Author	Year	N	Organism	Length of Anti-fungal Therapy	Length of Interstage	Drug Holiday	Outcome
Reddy [17]	2013	1	*C. tropicalis*	18	20 w	2 w	cured
Wang [18]	2015	5	Candida spp	8 w after RA (6-10) 2 w after reimplantation	6 m	>2 m	5 cured
Geng [19]	2016	8	*C. albicans* (3) Mould *C. freyschussii* Aspergillus spp *C. parapsilosis* *C. glabrata*	2.8 m after RA (1.5-6) 1m after reimplantation (1m-46 days)	4.3 m (3-7)	6 w (2w-10w)	7 cured
Sebastian [20]	2017	1	*C. tropicalis*	24 w	9 m	3 m	cure

RA, resection arthroplasty

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QUESTION 3: Can debridement, antibiotics and implant retention (DAIR) be used to treat acute fungal periprosthetic joint infections (PJIs)?

RECOMMENDATION: DAIR has a relatively high failure rate in fungal PJIs, especially for immunocompromised patients. DAIR should be reserved for patients with truly acute PJIs after an index arthroplasty and in healthy patients (Type A). If DAIR is performed for fungal PJIs, consideration should be given to anti-fungal suppression therapy.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 91%, Disagree: 5%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

PJIs caused by fungal pathogens are a rare occurrence accounting for <1% of all PJIs [1]. Surgical treatments for fungal PJIs include DAIR, one-stage exchange arthroplasty and two-stage exchange arthroplasty. The difficultly in the treatment of fungal PJIs can be attributed to the rarity of fungal PJIs that have confined our understanding of this infectious entity and the often-immunocompromised status of patients who develop these infections in the first place. Although some general agreements have been reached with recommendations proposed by the International Consensus Meeting (ICM) and Infectious Diseases Society of America (IDSA) [2,3], many issues related to fungal PJIs remain unresolved. The most optimal surgical option for patients with fungal PJIs, the dose and the type of antifungals to be added to the polymethyl methacrylate (PMMA) spacer, the optimal duration of systemic antifungal treatment and many other issues still remain unanswered.

In addition, despite offering a potential explanation above, the exact reason for the less optimal outcomes of treatment of fungal PJIs remains unknown. It is, however, known that patients with

fungal PJIs often have an immunocompromised condition, such as diabetes mellitus, rheumatoid arthritis and cancer, which may markedly contribute to the high failure rate of treatments [3]. In addition, the complexity of the fungal biofilm in having a highly heterogeneous structure in response to environmental conditions, such as differences in pH, oxygen availability and redox potential, could also contribute to the suboptimal outcomes of treatment [4].

Overall, DAIR has been reported to have a relatively high failure rate in patients with PJIs caused by resistant organisms and poor hosts. DAIR as a surgical option for patients with fungal PJIs is questionable [5], and a study published in the *New England Journal of Medicine* listed fungal PJIs as a contraindication for DAIR [6]. A search of Medline, PubMed, Embase, Web of Science and Medscape revealed no reports in the setting of DAIR for acute fungal PJIs. The review of the English literature from 1979 to 2018 identified 22 fungal PJIs undergoing DAIR [7–19]. An overall high failure rate (82%, 18 of 22) was reported for these patients. Additionally, one study by Azzam et al. demonstrated a 100% failure rate for seven patients in their cohort undergoing DAIR [16]. Among the seven patients who failed, five needed resection arthroplasty and two needed chronic suppression with oral fluconazole [16]. Furthermore, Badrul et al. reported a fungal PJI case treated with debridement and oral fluconazole for a year. But, the infection was never totally cured and a secondary infection with methicillin-resistant *Staphylococcus aureus* (MRSA) developed [14]. Fabry et al. also reported a failure in a patient who underwent two debridements and an eight-month oral antifungal therapy regimen [15]. However, a few case reports demonstrated successful results at a minimum follow-up of two years and all of them required a six-months to one-year antifungal agent treatment after irrigation and debridement alone [9,11,12,18,19].

Given the fact that literature is not definitive on this issue and based on the available reports, we recommend that DAIR for fungal PJIs should be limited to those with early presentation, good soft tissue coverage, well-fixed implants and are healthy patients (Host type A). If DAIR is performed for patients with fungal PJIs, long-term suppression (six months or longer) with antifungal agents should also be considered.

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QUESTION 4: Which antifungals, route of administration and duration of treatment should be utilized to treat fungal periprosthetic joint infections (PJIs)?

RECOMMENDATION: Fluconazole, by both oral and intravenous routes, is currently the treatment of choice for PJIs due to susceptible fungi, including the *Candida* species which are responsible for the majority of fungal PJI cases. Amphotericin B lipid formulations or echinocandins given intravenously are secondary considerations, but may be less well tolerated. Culture data including antifungal susceptibilities should be used to guide therapy. Two-stage revision is currently the standard of care. Antifungal treatment should be administered during the spacer interval with a minimum treatment duration of six weeks. Following revision, treatment with oral fluconazole (400mg daily) should be continued for three to six months, if tolerated.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 92%, Disagree: 3%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

Fungal PJIs are uncommon, accounting for approximately 1% of PJIs [1,2]. *Candida* species, in particular *Candida albicans*, are by far the most common pathogen [1,3]. Concomitant bacterial infection may occur in up to 20% of cases [4]. Risk factors for fungal