after total knee arthroplasty. JBJS Essent Surg Tech **2019**; 9:e38.1–2.
7. Shah NB, Hersh BL, Kreger A, et al. Benefits and adverse events associated with extended antibiotic use in total knee arthroplasty periprosthetic joint infection. Clin Infect Dis **2020**; 70:559–65.
8. Puhto AP, Puhto T, Syrjala H. Short-course antibiotics for prosthetic joint infections treated with prosthesis retention. Clin Microbiol Infect **2012**; 18:1143–8.
9. Byren I, Bejon P, Atkins BL, et al. One hundred and twelve infected arthroplasties treated with 'DAIR' (debridement, antibiotics and implant retention): antibiotic duration and outcome. J Antimicrob Chemother **2009**; 63:1264–71.
10. Chaussade H, Uçkay I, Vuagnat A, et al. Antibiotic therapy duration for prosthetic joint infections treated by debridement and implant retention (DAIR): similar long-term remission for 6 weeks as compared to 12 weeks. Int J Infect Dis **2017**; 63:37–42.
11. Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis **2013**; 56:e1–25.
12. Argenson JN, Arndt M, Babis G, et al. Hip and knee section, treatment, debridement and retention of implant: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty **2019**; 34:S399–419.
13. Li H-K, Rombach I, Zambellas R, et al. Oral versus intravenous antibiotics for bone and joint infection. N Engl J Med **2019**; 380:425–36.
14. Manning L, Metcalf S, Dymock M, et al. Short versus standard course intravenous antibiotics for peri-prosthetic joint infections managed with debridement and implant retention: a randomised pilot trial using a desirability of outcome ranking (DOOR) endpoint. Int J Antimicrob Agents **2022**; 60:106598.
15. Tai DBG, Patel R, Abdel MP, Berbari EF, Tande AJ. Microbiology of hip and knee periprosthetic joint infections: a database study. Clin Microbiol Infect **2022**; 28: 255–9.
16. Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant–related staphylococcal infections: a randomized controlled trial. JAMA **1998**; 279: 1537–41.
17. Karlsen ØE, Borgen P, Bragnes B, et al. Rifampin combination therapy in staphylococcal prosthetic joint infections: a randomized controlled trial. J Orthop Surg Res **2020**; 15:365.
18. Becker A, Kreitmann L, Triffaut-Fillit C, et al. Duration of rifampin therapy is a key determinant of improved outcomes in early-onset acute prosthetic joint infection due to Staphylococcus treated with a debridement, antibiotics and implant retention (DAIR): a retrospective multicenter study in France. J Bone Joint Infect **2020**; 5:28–34.
19. El Helou OC, Berbari EF, Lahr BD, et al. Efficacy and safety of rifampin containing regimen for staphylococcal prosthetic joint infections treated with debridement and retention. Eur J Clin Microbiol Infect Dis **2010**; 29:961–7.
20. Malchau H, Garellick G, Berry D, et al. Arthroplasty implant registries over the past five decades: development, current, and future impact. J Orthop Res **2018**; 36:2319–30.
21. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inform **2019**; 95: 103208.
22. Shohat N, Bauer T, Buttaro M, et al. Hip and knee section, what is the definition of a periprosthetic joint infection (PJI) of the knee and the hip? Can the same criteria

be used for both joints?: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty **2019**; 34:S325–7.
23. Centers for Disease Control and Prevention. 2022 NHSN Bone and Joint Infection. Atlanta, Georgia: Centers for Disease Control and Prevention, **2022**.
24. White H. Maximum likelihood estimation of misspecified models. Econometrica **1982**; 50:1–25.
25. Bernard L, Arvieux C, Brunschweiler B, et al. Antibiotic therapy for 6 or 12 weeks for prosthetic joint infection. N Engl J Med **2021**; 384:1991–2001.
26. Beldman M, Löwik C, Soriano A, et al. If, when, and how to use rifampin in acute staphylococcal periprosthetic joint infections, a multicentre observational study. Clin Infect Dis **2021**; 73:1634–41.
27. Tonnelier M, Bouras A, Joseph C, et al. Impact of rifampicin dose in bone and joint prosthetic device infections due to Staphylococcus spp: a retrospective single-center study in France. BMC Infect Dis **2021**; 21:174.
28. Scheper H, Gerritsen LM, Pijls BG, Van Asten SA, Visser LG, De Boer MGJ. Outcome of debridement, antibiotics, and implant retention for staphylococcal hip and knee prosthetic joint infections, focused on rifampicin use: a systematic review and meta-analysis. Open Forum Infect Dis **2021**; 8:ofab298.
29. Vollmer NJ, Rivera CG, Stevens RW, et al. Safety and tolerability of fluoroquinolones in patients with staphylococcal periprosthetic joint infections. Clin Infect Dis **2021**; 73:850–6.