Review

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Surgical procedures for the treatment of fungal periprosthetic infection following hip arthroplasty: a systematic scoping review

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Background: There has been limited literature synthesizing the therapeutic effects of surgical procedures for fungal periprosthetic joint infection (PJI) following hip arthroplasty. The authors' current study aims to comprehensively review and analyze those relevant literature, and carefully make recommendations for future clinical practices.

Methods: Our current study was carried out in accordance with the PRISMA 2020 statement. Studies regarding the surgical management of fungal PJI following hip arthroplasty were collected via a thorough search of PubMed, Embase and Google scholar databases. The search was lastly performed in March 2023. Non-English language, reviews, articles with duplicated data, and articles without clear information about the type of fungal pathogens and treatment options were excluded. The authors evaluated their systematic review compliance by using AMSTAR 2 criteria and fell in moderate quality. Clinical outcomes of different surgical procedures were evaluated, and a binary logistic regression model was used to identify the risks associated with treatment failure. Data analyses were performed using the SPSS version 19.0.

Results: A total of 33 articles encompassing 80 patients with fungal PJI following hip arthroplasty were identified. Candida albicans was the most frequently isolated fungus (56.3%, 45/80). The overall treatment success was achieved in 71.1% (54/76) of the reported cases. Univariate analysis showed that the differences of success rate were not significant between publication periods, genders, ages, specimen collection methods, and fungal pathogens. Treatment success rate was 47.4% (9/19) in fungal PJI cases with bacterial co-infection, significantly lower than those without [vs. 79.0% (45/57), $P = 0.017$]. The pooled success rate for surgical debridement, spacer implantation, resection arthroplasty, one-stage revision, and two-stage revision was 50.0% (4/8), 42.9% (3/7), 55.0% (11/20), 86.7% (13/15), and 88.5% (23/26), respectively, with significant differences between them ($P = 0.009$). A binary logistic regression model showed that bacterial co-infection and surgical option were the two significant risk factors associated with treatment failure for fungal PJI following hip arthroplasty.

Discussion: Regarding the surgical treatment of fungal PJI following hip arthroplasty, patients with bacterial co-infection, and those treated with surgical procedures such as debridement, spacer implantation, and resection arthroplasty should be aware of the higher risks of failure. Nonetheless, future multiple-centre cohort studies are required to establish the optimal treatment.

Keywords: fungal infection, hip arthroplasty, periprosthetic joint infection, surgery

Introduction

Fungal periprosthetic joint infection (PJI) is a refractory complication occurs in approximately 1% of all joint infections[1]. The incidence of fungal PJI is expected to increase over time due to the ageing population and the increased numbers of joint replacement being conducted every year around the world. The diagnosis of fungal PJI is trickier compared to typical bacterial PJI owing to its insidious onset and nonspecific clinical manifestations, which usually makes the treatment delayed and aimless in many scenarios[2].

Early in 1983, Goodman *et al.*[3] reported two cases of yeast infection of prosthetic joints and suggested removal of the prosthetic device for infection clearance. Afterwards, large numbers of fungal PJI following hip arthroplasty have been reported during the past decades. A recent review outlined the diagnostic as well as the management options for fungal PJI at its best[4]. However,

HIGHLIGHTS

- Hip fungal periprosthetic joint infection (PJI) cases from China were younger than those from other countries.
- Bacterial co-infection increased surgical failure rate for hip fungal PJI.
- Two-stage or one-stage revision tends to have better outcomes for hip fungal PJI.

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the authors did not differentiate between hip and knee arthroplasty cases when illuminating the results. A systematic review (published in 2015) focusing on the surgical treatments and clinical outcomes of Candida PJI following hip arthroplasty recommended surgical debridement with prosthesis removal or two-stage revision for the treatment[5]. Different from that, another similar systematic review published in 2020 suggested better clinical outcome with one-stage or two-stage revision[6]. We also found a more recent review meticulously summarized the diagnostic methods and the medical and surgical treatment options for fungal hip PJI[7]. However, the authors did not investigate and compare the clinical outcomes between different treatment options.

Regarding the causative pathogens of fungal PJI, Candida species are most frequent, while non-Candida fungal species have been increasingly isolated in recent years, which might be attributed to improved diagnostic methods or altered medical practices[8,9]. Considering the limited literature synthesizing the clinical outcomes of surgical management of Candida and non-Candida PJI following hip arthroplasty, our current study aims to comprehensively review and analyze those relevant literature, and carefully make recommendations for the future clinical practices.

Materials and methods

Literature search and article selection

Our current study was carried out in accordance with the PRISMA (Preferred Reporting Item for Systematic Reviews and Meta-Analyses) 2020 statement[10], Supplemental Digital Content 1, http://links.lww.com/MS9/A392. This study was also registered in Research Registry with identifying number reviewregistry1770 with a link: https://researchregistry.knack.com/research-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviews meta-analysesdetails/6590118fbaa9e80029f82f70/). We evaluated our systematic review compliance by using AMSTAR 2 criteria and fell in moderate quality[11], Supplemental Digital Content 2, http://links.lww.com/MS9/A393. PubMed, Web of Science and Scopus databases were searched to collect citations regarding fungal PJI following hip arthroplasty. The search items included “hip”, “replacement”, “arthroplasty”, “prosthetic”, “prosthesis”, “infection”, “fungal”, and “candida”. All retrieved records were added to an EndNote (Version X9, Thomson Reuter, New York, NY) library. A cross-reference search was performed to acquire the further relevant articles. No limit was applied to the publication date. The search was lastly performed in March 2023.

Exclusion criteria were (1) articles written in non-English language, and (2) reviews, articles with duplicated data, and (3) articles without clear information about the type of fungal pathogens and treatment options. Two reviewers independently screened the titles and abstracts of the retrieved records for eligibility, and disagreements were resolved with a third reviewer adjudication.

Data extraction and quality assessment

The following data were extracted: patient demographics, specimen collection methods, causative pathogens, surgical options, and clinical outcomes. Preoperative hip joint aspiration was reported in 45 cases and positive culture outcomes were reported in 28 (62.2%) of them. Fungal PJI of the remaining cases were determined by positive culture outcomes from intraoperative specimens. Treatment success was defined as a well-functioning joint without relapse of fungal or bacterial infection after surgical treatment during a follow-up of at least 6 months. Recurrence of PJI attributable to the original microorganism (relapse of infection) or a different strain (reinfection), development of a sinus tract, or death related to the PJI were considered as treatment failure.

Quality of studies were graded based on Oxford Centre for Evidence-Based Medicine (OCEBM) levels of evidence[12,13]. Two reviewers independently proceeded the assessment, and inconsistence was resolved by discussion and consensus.

Statistical analysis

Descriptive statistics were calculated for all the variables. Continuous variables were reported as mean values and standard deviations, and compared using the One-way analysis of variance (ANOVA) with a Fisher’s Least Significant Difference (LSD) test. Categorical variables were reported as numbers and percentages, and compared using the χ^2 or Fisher’s exact test. Variables in the univariate analysis were further included in the binary logistic regression with the forward stepwise method of variable selection. Odds ratios (ORs) with 95% CIs were calculated. A P value of less than 0.05 indicated statistical significance. All statistical analyses were performed using SPSS version 19.0 software (SPSS Inc).

Results

Article characteristics and patient demographics

A flow diagram explaining the literature search and article selection is shown in Fig. 1. A total of 33 articles (case reports and case series: OCEBM level 4) published between 1988 and 2021 reporting surgical treatment of fungal PJI following hip arthroplasty were identified, as listed in Table 1[14–46]. Those articles

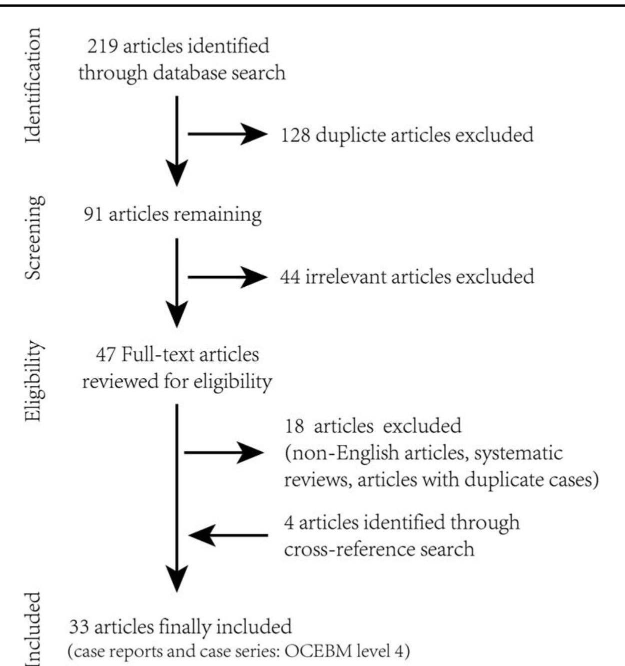

Figure 1. A flow diagram explaining the literature search and article selection.

Table 1

The basic characteristics of the 80 patients with fungal PJI following hip arthroplasty

Year	Author ref	Country	Cases (*n*)	Age/sex	Fungal pathogens[b]	Bacterial pathogens	Treatment regimens	Clinical outcomes
1988	Lambertus *et al.*[14]	USA	1	61/M	C. t [h]	/	RA	Success
1989	Darouiche *et al.*[15]	USA	3	62/M	C. a [h]	/	RA	Success
				72/M	C. t [h]	/	RA	Success
				78/F	C. a [h]	/	RA	Success
1996	Cardinal *et al.*[16]	USA	3	42/F	C. a [t]	/	RA	Failure
				67/F	C. a [t]	S. epidermidis	RA	Success
				57/M	C. a [t]	P. aeruginosa, Enterobacter cloacae, Streptococcus, Bacillus	RA	Failure
1997	Nayeri *et al.*[17]	Sweden	1	62/F	C. g [t]	/	1SR	Success
1998	Fowler *et al.*[18]	USA	1	84/F	H. c [t]	/	DAIR	Success
2001	Ramamohan *et al.*[19]	UK	1	65/F	C. g [h]	/	2SR	Success
2000	Marra *et al.*[20]	France	1	59/M	C. a [h]	/	Spacer	Failure
2001	Bruce *et al.*[21]	UK	2	51/F	C. pa [t]	/	2SR	Success
				68/F	C. a [t]	/	2SR	Success
2002	Phelan *et al.*[22]	USA	3	83/M	C. a [t]	/	2SR	Success
				60/F	C. a [t]	/	2SR	Success
				75/F	C. a [t]	/	2SR	Success
2004	Lazzarini *et al.*[23]	Italy	1	63/M	C. a [h]	/	RA	Success
2005	Lejko-Zupanc *et al.*[24]	Slovenia	1	73/M	C. g [t]	/	RA	Success
2009	Johannsson *et al.*[25]	USA	1	84/M	Cry. n [h]	/	RA	NA
2010	Kelesidis *et al.*[26]	USA	1	93/F	C. a [t]	/	1SR	Success
2010	Dutronc *et al.*[27]	France	3	85/F	C. a [t]	/	DAIR	Success
				66/M	C. pa [t]	/	2SR	Success
				77/F	C. pa [t]	/	RA	Success
2011	Gottesman *et al.*[28]	Israel	1	56/F	P. b [h]	/	2SR	Success
2012	Hall *et al.*[29]	UK	1	60/F	C. g [t]	P. aeruginosa, E. coli	RA	NA
2012	Anagnostakos *et al.*[30]	Germany	4	68/F	C. a [h]	/	2SR	Success
				77/M	C. li [h]	/	2SR	Success
				51/F	C. a [h]	/	2SR	Success
				78/M	C. g [h]	/	2SR	Success
2013	Artiaco *et al.*[31]	Italy	1	70/F	C. a [h]	/	DAIR	Failure
2013	Deelstra *et al.*[32]	Netherlands	1	73/F	C. a [t]	CoNS	2SR	Success
2013	Ueng *et al.*[33]	Taiwan	7	66/M	C. pa [h]	/	2SR	Success
				62/F	C. a [t]	MSSA	RA	Failure
				67/M	C. t [h]	/	RA	Failure
				66/M	C. pa [t]	MRSA	RA	Failure
				75/M	C. a [t]	/	Spacer	Failure/D[a]
				31/M	C. a [t]	MRSA	2SR	Failure/D[a]
				41/M	C. a [t]	MSSA	Spacer	Failure/D[a]
2013	Chiu *et al.*[34]	Hong Kong	1	71/M	C. pa [h]	/	RA	Success
2013	Lidder *et al.*[35]	UK	1	76/F	C. t [t]	/	2SR	Success
2014	Shah *et al.*[36]	USA	1	77/F	Cry. n [t]	/	Dm	Success
2014	Klatte *et al.*[37]	Germany	6	67/M	C. a [h]	/	1SR	Success
				78/F	C. a [h]	/	1SR	Success
				81/F	C. g [h]	/	1SR	Success
				88/M	C. a [h]	/	1SR	Success
				62/F	C. a [h]	/	1SR	Success
				31/M	C. a [h]	/	1SR	Success
2017	Cobo *et al.*[38]	Spain	1	77/M	C. g [t]	/	Dm	Success
2016	Jenny *et al.*[39]	France	1	78/F	C. a [t]	/	1SR	Success
2018	Burgo *et al.*[40]	Argentina	1	73/F	T. i [h]	/	Spacer	Success
2018	Sebastian *et al.*[41]	India	1	53/M	C. t [h]	MRSH	2SR	Success
2017	Ji *et al.*[42]	China	4	74/M	C. a [t]	/	1SR	Success
				47/F	C. pt [t]	/	1SR	Success
				59/M	C. a [t]	/	1SR	Success
				67/F	C. a [t]	Str. viridians, E. coli	1SR	Failure
2018	Brown *et al.*[43]	USA	13	77/F	Pm [NA]	P. acnes	Spacer	Failure
				84/F	C. a [NA]	/	DAIRE	Failure
				75/F	C. a [NA]	/	2SR	Success
				60/M	Ab [NA]	/	2SR	Success
				68/M	C. a [NA]	/	2SR	Failure

Table 1

(Continued)

Year	Author ref	Country	Cases (*n*)	Age/sex	Fungal pathogens[b]	Bacterial pathogens	Treatment regimens	Clinical outcomes
				37/M	C. a [NA]	/	DAIRE	Failure
				63/F	C. a [NA]	P. acnes	Spacer	Success
				89/M	Coc. i [NA]	/	2SR	Success
				56/F	C. a [NA]	/	RA	Success
				75/F	C. pa [NA]	/	RA	Failure
				61/F	C. g [NA]	/	RA	Failure
				45/M	C. a [NA]	/	2SR	Failure
				76/M	C. a [NA]	MRSA	DAIRE	Failure
2018	Gao *et al.*[44]	China	5	62/F	C. t [h]	S. epidermidis, E. coli	Spacer	Failure
				42/M	C. a [t]	Acinetobacter lwoffii	2SR	Success
				53/F	C. a [t]	S. aureus	2SR	Success
				43/F	C. a [t]	Enterococcus faecalis	2SR	Success
				78/M	C. g [t]	G- bacilli	RA	Failure
2020	Saconi *et al.*[45]	Brazil	6	64/F	C. pa [t]	S. aureus	RA	NA
				61/F	C. pa [t]	/	1SR	Success
				66/M	C. lu [t]	/	1SR	Failure
				63/M	C. a [t]	/	1SR	NA
				53/F	C. a [t]	/	RA	Success
				61/M	C. a [t]	S. haemolyticus, Enterococcus faecalis, P. aeruginosa	RA	Success
2021	Lin *et al.*[46]	China	1	76/F	C. a [t]	S. hominis	2SR	Success

1SR, one-stage revision; 2SR, two-stage revision; Ab, Aureobasidium; C. a, *C. albicans*; C. g, *C. glabrata*; C. li, *C. lipolytica*; C. lu, *C. lusitaniae*; Coc. i, *Coccidioides immitis*; CoNS, coagulase-negative staphylococci; C. p, C. parapsilosis; C. pt, C. pseudotropicalis; Cry. N, *Cryptococcus neoformans*; C. t, C. tropicalis; DAIR, debridement, antibiotics, and implant retention; DAIRE, DAIR plus modular polyethylene exchange; Dm, debridement; E. coli, *Escherichia coli*; H. c, *Histoplasma capsulatum*; F, female; M, male; MRSA, methicillin-resistant Staphylococcus aureus; MRSH, methicillin-resistant Staphylococcus haemolyticus; MSSA, methicillin-susceptible Staphylococcus aureus; NA, not available; P. acnes, *Propionibacterium acnes*; P. aeruginosa, *Pseudomonas aeruginosa*; P. b, *Pseudallescheria boydii*; PJI, periprosthetic joint infection; Pm, Pithomyces; RA, resection arthroplasty; S. aureus, *Staphylococcus aureus*; Spacer, prosthetic articulating spacer implantation; T. i, *Trichosporon inkin*.

[a]D, died owing to the uncontrolled candida infection and deteriorating candidemia sepsis.

[b]Fungal pathogens were detected via hip aspiration (h) or intraoperative specimens (i).

involved 80 patients, including 43 females and 37 males. The mean age of patients at diagnosis was 65.9 years, ranging from 31 to 93 years. There were no significant differences in patient age between genders (females: 67.2 ± 11.9 vs. males: 64.5 ± 14.8 years, $P = 0.367$) and between publication periods (1988–2010: 69.0 ± 12.2 vs. 2011–2021: 64.7 ± 13.6 years, $P = 0.191$). Patients from China were significantly younger than those from the USA (60.0 ± 14.0 vs. 68.9 ± 14.2 years, $P = 0.044$) and from other countries (60.0 ± 14.0 vs. 66.7 ± 11.4 years, $P = 0.045$). For detailed information about the patient demographics, indications for initial hip arthroplasty, comorbidities or predisposing factors, major complaints on admission, treatment regimes, fungal and bacterial pathogens, and clinical outcomes, please check our supplemental file, Supplemental Digital Content 3, http://links.lww.com/MS9/A394 (https://lww.figshare.com/s/cb53626910bd7d7dfa14).

Fungal pathogens and bacterial co-infection

The most frequently identified fungal pathogens were Candida species (90.0%, 72/80). C. albicans was identified in 45 cases (56.3%), C. parapsilosis in 9 cases (11.3%), C. glabrata in 9 cases (11.3%), C. tropicalis in 6 cases (7.5%), C. lipolytica in 1 case, C. pseudotropicalis in 1 case, and C. lusitaniae in 1 case. Non-Candidal fungal species, including cryptococcus neoformans, histoplasma capsulatum, pseudallescheria boydii, trichosporon inkin, pithomyces, aureobasidium, and coccidioides immitis, were identified in 8 cases, as shown in Fig. 2. Bacterial co-infection was reported in 21 cases (26.3%), including 5 of them were infected with multiple bacterial species.

Surgical procedures and antifungal drugs

Eight cases were treated with surgical debridement (including debridement, antibiotics, and implant retention (DAIR) with or

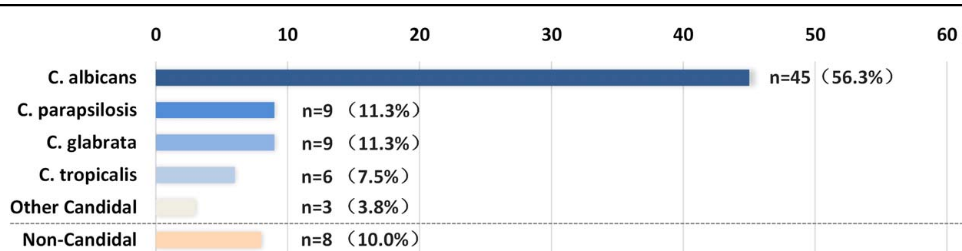

Figure 2. Fungal pathogens isolated from the included cases.

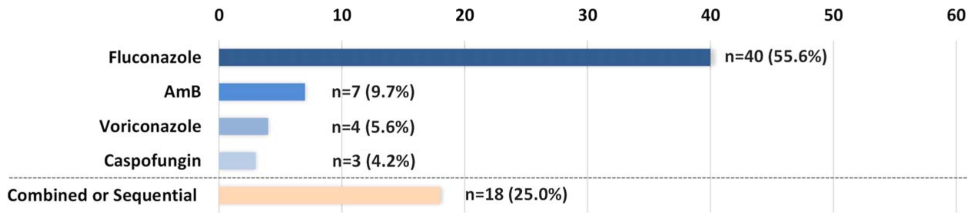

Figure 3. Antifungal drugs for the treatment of fungal periprosthetic joint infection following hip arthroplasty.

without modular polyethylene exchange), 7 cases with prosthetic articulating spacer implantation, 23 cases with resection arthroplasty, 16 cases with one-stage revision, and 26 cases with two-stage revision.

Systematic (oral or intravenous) administration of antifungal drugs was described in 72 cases. Among them, 54 cases (75.0%) were treated with monotherapy, and 18 cases (25.0%) were treated with combined or sequential antifungal drugs. For monotherapy, fluconazole was most commonly used (55.6%, 40/72), followed with amphotericin B (9.7%, 7/72) and voriconazole (5.6%, 4/72), as shown in Fig. 3.

Clinical outcomes

The overall treatment success was achieved in 71.1% (54/76) of the reported cases. The clinical outcomes were not available in 4 cases due to no mention or loss to follow-up. Death was reported in 5 cases, including 1 died of end-stage renal disease before a revision arthroplasty, 1 died more than four years later with no sign of recurrence of the infection, and 3 died owing to the uncontrolled candida infection and deteriorating candidemia sepsis.

Univariate analysis

Univariate analysis indicated that the differences of success rate were not significant between publication periods, genders, ages, and specimen collection methods, as shown in Table 2. By fungal pathogens, treatment success was achieved in 68.2% (30/44) of C. albicans PJI cases, 72.0% (18/25) of non-C. albicans Candida (NCAC) PJI cases, and 85.7% (6/7) of non-Candida PJI cases, and the differences between them were not statistically significant ($P=0.749$). Treatment success was reported in 47.4% (9/19) of the PJI cases with bacterial co-infection, significantly lower than those without bacterial co-infection (vs. 79.0% (45/57), $P=0.017$). The pooled success rate for surgical debridement, spacer implantation, resection arthroplasty, one-stage revision, and two-stage revision was 50.0% (4/8), 42.9% (3/7), 55.0% (11/20), 86.7% (13/15), and 88.5% (23/26), respectively, and the differences between them were significant ($P=0.009$).

Binary logistic regression analysis

The fit of the binary logistic regression model was tested with the Hosmer–Lemeshow test ($P=0.883$), and the overall correctly classified percentage was 77.6%. As shown by the model, after adjusting for age, sex, publication year, specimen collection method, and fungal pathogen, bacterial co-infection and surgical option were the two significant risk factors associated with the treatment failure for fungal PJI following hip arthroplasty. Patients with bacterial co-infection presented a OR of 4.5 (95% CI 1.2–16.8, $P=0.024$) compared to those without bacterial co-infection. Surgical procedures such as debridement, spacer implantation, and resection arthroplasty presented a OR of 11.7 (95% CI 1.6–84.3, $P=0.014$), 8.1 (95% CI 1.1–61.2, $P=0.044$), and 7.2 (95% CI 1.5–35.2, $P=0.015$), respectively, compared to two-stage revision, while one-stage revision presented a OR of 1.8 (95% CI 0.2–13.8) compared to two-stage revision, without statistical significance ($P=0.560$), as shown in Table 3 and Fig. 4.

Discussion

Regarding the pathogenesis of fungal PJI, several possible routes have been postulated, including direct inoculation during surgery, bloodstream dissemination, contiguous infection spread, and recurrence from a previously infected joint[47]. As far as the

Table 2

Analysis of clinical outcomes of fungal PJI following hip arthroplasty by univariate analysis

	Success ($n=54$)	Failure ($n=22$)	
Outcomes variables	***n*** **(%)**	***n*** **(%)**	***P***
Publication year			
1998–2000	7 (77.8)	2 (22.2)	0.158
2001–2010	12 (92.3)	1 (7.7)	
2021–2022	35 (64.8)	19 (35.2)	
Sex			
Male	32 (78.0)	9 (22.0)	0.205
Female	22 (62.9)	13 (37.1)	
Age			
< 60 years	12 (70.6)	5 (29.4)	0.676
60–80 years	7 (87.5)	1 (12.5)	
> 80 years	35 (68.6)	16 (31.4)	
Specimen collection method			
Hip aspiration	23 (85.2)	4 (14.8)	0.064
Intraoperative specimen	31 (63.3)	18 (36.7)	
Fungal pathogen			
C. albicans	30 (68.2)	14 (31.8)	0.749
NCAC	18 (72.0)	7 (28.0)	
Non-Candida	6 (85.7)	1 (14.3)	
Bacterial co-infection			
No	46 (79.3)	12 (20.7)	0.017*
Yes	8 (44.4)	10 (55.6)	
Surgical option			
Debridement	4 (50.0)	4 (50.0)	0.009*
Spacer	3 (42.9)	4 (57.1)	
Resection	11 (55.0)	9 (45.0)	
One-stage revision	13 (86.7)	2 (13.3)	
Two-stage revision	23 (88.5)	3 (11.5)	

NCAC, non-C. albicans Candida; PJI, periprosthetic joint infection.
**P* value <0.05 with statistical significance.

Table 3

Multivariate analysis of risk factors associated with treatment failure for fungal PJI following hip arthroplasty

Variables	Odds ratio	95% CI	*P*
Bacterial co-infection			
No	Reference	Reference	
Yes	4.5	1.2–16.8	0.024*
Surgical option			
Two-stage revision	Reference	Reference	
One-stage revision	1.8	0.2–13.8	0.560
Debridement	11.7	1.6–84.3	0.014*
Spacer	8.1	1.1–61.2	0.044*
Resection	7.2	1.5–35.2	0.015*

PJI, periprosthetic joint infection.
**P* value <0.05 with statistical significance.

responsible fungal pathogens in our present study, the most frequent were Candida species (90.0%, 72/80). Among them, C. albicans and NCAC species accounted for 62.5% (45/72) and 37.5% (27/72), respectively. Those findings were consistent to the previous systemic review study on Candida infection following total hip arthroplasty by Kim *el al.*[5], in which the authors reported that C. albicans was the most frequently identified candida pathogen with a pooled percentage of 58%. The pathogenicity of fungi is attributed to multiple virulence factors, involving the adherence to host tissues and medical devices, formation of biofilms, and production of hydrolytic enzymes[48]. According to the NIH, biofilms account for over 80% of all microbial infections in the body[49]. Biofilm-growing cells are more resistant to antibiotics and host immune system. At present no drugs are in clinical use that specifically target fungal biofilms[50]. Therefore, treatment of prosthesis-associated fungal infection usually requires surgical removal and later new prosthesis replacement.

Based on the clinical practice guidelines by the Infectious Diseases Society of America, DAIR is recommended for an early PJI provided that the prosthesis is stable, the duration of symptoms is no more than 3 weeks, the skin and soft tissues are intact, and the causative pathogen is susceptible to a biofilm-active agent[51]. For bacterial PJI, previous studies have shown that the success rates of DAIR vary widely from 37.0 to 87.0%[52–54]. Moreover, Svensson *et al.*[55] analyzed 575 patients treated with DAIR for a first-time PJI after a primary total hip arthroplasty and found that DAIR with component exchange was associated with a significant lower reoperation rate (28.0%) compared with non-exchange (44.1%). In our current review, the pooled success rate for surgical debridement (including DAIR with or without modular polyethylene exchange) was 50.0% (4/8). Unfortunately, because of the paucity of data we were unable to conduct a subgroup analysis to investigate whether DAIR with component exchange would be better than DAIR alone in the surgical treatment of fungal PJI of the hip.

As reported in our current review, two-stage revision was the most preferred surgical option (32.5%, 26/80) to treat a fungal PJI following hip arthroplasty, with a pooled success rate of 88.5% (23/26), which is relative higher than the data from a previous review by Schoof *et al.*[56] in 2015. They reported that 77.3% of the fungal PJIs could be controlled with a two-stage revision procedure. Compared with two-stage revision, one-stage revision has the advantages of lower technical difficulty, earlier functional recovery, decreased complications, and less hospitalization expense[57]. The pooled success rate of one-stage revision (86.7%, 13/15) in our current review was comparable to that of two-stage revision (88.5%, 23/26). Using the binary logistic regression analysis, surgical option was identified as one of the two significant risk factors associated with the treatment failure for fungal PJI following hip arthroplasty. However, unlike other surgical procedures such as debridement, spacer implantation, and resection arthroplasty, one-stage revision presented a OR of 1.8 (95% CI 0.2–13.8) compared to two-stage revision without statistical significance ($P = 0.560$). It seems that further high-quality studies with large sample size and high level of evidence are required to establish the optimal treatment.

Bacterial co-infection adds to the difficulties in treating fungal PJI, due to the more virulent biofilm produced by bacteria and fungi synergistically. Bacterial co-infection was reported in 21 (26.3%) of the enroled 80 fungal PJI cases following hip arthroplasty. Treatment success was reported in 47.4% (9/19) of those cases with bacterial co-infection, significantly lower than those without bacterial co-infection [vs. 79.0% (45/57), $P = 0.017$]. Sidhu *et al.*[58] reported a relative lower rate (1.9%) of co-infective bacterial and fungal PJIs (8 cases after total hip arthroplasties and 14 after total knee arthroplasties) among the 1189 PJI cases presenting to their institution. They found the overall rate of infection eradication after two and five years was 50.0% and 38.9%, respectively, which was comparable to the results from our current review. Moreover, they concluded that the risk of failure to eradicate infection with the requirement of amputation among those cases was heightened when the fungal organism was joined by polymicrobial and multidrug-resistant bacterial organisms. Resection arthroplasty is considered as a salvage procedure in situations of refractory infections, high

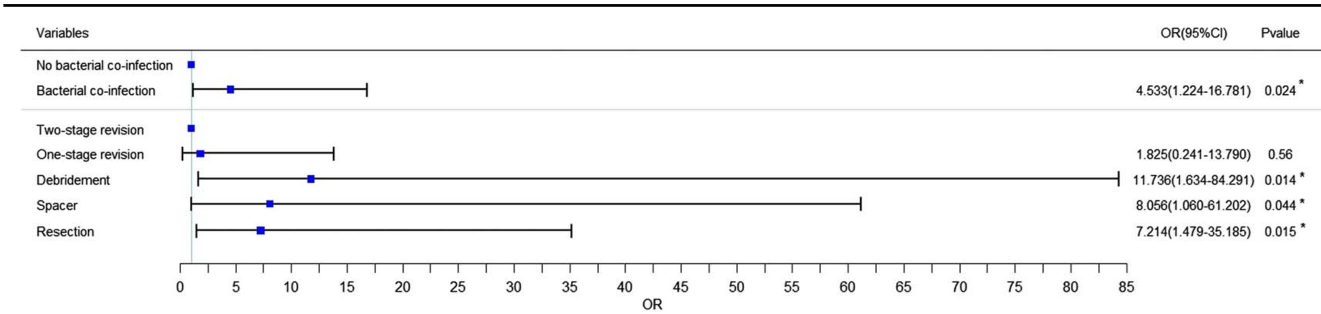

Figure 4. Forest plot of risk factors associated with treatment failure for fungal periprosthetic joint infection following hip arthroplasty. OR, odds ratio.

surgical risks, or further prosthetic reimplantation is refused by patients[59].

Despite the strengths of this systematic scoping review in providing a comprehensive insight into the surgical procedures of fungal PJI following hip arthroplasty, we acknowledge several limitations to this review. Firstly, all the included studies are case reports or series with low levels of evidence and large heterogeneities because of the rarity of fungal PJIs. Thus, the inferential statistical conclusions drawn from the pooled results should be prudently interpreted. Secondly, we excluded some relevant articles published in other languages such as Chinese, French, German, and Japanese, which inevitably generated information bias in the following statistical analysis. Moreover, given the length limitation, some aspects in the management of fungal PJI of the hip, such as the optimal diagnostic method, selection of ideal antifungal drug, route and duration of antifungal drug administration, and impregnation of antifungal drugs into bone cement were not investigated and discussed herein. For details about these aspects, readers may refer to those previous reviews[1,5,56].

Conclusions

Regarding the surgical treatment of fungal PJI following hip arthroplasty, patients with bacterial co-infection, and those treated with surgical procedures such as debridement, spacer implantation, and resection arthroplasty should be aware of the higher risks of failure. Nonetheless, future multiple-centre cohort studies are required to establish the optimal treatment.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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Author contribution

Y.G. and Y.T. had the idea for the article. Literature search, data collection and analysis were performed by Y.G. and H.Z. The first draft of the manuscript was written by Y.J.T. Z.Z. and Y.G. critically revised the work. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no competing interests.

Research registration unique identifying number (UIN)

Our current study was registered in Research Registry with identifying number reviewregistry1770 with a link: https://researchregistry.knack.com/research-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/6590118fbaa9e80029f82f70/).

Guarantor

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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