Prospective Cohort Study Identifying Risk Factors Associated With Treatment Failure For Acute Periprosthetic Joint Infections After Debridement Antibiotics And Implant Retention

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INTRODUCTION:

Periprosthetic joint infections (PJI) are common and serious complications following knee and hip arthroplasty. Our previous retrospective study suggested extended antibiotics following DAIR decreased failure rates and were not associated with increased adverse events. Further, extended antibiotics beyond one year did not provide additional benefits. These observations were tested in a prospective cohort study.

The objectives of our study included: 1) identifying protective and risk factors that cause PJI treatment failure 2) determining if extended antibiotic exposes patients to more adverse events 3) comparing the rates of treatment failure between patients who underwent DAIR with and without the use of extended oral antibiotics.

METHODS:

A multicenter prospective cohort of patients who underwent DAIR for total knee arthroplasty PJI and received primary antibiotics were compared to patients that received primary antibiotics combined with extended antibiotics for one year. Participants had a minimum of 2-year follow-up. The primary outcome of interest was the failure rate derived from the survival time between the DAIR procedure and future treatment failure. Secondary endpoints included adverse events associated with antibiotics.

RESULTS:

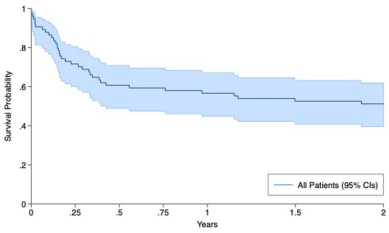
A prospective cohort of 79 patients were followed where 39 participants (52.7%) received primary antibiotics and 35 participants (47.3%) received both primary and extended antibiotics following DAIR. Multivariable time-to-event analyses revealed that extended antibiotic use as an independent predictor of treatment success. Infection-free survival differed significantly between the two treatment regimens, as the hazard of PJI failure was significantly lower for extended antibiotics as compared to primary antibiotics alone (adjusted HR=0.46 [0.24, 0.87], p= 0.017). Adverse event rates did not significantly differ between patients treated with primary antibiotics only versus primary combined with extended antibiotics.

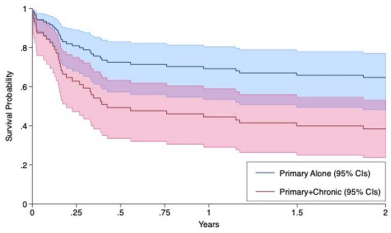
DISCUSSION AND CONCLUSION:

The use of extended antibiotics in the treatment of PJI is controversial. Several studies have suggested that extended oral antibiotics can be used to prevent PJIs in high-risk patients. Other studies have not demonstrated these results. All of these studies were retrospective. We had previously observed that extended antibiotic therapy decreased treatment failure following DAIR, was not associated with additional adverse events as compared to primary antibiotics, and there was no further benefit with continued antibiotic therapy after a one-year time period. A limitation of our previous study was that it was retrospective. Therefore, this prospective cohort study was performed to test if one year of extended antibiotics decreased treatment failure and had limited adverse events as compared to primary antibiotics alone.

Our prospective study observed that antibiotic duration is a statistically significant predictor of PJI failure, with longer antibiotic duration resulting in decreased PJI treatment failure rates. A statistically significant difference in hazard rates for PJI failures in patients treated with extended antibiotics versus primary antibiotic therapy alone was noted (adjusted HR= 0.46 [0.24, 0.87], p=0.017). This is shown in Table 2 and visualized on our Kaplan Meier Survival Curve in Figure 2. These findings reinforce initial observations that extended antibiotic therapy could help prevent PJI treatment failure. This falls in line with literature that has shown patients who received extended antibiotic therapy after a DAIR have improved infection-free survival versus patients who do not receive such therapy. We hypothesize that a longer duration provides additional benefit given that many organisms have the ability to produce antibiotic tolerant biofilms on the implant surface, resulting in eventual treatment failure. Antibiotic therapy beyond they 6-week mark for individuals who undergo PJI may help overcome the antibiotic tolerance seen in common infectious PJI pathogens.

This prospective cohort study supports previous observations that extended antibiotics for one year was associated with lower failure rates as compared to primary antibiotics alone. Extended antibiotics after primary antibiotics was not found to be associated with increased adverse events as compared to only primary antibiotics.





Predicting Factors	Unadjusted HR (95% CI)	Unadjusted P Value	Adjusted HR	Adjusted P Value
Abx Duration		**0.043**		**0.017**
Primary Alone	(reference level)		(reference level)	
Primary+ Chronic	0.53 (0.28, 0.98)		0.46 (0.24, 0.87)	
Age	0.98 (0.96, 1.01)	0.219	---	---
BMI	0.99 (0.95, 1.03)	0.596	---	---
Sex		0.091		**0.036**
Male	(reference level)		(reference level)	
Female	0.58 (0.30, 1.11)		0.49 (0.25, 0.95)	
CCMI	0.92 (0.79, 1.08)	0.281	---	---
DM	0.77 (0.34, 1.75)	0.538	---	---
RA	1.27 (0.50, 3.25)	0.616	---	---
ASA Score		0.199	---	---
1-2	(reference level)			
3	1.65 (0.68, 4.00)			
4	3.40 (0.93, 12.42)			
Host Score		0.588	---	---
A	(reference level)			
B	0.68 (0.31, 1.47)			
C	0.78 (0.10, 6.27)			
Time Symptomatic			---	---
<1 week	(reference)	0.861		
2-4 weeks	1.08 (0.45, 2.59)			
>4 weeks	NA (nobody >4 weeks)			
Primary Organism		0.262	---	---
Culture Negative	(reference)			
Staph Aureus	1.45 (0.68, 3.21)			
Other	0.80 (0.36, 1.78)			

Table 2: Multivariable Analysis of Predictors of Treatment Success