



Comparison of Outcomes between Fungal and Non-fungal Periprosthetic Joint Infections in Total Knee Arthroplasty: A Propensity Score-Matched Analysis

Hong Yeol Yang, MD, PhD

Jong Keun Seon, MD, PhD

**Dept. of Orthopaedic Surgery
Chonnam National University Hwasun Hospital
Chonnam National University College of Medicine**

INTRODUCTION

Periprosthetic Joint Infection (PJI)

❖ **PJI remains a serious complication of TKA that increases patient morbidity and mortality and leads to a poor outcome**

Pulido L et al., CORR, 2008
Phelan DM et al, Clin Infect Dis, 2002
Azzam K et al., JBJS, 2009

❖ **Fungal PJIs**

- Approximately 1% of all PJIs, relatively underreported
- Devasting clinical course
- Exact understanding of fungal PJIs is challenging but crucial

Kuo FC et al., J Arthroplasty 2018
Ueng SW et al, CORR, 2013

Treatment of Fungal PJIs

❖ Optimum treatment varies btw patients and remains unclear

- Antifungal suppression alone
- Debridement with retained prosthesis
- Single-stage implant exchange
- **TOC**: Two-stage exchange arthroplasty with fungal suppression

Brown TS et al., J Arthroplasty, 2018

Kuiper JW et al., Acta Orthop, 2013

❖ However, there remains a paucity of data to draw valid conclusions about the preferred fungal PJI treatment protocol

Ueng SW et al., CORR, 2013

Cowen LE et al, Mat Rev Microbiol, 2008

Purpose

- ❖ **We reported on fungal PJIs treated with two-stage exchange knee arthroplasty combined with antifungal treatment at a single institution.**

- ❖ **The specific aims were to compare the clinical characteristics, and implant survivorship between fungal and non-fungal PJIs**

METHODS

Patients

❖ **262 patients diagnosed with PJIs and treated with two-stage exchange arthroplasty after TKA from 2001 to 2020 were included**

❖ **Inclusion criteria**

- Definite organism was isolated from either tissue culture or synovial fluid during PJI treatment based on Musculoskeletal Infection Society (MSIS) criteria
- Cultured microorganisms were classified into two groups
: *fungal species (n = 41)* and other *non-fungal species (n = 221)*

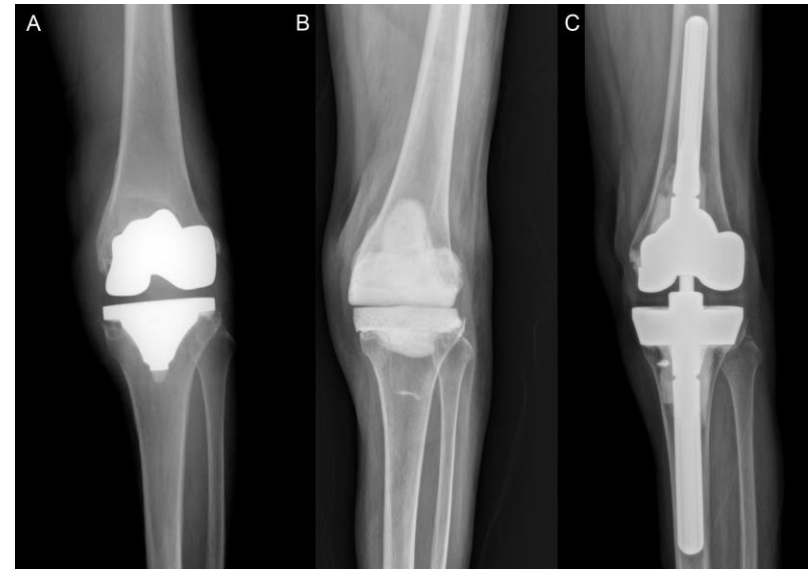
❖ Propensity Score Matching (PSM) Analysis

- Age, sex, body mass index (BMI), Charlson Comorbidity Index (CCI), and American Society of Anesthesiologists (ASA) grade
- One-to-one matching was performed using a variable-ratio, parallel, and balanced nearest-neighbor approach
- A caliper width of 0.2 standard deviations (SDs) of the propensity score

Treatment

❖ Fungal PJIs

- Two-stage exchange arthroplasty
- 100–400 mg of amphotericin B per each pack of cement
- A systemic antifungal therapy based on susceptibility (at least 6 wks)
- Reimplantation
 - ✓ Serum CRP less than 1.0 mg/dL
 - ✓ No clinical signs of persistent infection



Treatment

❖ Non-fungal PJIs

- Two-stage exchange arthroplasty
- 4 g of vancomycin and 2 g of cefotaxime per each pack of cement
- Same manner described for the fungal PJI group

Clinical Investigation

- ❖ **Clinical examination: preoperatively and 2 years after surgery**
 - WOMAC Score
 - Range of motion

- ❖ **Radiologic evaluation was performed to identify the presence of radiolucent lines at the bone-cement interface or osteolysis to exclude re-infection**

Survival

❖ Definition of “Treatment Success”

- **Def:** a well-functioning arthroplasty without any signs of a PJI after a minimum follow-up of two years after reimplantation
- **Failure:** reinfection with the same or different microorganisms and resection arthroplasty, amputation, or death due to a related infection

❖ Possible factors influencing survival

- Age, sex, BMI, CCI, ASA, interval from TKA to PJI, prior DAIR, prosthesis-free interval, antifungal agent, *Candida* species, and co-bacterial organisms

Statistical Analysis

- ❖ **Paired and independent t-tests/ Wilcoxon signed rank test and Mann-Whitney test for continuous variables**
- ❖ **Chi-square test or Fisher's exact test for categorical variables**
- ❖ **Kaplan-Meier analysis for survival probability**
- ❖ **Cox hazards models for relationship btw factors and survivorship**

RESULTS

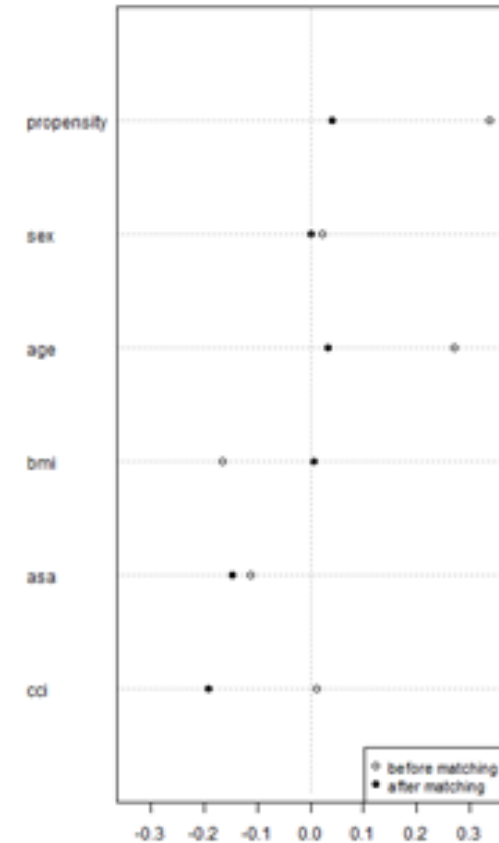
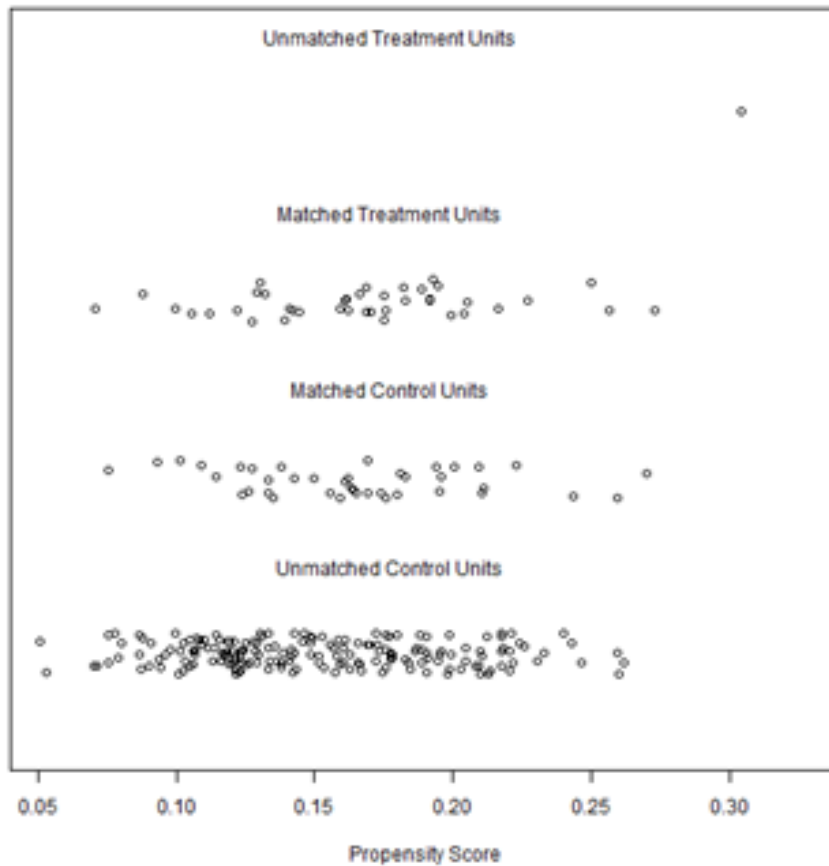
Demographics

Variable	Before Matching			After Matching		
	Fungal Group (n = 41)	Non-fungal Group (n = 221)	<i>P</i> Value†	Fungal Group (n = 40)	Non-fungal Group (n = 40)	<i>P</i> Value†
Age	77.6 ± 7.6	75.6 ± 7.8	0.121	77.4 ± 7.6	77.2 ± 7.2	0.881
Sex (no. [%])			0.999			0.148
Male	10 (24.4)	56 (25.3)		9 (22.5)	16 (40.0)	
Female	31 (75.6)	165 (74.7)		31 (67.5)	24 (60.0)	
BMI, kg/m ²	24.5 ± 3.7	25.1 ± 3.4	0.301	24.5 ± 3.7	24.2 ± 2.9	0.682
CCI	1.2 ± 2.2	1.1 ± 1.3	0.939	0.9 ± 1.1	1.2 ± 1.2	0.238
ASA score			0.814			0.880
1	2 (4.9)	6 (2.7)		0 (0)	0 (0)	
2	29 (70.7)	155 (70.1)		2 (5.0)	2 (5.0)	
3	10 (24.4)	58 (26.2)		28 (70.0)	26 (65.0)	
4	0 (0)	2 (0.9)		10 (25.0)	12 (30.0)	

PSM yielded 40 pairs and no statistical differences between groups

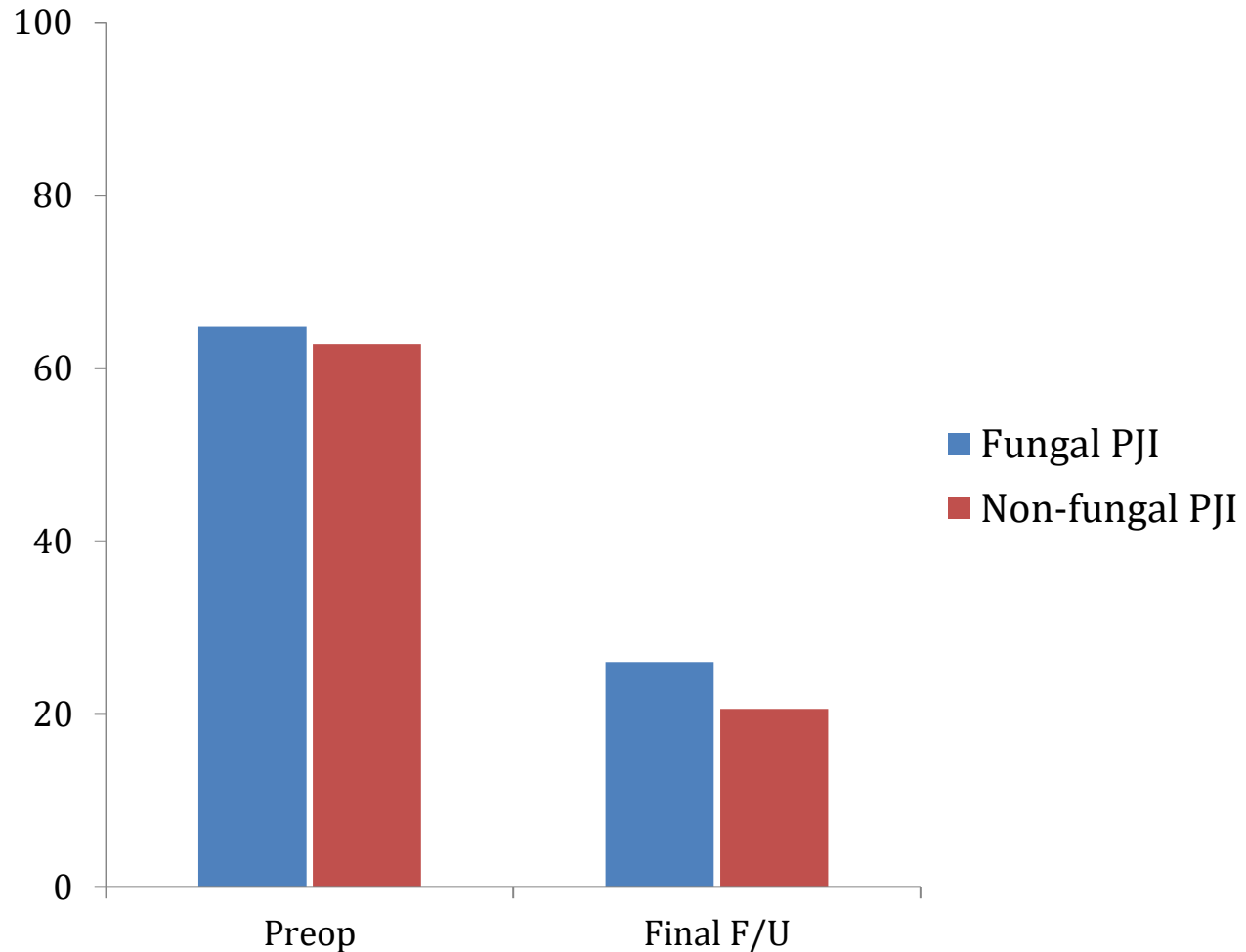
PSM Analysis

Distribution of Propensity Scores



The covariates between groups was considered balanced (SMDs<0.2)

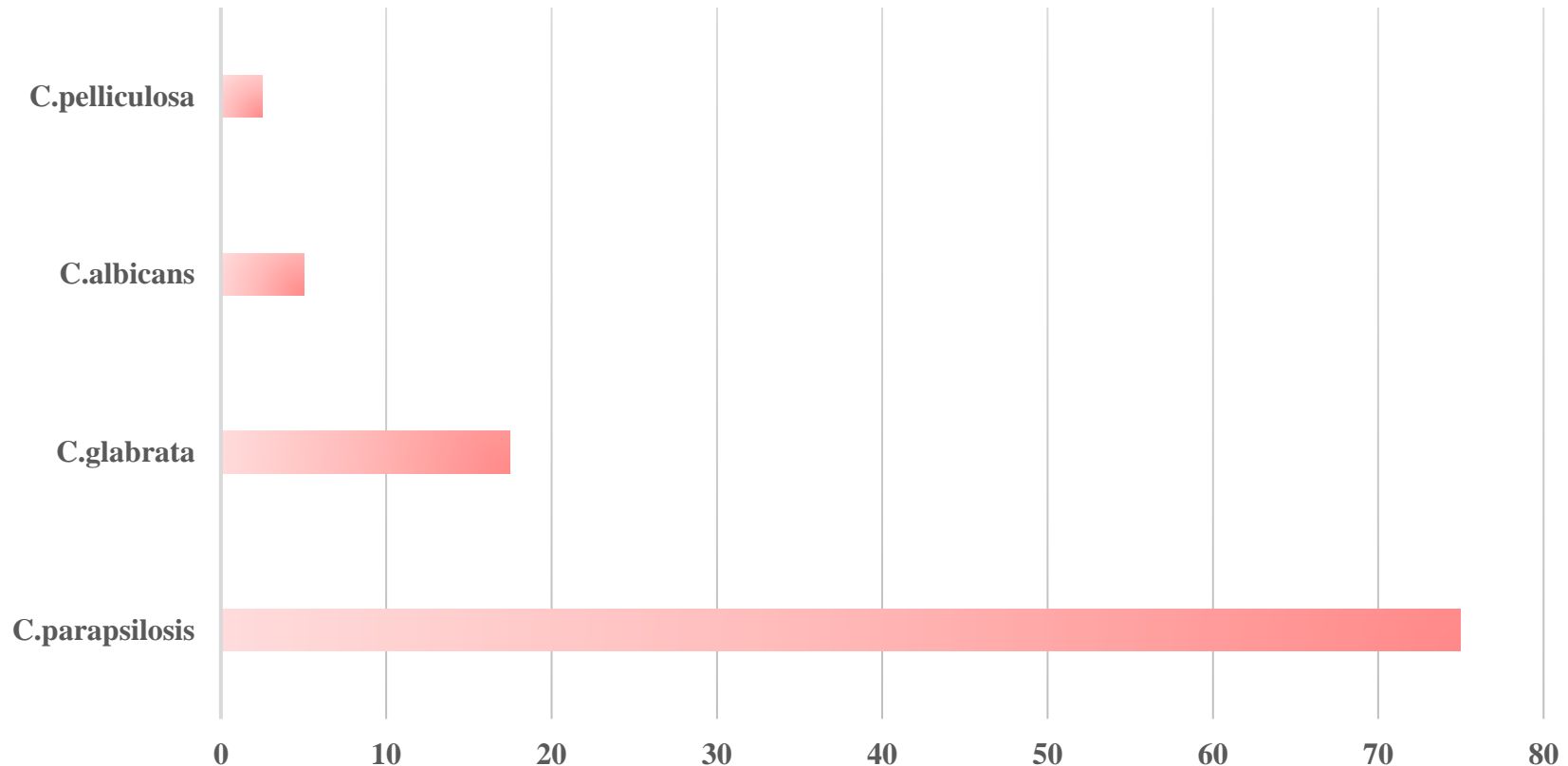
PROMs (WOMAC Total)



No Significant difference of Postoperative WOMAC between two groups

Clinical Characteristics

CANDIDA SPECIES



***C. parapsilosis* was the most commonly isolated organism (75.0%)**

Clinical Data

	Fungal Group (n = 40)	Control Group (n = 40)	P Value [†]
Immunosuppression	4 (25.0)	6 (15.0)	0.213
Laboratory analysis			
CRP (mg/L) at diagnosis	8.0	6.4	0.615
ESR (mm/h) at diagnosis	59.0	56.2	0.575
Co-bacterial organism			
<i>Staphylococcus aureus</i>	2 (5.0) [‡]	4 (10.0)	
CoNS	0 (0)	2 (5.0)	
Antibiotic-resistant species (MRSA, MRSE)	7 (17.5) [‡]	10 (25.0)	
<i>Streptococcus</i>	0 (0)	8 (20.0)	
<i>Enterococcus</i>	1 (2.5) [‡]	3 (7.5)	
Gram negative	3 (7.5) [‡]	1 (2.5)	
Culture negative	N/A	12 (30.0)	

Concomitant infection with a bacterial species occurred in 13 knees

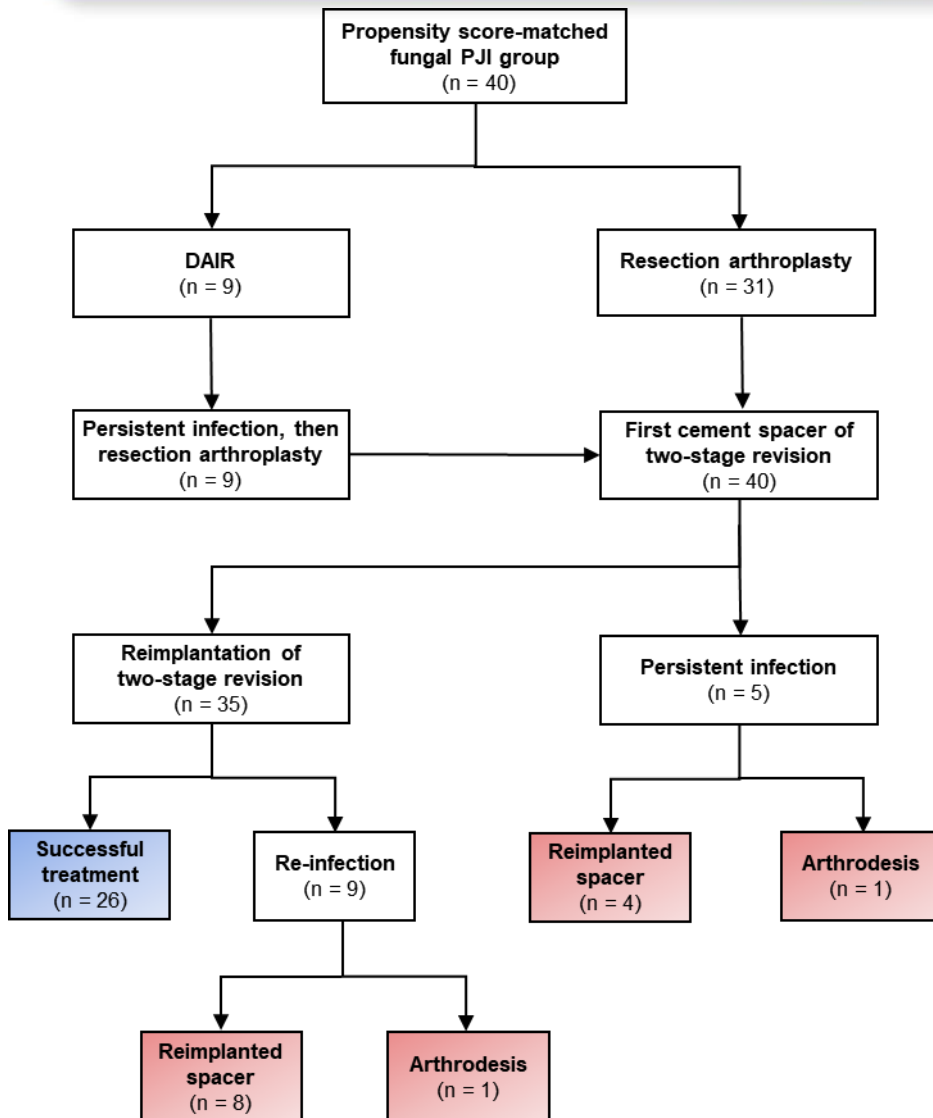
PJI Treatment Characteristics

	Fungal PJI (n = 40)	Non-fungal PJI (n = 40)	P Value [†]
Prior surgery before second-stage arthroplasty			0.792
DAIR procedure for infection eradication without AICs	9 (22.5)	10 (25.0)	
First-stage surgeries with AICs	31 (77.5)	30 (75.0)	
Interval from the first-stage to second-stage surgery (<i>months</i>)	6.7 ± 5.8	4.1 ± 2.5	0.020
Duration of systemic antimicrobial treatment (<i>months</i>)	5.6 ± 4.5	1.4 ± 0.8	0.001

❖ Fungal PJI group > Non-fungal PJI group

- Mean prosthesis-free interval: **2 months**
- Duration of IV antimicrobial agent (m/c, fluconazole): **4 months**

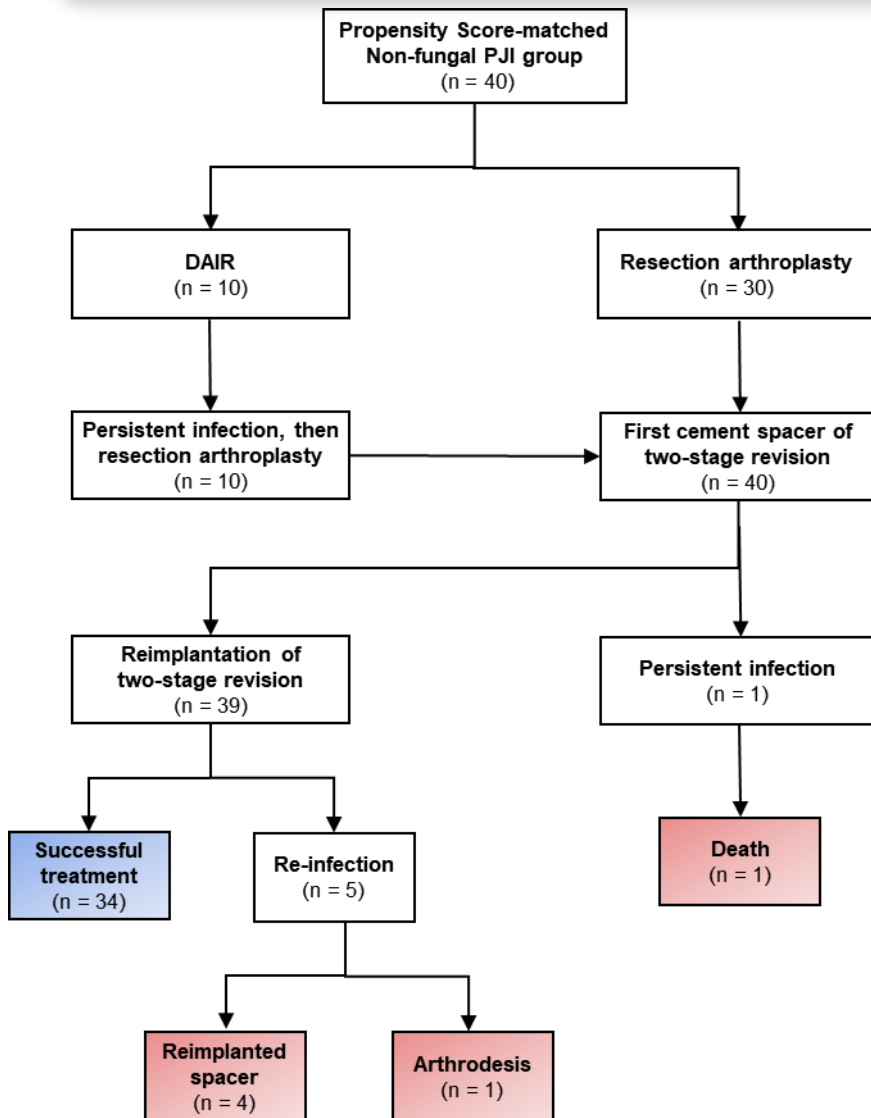
Treatment Success of Fungal PJI



❖ Fungal PJI group (n = 40)

- **Prior DAIR:** 9 (22.5%)
- **Second-stage revision:** 35 (87.5%)
- **Success:** 26 (65.0%)
- **Fail:** 14 (35.0%)
 - ✓ Arthrodesis: 2 pts
 - ✓ Reimplanted spacer: 12 pts

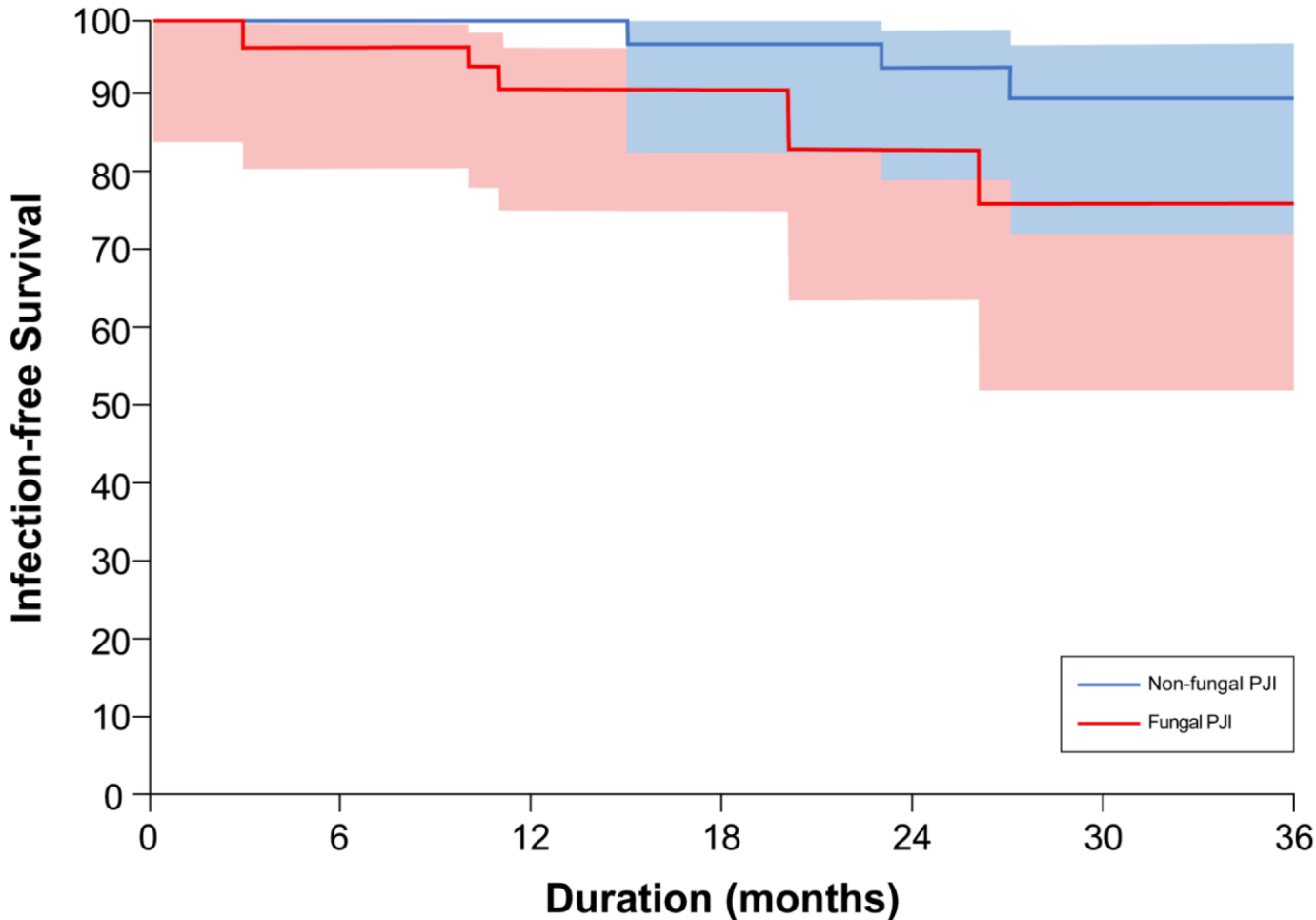
Treatment Success of Non-fungal PJI



❖ Non-fungal PJI group (n = 40)

- **Prior DAIR:** 10 (25.0%)
- **Second-stage revision:** 39 (97.5%)
- **Success:** 34 (85.0%)
- **Fail:** 6 (15.0%)
 - ✓ Arthrodesis: 1 pt
 - ✓ Death: 1 pt
 - ✓ Reimplanted spacer: 4 pts

Survivorship



No differences of survivorship free from reinfection (log-rank, $p=.270$)

Risk Factor Analysis

	Univariate Analysis	
	Hazard Ratio (95% CI)	P Value*
Age	0.936 (0.833 to 1.053)	0.275
Female sex	1.345 (0.269 to 6.703)	0.718
BMI	0.843 (0.646 to 1.100)	0.210
CCI	1.068 (0.584 to 1.953)	0.830
ASA score	2.201 (0.608 to 7.966)	0.229
Interval from index surgery to fungal PJI	0.994 (0.971 to 1.017)	0.598
Prior DAIR procedure for infection eradication	1.385 (0.278 to 6.902)	0.691
Duration of prosthesis-free interval	1.128 (1.003 to 1.268)	0.043
Mean length of antifungal treatment	0.815 (0.586 to 1.135)	0.226
<i>Candida</i> strain		
<i>C. parapsilosis</i> vs Non- <i>parapsilosis Candida</i> species	0.359 (0.084 to 1.533)	0.167
Bacterial co-infections	0.380 (0.046 to 3.127)	0.368

A risk factor for failure was duration of the prosthesis-free interval

CASE (70/F)

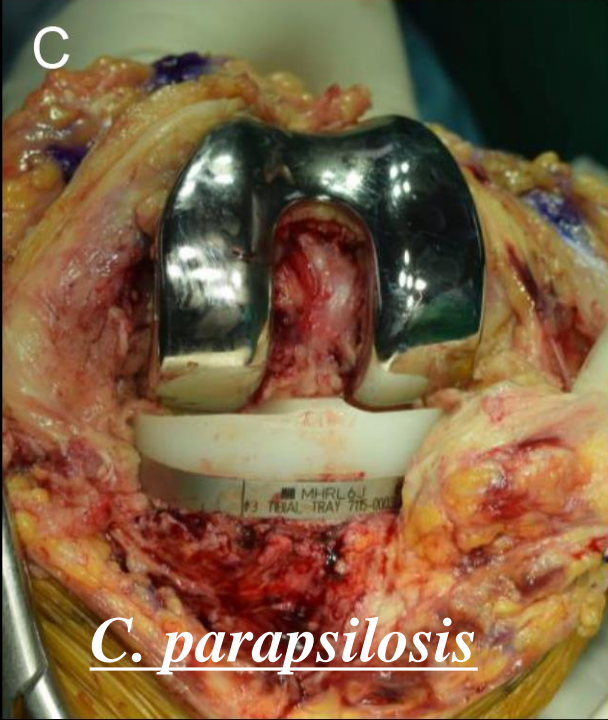
A



B



C



C. parapsilosis

D



A



B



CONCLUSIONS

Takeaway

- ❖ **Fungal PJIs had a 20% lower treatment success rate than non-fungal PJIs despite two-stage revision arthroplasty**
- ❖ **Fungal PJIs are more difficult to eradicate and thus may require a different and more aggressive treatment algorithm**
- ❖ **The optimum fungal PJI treatment remains to be determined and is a subject for further research.**

Thank You

