

HK92: What is the optimal management of patients undergoing revision arthroplasty for presumed aseptic failure in whom a single culture isolates an organism?

Jason M. Jennings, Benjamin Ricciardi, Edward Vasarhelyi, Georgios Komnos, George Babis, Carolyn Kramer, Rajeev K. Sharma, Udit Vinayak, Nicholas C. Arpey

Response/Recommendation:

Assuming that the patient undergoing revision had negative work up for periprosthetic joint infection (PJI) and only one out of at least three cultures turned positive, then the single culture can be ignored. The circumstances when a single positive culture may lead to the need for additional antibiotic treatment is when the isolated organism is the same as the original infective organism and/or PJI could not be ruled out with confidence prior to surgery. .

Strength of recommendation: Moderate

Delegate Vote:

Rationale:

Periprosthetic joint infection (PJI) may be present in patients undergoing revision THA and TKA for aseptic failure, even when preoperative workup is negative.¹ Since the treatment of septic and aseptic failure differs significantly, an accurate diagnosis is essential for proper management. Therefore, it is recommended that intraoperative samples be sent for culture in all revision THA and TKA cases, regardless of the suspected cause of failure.² Current guidelines define a single positive culture as a “minor criterion” for PJI, contributing two points to a score that classifies a joint as “infected” if it reaches six or more points.³ Patients who meet the criteria for PJI should be treated accordingly. However, the optimal management of patients undergoing revision arthroplasty for presumed aseptic failure where a single culture isolates an organism (in the absence of other supporting criteria for PJI) remains uncertain.

Twelve studies have evaluated this patient population. Of the included 10,228 presumed aseptic revisions, single positive cultures occurred in 860 cases (8.4%). The most commonly isolated pathogens were slow growing bacteria, predominantly coagulase negative staphylococcus and *Cutibacterium acnes*. Ten of the studies reported no statistically significant influence on the revision-free (RFS) or infection-free (IFS) survival following a single positive culture. Goh et al. conducted a retrospective review of patients at their institution who underwent presumed aseptic revision THA and TKA and compared the outcomes of patients who had a single positive culture (n = 196) or multiple positive cultures for distinct organisms (n = 19) to those who had negative cultures (n = 3,019). No patients with positive cultures were treated with antibiotics.⁴ The authors demonstrated no significant difference in all-cause reoperation (14.0% vs 12.3%, p = 0.484) or PJI (3.3% vs 1.9%, p = 0.151) between the groups at mean follow-up of 10.8 years. Furthermore, single culture positivity was not associated with the rate of all-cause reoperation (OR 0.995, 95% CI 0.606-1.635, p = 0.985) or PJI (OR 0.662, 95% CI 0.231-1.898, p = 0.443) on multivariate regression analysis. In their cohort of single component THA or TKA revisions, Vargas-Reveron et al. demonstrated that the presence of a single positive culture (n = 35) was not associated with a higher re-revision rate at 5 years than in those with negative

cultures (n = 97) (5.7% vs 3.1%, $p > 0.05$). Six patients with a single positive culture were treated with antibiotics for 4 weeks.⁵ Leal et al. and Wu et al. each performed a retrospective study of patients with unsuspected positive intraoperative cultures in presumed aseptic revision THA and TKA using a database from the same single tertiary academic medical center. When comparing 5-year IFS between patients who had a single positive culture with a new organism (hip: n = 59, knee: n = 49) and negative cultures (hip: n = 530, knee: n = 630), there was no difference for both the hip (86% vs 92%, $p = 0.400$) and the knee (89% vs 96, $p = 0.390$) cohorts. However, patients who had a single positive culture with the same organism from a prior PJI (n = 1) had a significantly lower 5-year IFS when compared to patients with negative cultures (0% vs 92%, $P < 0.001$). Cox proportional hazards regression analysis suggested that a single positive culture did not increase the likelihood of subsequent revision for infection in the hip cohort (HR = 1.27, 95% CI 0.555-2.910, $p = 0.570$), but it did in the knee cohort (HR = 4.2, 95% CI 1.285-13.960, $P = 0.018$). Of the 59 hip patients and 49 knee patients with single positive cultures, 18 and 13 were treated with postoperative antibiotics, respectively. The one patient who had a single positive culture with the same organism from a prior PJI was not treated with postoperative antibiotics.^{6,7} In separate studies, Neufeld et al. retrospectively reviewed patients at their institution who underwent presumed aseptic THA and TKA revisions to assess the impact of unexpected positive cultures on outcomes. There were 62 knee revisions with a single positive culture, 18 of which were treated with postoperative antibiotics (56% oral antibiotics alone, 100% for less than 6 weeks), and 74 hip revisions with a single positive culture, 15 of which received postoperative antibiotic treatment (40% oral antibiotics alone, 73% for less than 6 weeks). In the knee cohort, 3 patients with a single positive culture developed a subsequent PJI, none of which were caused by the same organism identified at the time of revision. In the hip cohort, 8 patients with a single positive culture developed a subsequent PJI, only two of which were caused by the same organism identified at the time of revision. No patient with a single positive culture who was treated with observation alone developed a subsequent PJI from the same organism identified at the time of revision. However, they did not include patients with negative cultures as a control, so comparisons between the groups could not be made.^{8,9} For patients undergoing revision TKA after unicompartmental arthroplasty, Lara-Taranchenko et al. demonstrated no difference in the risk of re-intervention between patients with a single positive culture (n = 8) and those with negative cultures (n = 254) (0% vs 3.2%, $P = 0.84$) at average follow-up of 8.3 months. None of the patients with single positive cultures were treated with postoperative antibiotics.¹⁰ In their cohort of TKA revisions for presumed aseptic failure, Kloos et al. had 35 patients with a single positive culture, none of which received postoperative antibiotics or were re-revised for PJI at 2 years. Patients who had a single positive culture of a virulent organism were treated as infected in their study.¹¹ Hoch et al. investigated patients undergoing presumed aseptic revision arthroplasty in which cutibacterium acnes was identified on a single positive culture. Contamination was defined as a single positive culture in the absence of two or more clinical criteria suggesting infection (elevated inflammatory markers, intraoperative abnormalities, local signs of infection, or a history of two or more prior local surgeries). None of the 16 patients with single positive cultures were revised for PJI at minimum 2-year follow-up, irrespective of treatment with postoperative antibiotics.¹² Schwarze et al. also conducted a retrospective review of patients at their institution who underwent presumed aseptic revision THA and TKA. The authors found that a single positive culture had no influence on 2- and 5-year RFS for both hip and knee patients when compared to the cohort with negative cultures (hip: 66.2% vs 76.7% and 59.8% vs 70.6%, $P = 0.13$; knee: 78.4% vs 76.6% and 59.9%

vs 63.5%, $P = 0.85$). Similarly, a single positive culture had no influence on 2-year IFS for both hip and knee patients when compared to the group with negative cultures (hip: 90.9% vs 95.4%, $P = 0.17$; knee: 91.9% vs 96.7%, $P = 0.79$). Of the 119 cases of single positive cultures in their cohort, 59 patients received antibiotic treatment. Postoperative antibiotic treatment did not demonstrate a significant influence on IFS at 2-year follow-up though (no antibiotic treatment 95.0% IFS, antibiotic treatment 85.8% IFS, $P = 0.2$).¹³

The other two studies reported a statistically significant influence of a single positive culture on RFS and IFS. In their retrospective review of presumed aseptic revision THA from a national registry, Milandt et al. found an increased risk for all cause re-revision (RR 1.73, 95% CI 1.07-2.80, $P = 0.020$) and re-revision due to PJI (RR 2.44, 95% CI 1.02-5.84, $P = 0.045$) at 1-year follow-up for patients with a single positive culture compared to patients with negative cultures. Interestingly, patients with two or more positive cultures did not have an increased risk of all-cause re-revision (RR 1.52, 95% CI 0.82-2.80, $P = 0.180$) or revision due to PJI (RR 2.28, 95% CI 0.81-6.43, $P = 0.120$) at 1-year follow-up when compared to patients with negative cultures. Of the 170 patients with a single positive culture, 42 were prescribed postoperative antibiotics. Revisions with two or more positive cultures (57 out of 112, 51%) were more likely to be prescribed antibiotics than patients with a single positive culture (42 out of 170, 25%) or negative cultures (486 out of 2023, 24%) ($P = <0.001$). There was no difference in the prevalence of postoperative antibiotic treatment between the single positive culture patients and culture-negative patients ($P = 0.840$).¹⁴ Hipfl et al. conducted a retrospective analysis of patients undergoing revision THA for presumed aseptic loosening at their institution and compared outcomes of patients who had a single positive culture with a low-virulence organism ($n = 37$) or multiple positive cultures for different organisms ($n = 4$) to those who had a low-grade infection (defined as two positive cultures or a single positive culture with a high-virulence organism, $n = 36$) or negative cultures ($n = 197$). They demonstrated a 7-year IFS of 87.4% in patients with a single positive culture, 94.4% in patients with a low-grade infection, and 97.5% in patients with negative cultures ($P = 0.021$). No patients with single positive cultures were treated with postoperative antibiotics, whereas patients with low-grade infections received 6 weeks of targeted antibiotic treatment.¹⁵

Conclusion

Most studies reviewed demonstrate no statistical difference in RFS or IFS for patients undergoing revision THA and TKA due to presumed aseptic failure where a single culture isolates an organism in the absence of other supporting criteria for PJI. However, all of the studies are retrospective, the majority utilize a single institution database, and each has its own approach to postoperative management. Some patients with single positive cultures are observed, while others are treated with 4 to 6 weeks of postoperative antibiotics. It is important to note that two studies demonstrate an increased risk of re-revision for PJI in patients with single positive cultures, which the authors believe could potentially be reduced if postoperative antibiotic treatment for them was more consistent. While the data clearly suggests that another operation is not necessary for patients with single positive cultures following revision THA or TKA, the optimal management of these patients (i.e. observation versus antibiotics) is unclear. Treatment is based largely on clinical suspicion and surgeon preference. Care should be taken if a single culture yields a virulent organism or the same organism that was isolated in a prior PJI as this could represent a true PJI.

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