

The fate of unexpected intraoperative fungal cultures in periprosthetic joint infection: Comparable outcomes to recalcitrant bacterial periprosthetic joint infection

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Background

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- Periprosthetic joint infection (PJI) is most associated with bacterial organisms; however, fungal organisms may occasionally be identified from intraoperative cultures^{1, 2, 3}
 - Intraoperative fungal cultures are uncommon, and the clinical significance of an unexpected positive fungal culture obtained during PJI treatment remains poorly defined^{2, 3}
 - Fungal PJI is generally associated with chronic and recalcitrant infection, often occurring in patients with substantial comorbidity and a history of multiple surgical procedures^{4, 5}
 - Because fungal PJI may represent a particularly complex form of infection, outcomes were also compared with a cohort of patients with similarly complex, recalcitrant bacterial PJI⁶

- Aim**
- To evaluate clinical outcomes in patients undergoing PJI treatment in whom an unexpected positive intraoperative fungal culture was obtained
 - As a secondary objective, to compare outcomes of fungal PJI with a cohort of patients with similarly complex and recalcitrant bacterial PJI

- Hypotheses**
- Patients with unexpected intraoperative fungal cultures would demonstrate poor clinical outcomes given the chronic and recalcitrant nature of fungal PJI
 - Outcomes following fungal PJI treatment would be comparable to those observed in patients with similarly complex, recalcitrant bacterial PJI

Methods

- Study Design**
 - A multi-center retrospective review was performed of patients who underwent treatment for hip or knee PJI
 - Patients with positive fungal cultures during PJI treatment were identified and categorized according to whether the fungal infection was recognized preoperatively or unexpectedly identified intraoperatively
 - A comparison cohort consisting of patients with comparable recalcitrant bacterial PJI was also identified
- Outcomes**
 - Clinical outcomes were assessed using the Musculoskeletal Infection Society Outcome Reporting Tool (MSIS-ORT)⁷
 - Failure was evaluated using MSIS-ORT Tier 1 criteria, defined as further surgery and/or continued antibiotic treatment, with the study specifically reporting the Tier 1 endpoint of no further surgery and being off antibiotics
 - MSIS-ORT Tier 1 and Tier 2 criteria were also evaluated, incorporating patients who had no further surgery with or without ongoing antibiotic treatment
- Data Analysis**
 - Survival analysis was performed using Kaplan-Meier methods, with log-rank testing used to compare survival distributions between fungal and bacterial cohorts

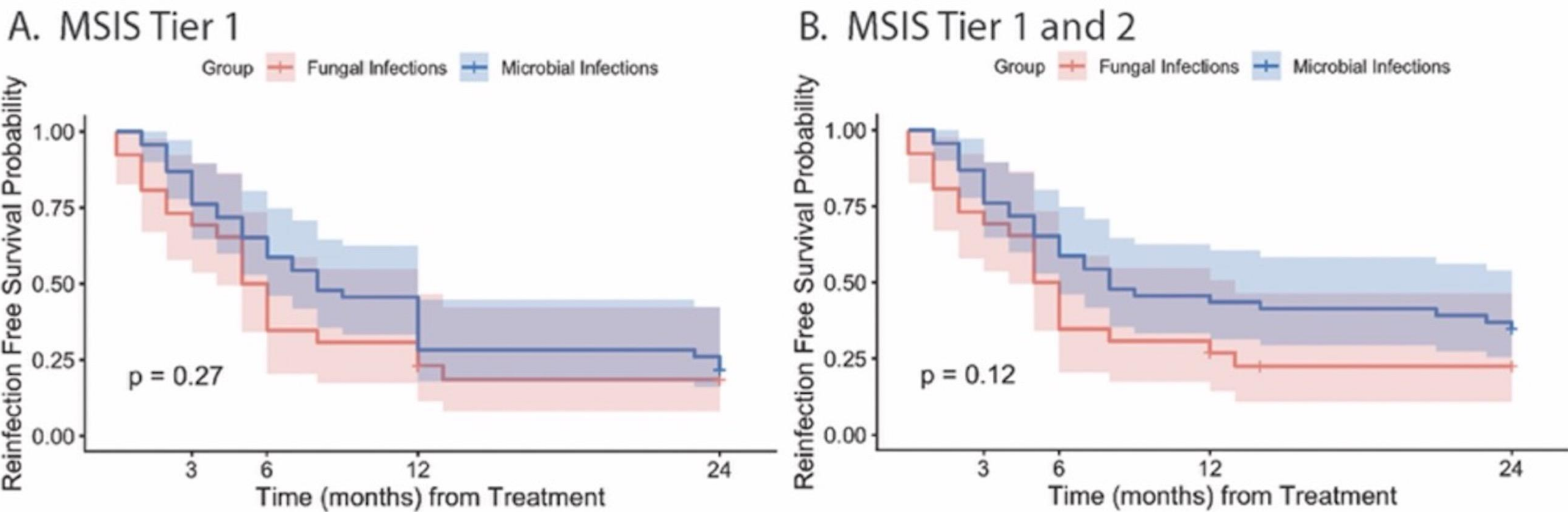
Tier 1. Infection control with no continued antibiotic therapy
Tier 2. Infection control with the patient on suppressive antibiotic therapy
Tier 3. Need for reoperation and/or revision and/or spacer retention (assigned to subgroups A, B, C, D, E, and F based on the type of reoperation)
 A. Aseptic revision at > 1 year from initiation of PJI treatment
 B. Septic revision (including debridement, antibiotics, and implant retention [DAIR]) at >1 year from initiation of PJI treatment (excluding amputation, resection arthroplasty, and arthrodesis)
 C. Aseptic revision at ≤1 year from initiation of PJI treatment
 D. Septic revision (including DAIR) at ≤1 year from initiation of PJI treatment (excluding amputation, resection arthroplasty, and arthrodesis)
 E. Amputation, resection arthroplasty, or arthrodesis
 F. Retained spacer
Tier 4. Death (assigned to subgroups A or B).
 A. Death ≤ 1 year from initiation of PJI treatment
 B. Death > 1 year from initiation of PJI treatment

Infection management outcome categories:
Successful: Tiers 1, 2
Failure due to secondary causes: Tiers 3A, 4B
Failure directly or indirectly related to PJI: Tiers 3B, 3C, 3D, 3E, 3F, 4A

Figure 1. 2019 MSIS-ORT⁷

Results

- Study Population**
 - The overall study population included **71 patients**
 - The intraoperative fungal cohort included **24 patients**
 - A cohort of **46 patients with comparable recalcitrant bacterial PJI** was identified for outcome comparison
 - Specialized fungal-specific culture methods were utilized in only **6.7% of all PJI cases**
- Fungal PJI Cohort**
 - MSIS-ORT Tier 1 criteria: **77% failure rate at 12 months**
 - At **24 months**, the Tier 1 failure rate increased to **82%**
 - MSIS-ORT Tier 1 and 2 criteria: **73% failure rate at 12 months**
 - At **24 months**, the combined Tier 1 and 2 failure rate was **78%**
 - None of the reported failures were attributable to repeat fungal disease
- Recalcitrant bacterial PJI Cohort**
 - MSIS-ORT Tier 1 criteria: failure rates were **72% at 12 months** and **78% at 24 months**
 - MSIS-ORT Tier 1 and 2 criteria: failure rates were **57% at 12 months** and **65% at 24 months**
- Kaplan-Meier survival curves demonstrated **no statistically significant difference** between fungal and bacterial cohorts using MSIS Tier 1 criteria (**P = 0.27**)
- No statistically significant difference was observed using MSIS Tier 1 and 2 criteria (**P = 0.12**)



C. Failure Rates of Fungal and Microbial PJIs at Various Time Points

Group	3 months	6 months	12 months	24 months	Log-rank P value
Fungal T1	0.31	0.65	0.77	0.82	0.27
Microbial T1	0.24	0.41	0.72	0.78	
Fungal T1 and T2	0.31	0.65	0.73	0.78	0.12
Microbial T1 and T2	0.24	0.41	0.57	0.65	

Figure 2. Comparative Kaplan-Meier survival analysis of fungal versus polymicrobial bacterial periprosthetic joint infection. (A) Failure rates at 3, 6, 12, and 24 months using MSIS Tier 1 criteria. (B) Failure rates at 3, 6, 12, and 24 months using MSIS Tier 1 and Tier 2 criteria. Shaded areas represent 95% confidence intervals. (C) Failure rates of both cohorts at 3, 6, 12, and 24 months.

Conclusion

- Fungal PJI was most encountered as an unexpected intraoperative culture finding, rather than as a diagnosis established preoperatively
- Despite treatment with a defined period of antifungal therapy, patients with fungal PJI demonstrated high rates of treatment failure
- Outcomes following fungal PJI treatment were similar to those observed in patients with comparably complex, recalcitrant bacterial PJI
- Clinical Significance**
 - The similarity in outcomes between fungal and recalcitrant bacterial PJI suggests that poor outcomes may not be explained primarily by fungal virulence alone
 - Instead, outcomes may be driven predominantly by the chronicity of infection, prior surgical burden, and host factors
 - These findings suggest that an unexpected intraoperative fungal culture may serve as a marker of an already complex and recalcitrant infection rather than necessarily indicating a uniquely aggressive infectious process
 - Overall, fungal PJI demonstrated poor clinical outcomes comparable to recalcitrant bacterial PJI, despite the absence of recurrent fungal disease as a major mechanism of failure

References

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