

What Culture Can't See: NGS Identifies Pathogens in 80% of Culture-Negative PJIs

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Background

- Culture-negative periprosthetic joint infection (PJI) accounts for 20–30% of all PJIs. These cases often receive broad empiric antibiotics, resulting in suboptimal coverage and limited ability to tailor therapy. Next-generation sequencing (NGS) detects microbial DNA independent of culture, offering a potential solution to this diagnostic gap.

Objectives

- Determine the diagnostic yield of NGS in culture-negative PJI.
- Identify the most frequently detected organisms and the proportion of polymicrobial infections.
- Assess how often NGS results lead to changes in antibiotic therapy.
- Compare clinical outcomes between NGS-guided culture-negative PJI and matched culture-positive PJI.
- Evaluate concordance between NGS and culture in matched culture-positive cases.

Methods

- Design: Retrospective cohort (Jan 2020 – Dec 2024) at a tertiary academic center.
- Inclusion: Patients meeting 2018 hip/knee PJI criteria.
- Cohort: 131 culture-negative PJIs with NGS performed on synovial fluid or periprosthetic tissue.
- Matched comparison: 131 culture-positive PJIs matched 1:1 by joint, age (± 5 years), and surgical strategy (DAIR, one-stage, two-stage).
- Variables: Age, sex, BMI, Charlson Comorbidity Index (CCI), joint, surgical strategy.

Cohort Demographics

- 262 total PJIs: 131 culture-negative, 131 culture-positive
- Matched for joint, age, and surgical strategy
- Mean age: 67 ± 9 years
- BMI: 30 ± 5
- Joint distribution: 62% knees, 38% hips
- CCI comparable ($p = 0.64$)

Results: Diagnostic Yield

- NGS detected microbial DNA in 105/131 cases (80%).
- DNA detected in 81.8% of culture-negative PJIs.
- Detection was independent of specimen type (synovial fluid vs tissue).

Results: Impact on Antibiotic Therapy

- NGS results led to antibiotic modification in 62.3% (82/131) of culture-negative PJIs.
- Adding antifungal therapy when *Candida* species were detected.
- Switching to targeted therapy for anaerobes and resistant gram-positive organisms.

Results: Clinical Outcomes

- Infection-related reoperation at 1 year:
- 27.5% (NGS-guided) vs 26.7% (matched culture-positive), $p = 0.89$
- Kaplan–Meier: No difference in infection-free survival (log-rank $p = 0.77$)

Limitations

- Retrospective design → potential selection bias.
- Pre-sampling antibiotic exposure inconsistently documented.
- NGS cannot distinguish viable vs nonviable organisms.

Conclusion

- NGS positivity in 82% of culture negative PJI
- Results were clinically actionable, leading to targeted antibiotic changes in >60% of cases.
- Infection-free survival and reoperation rates were comparable to culture-positive PJIs.
- 93% concordance with matched culture-positive cases supports reliability.
- NGS should be considered a valuable adjunct in the diagnostic workup of PJI.



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