## SH29. What is the clinical significance of polymicrobial PJI when using molecular techniques (NGS/PCR)?

## Vahid Entezari, MD; Eoghan Hurley, MD, Christopher Joyce, MD

Methodology: A comprehensive literature review was performed to identify all studies on polymicrobial prosthetic joint infection (PJI). Searches for the terms ("shoulder replacement" OR "shoulder arthroplasty") AND ("polymerase chain reaction" OR "next generation sequencing") was performed using the search engines PubMed and Google scholar which were searched through Jan 2025. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on polymicrobial PJI in joint arthroplasty. Exclusion criteria were non-English language articles, nonhuman studies, case reports, review papers, studies with less than <10 patients in the sample size, studies without clinical follow-up/infection rates, and technique papers without patient data. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria were followed. 16 articles met inclusion and exclusion criteria and were reviewed.

**Response/recommendation:** Polymicrobial PJI is detected in 5-40% of shoulder PJIs based on conventional cultures and this rate increases substantially after using NGS. There is low concordance between conventional cultures and molecular diagnostics in the shoulder PJI setting. It is unclear if more emphasis should be placed on polymicrobial PJI based on NGS/PCR results given possibility of false positivity and uncertain link to clinical outcomes.

## Strength of recommendation: Limited

Rationale: Majority of shoulder PJIs diagnosed by culture are monobacterial with Cutibacterium acnes and Coagulase-negative staphylococci (CONS) making up the majority of bacterial cultures at the time of revision. The incidence of polymicrobial shoulder PJI is 5-40% in the literature. The clinical significance of polymicrobial shoulder PJI is not well understood mainly due to small sample size and short follow up duration of studies. There is evidence in the hip and knee literature that suggests polymicrobial PJI is associated with worse clinical outcome. For example, a large multicenter study showed that among 345 PJIs, polymicrobial infection was present in 19% of cases and it was an independent predictor of failure of debridement, antibiotics and implant retention (DAIR) leading to higher earlier and late failures. Hampton et al conducted a case-control study of 106 patients after 2-stage revision for PJI and found that odds of polymicrobial PJI was 11-fold higher among patients with recurrent PJI. Another study evaluating risk factors of sinus tract after knee PJI showed a significantly higher rate of polymicrobial infection among patients with PJI with sinus tract compared to PJIs without sinus tract. Zmistowski et al. reported that polymicrobial PJI was an independent predictor of one-year mortality after revision arthroplasty.

Next generation sequencing (NGS) is an innovative and highly sensitive diagnostic tool that enables fast sequencing of multitudes of DNAs from PJI samples. A recent metanalysis included 22 studies with 2462 patients with PJI compared the diagnostic value of NGS and conventional cultures. They reported the pooled sensitivity, specificity and accuracy of NGS as 87%, 94% and 96% and conventional cultures as 63%, 98% and 82% respectively. Rao et al. analyzed superficial and deep specimens taken from 25 patients undergoing primary shoulder arthroplasty. They showed positive cultures in 40% of superficial and 12% of deep specimens while NGS was positive in 68% of superficial and 28% of deep specimens. Rogalski et al studied 41 patients undergoing

revision shoulder surgery and showed that NGS was positive in 46% of cases with 95% of them being poly microbial. They found positive NGS but not positive culture was associated with subsequent failure by infection and 67% of organisms that were cultured at subsequent failure, were present on NGS testing. Another study from the same institution reported that in 44 revision shoulder arthroplasties, positive cultures were present in 50% of cases and none had a polymicrobial infection while NGS was positive in 40% of cases and of those, 90% were polymicrobial. Authors emphasize the need for establishing normal and revision shoulder microbiota to distinguish between false positive and truly pathogenic organisms.

## References

- 1. Lora-Tamayo J et al. A large multicenter study of methicillin-susceptible and methicillin-resistant Staphylococcus aureus prosthetic joint infections managed with implant retention. Clin Infect Dis. 2013 Jan;56(2):182-94. doi: 10.1093/cid/cis746. Epub 2012 Aug 31. PMID: 22942204.
- 2. Hampton JP, Zhou JY, Kameni FN, et al. Host and microbial characteristics associated with recurrent prosthetic joint infections. J Orthop Res. 2024; 42: 560-567. doi:10.1002/jor.25768
- 3. Luo, T. David et al. Risk Factors and Microbiological Profile of Knee Periprosthetic Joint Infections With Sinus Tract The Journal of Arthroplasty, Volume 40, Issue 1, 214 217
- 4. Zmistowski B, Karam JA, Durinka JB, Casper DS, Parvizi J. Periprosthetic joint infection increases the risk of one-year mortality. J Bone Joint Surg Am. 2013 Dec 18;95(24):2177-84
- 5. Su, S. Et al. Higher diagnostic value of next-generation sequencing versus culture in periprosthetic joint infection: a systematic review and meta-analysis. Knee Surgery, Sports Traumatology, Arthroscopy, 2024. 32, 2277–2289. https://doi.org/10.1002/ksa.12227
- 6. Namdari S et al. Comparative study of cultures and next-generation sequencing in the diagnosis of shoulder prosthetic joint infections. J Shoulder Elbow Surg. 2019 Jan;28(1):1-8. doi: 10.1016/j.jse.2018.08.048. PMID: 30551780.
- 7. Rao AJ et al. Next-generation sequencing for diagnosis of infection: is more sensitive really better? J Shoulder Elbow Surg. 2020 Jan;29(1):20-26. doi:10.1016/j. jse.2019.07.039. Epub 2019 Oct 13. PMID: 31619355.
- 8. Rogalski, Brandon L. et al. An enhanced understanding of shoulder periprosthetic joint infection using next-generation sequencing: findings at the 3-year clinical follow-up Journal of Shoulder and Elbow Surgery, Volume 32, Issue 4, e168 e174
- 9. Namdari S et al. *Cutibacterium acnes* is less commonly identified by next-generation sequencing than culture in primary shoulder surgery. Shoulder Elbow. 2020 Jun;12(3):170-177. doi:10.1177/1758573219842160. Epub 2019 Apr 11. PMID:32565918; PMCID: PMC7285974.
- 10. Lee SY et al. A Meta-Analysis of Polymerase Chain Reaction for Prosthetic Joint Infection Diagnosis. Clin Lab. 2023 May 1;69(5). doi: 10.7754/Clin.Lab.2022.220833. PMID: 37145083.