Reviews

Debridement and implant retention in acute hematogenous periprosthetic joint infection after knee arthroplasty: a systematic review.

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Debridement, antibiotic, and implant retention (DAIR) can be used as a first surgical procedure for acute infections in patients who have well-fixed components. However, its use in hematogenous or late acute infections is still debated. This systematic review of literature aims to clarify the effectiveness of DAIR procedure in the treatment of hematogenous periprosthetic knee infections.

DAIR is an effective way to treat acute hematogenous PJIs of the knee and reaches its best efficacy when performed within one week from the onset of symptoms, modular components are exchanged, and a pathogen-oriented antibiotic therapy can be set. It is safe, economic, and effective technique, but has to be performed in a very narrow temporal window.

INTRODUCTION

Periprosthetic joint infection (PJI) represents a relatively rare but severe complication of total knee arthroplasties (TKA),[1] with life-threatening consequences and high costs for patients and the healthcare system.[2] Debridement of the infected tissues associated with implant removal or not represents the best treatment option facing PJI.[3-7] Moreover, radical debridement of all necrotic tissues, synovectomy, combined with replacement of mobile prosthetic parts, and systemic antibiotic treatment, namely DAIR, eight is reported to be effective in those patients affected acute postoperative implant infections. Early postoperative infection is usually defined as occurring within four weeks from index arthroplasty, although some authors consider any infection within three months (90 days) from the index arthroplasty as acute.[8] Conversely, hematogenous infections are often classified as 'late infections' since they can occur up to two years after joint arthroplasty, caused by blood spread of bacteria from a distant primary focus that can secondarily affect the joint space.[9-13] Although hematogenous PJIs characterized by immature bacterial biofilm can be effectively treated with DAIR, as acute infections, the results in terms of infection eradication rate are highly variable.

This systematic review of literature aims to I) evaluate demographic data and microbiological findings of patients affected by hematogenous periprosthetic knee infections II) clarify the effectiveness of the DAIR procedure in treating hematogenous periprosthetic knee infections.

MATERIALS AND METHODS

REGISTRATION

Before commencing the review, the protocol was registered online with PROSPERO (International Prospective Register of Systematic Reviews) (reg. prot. CRD42018064291).

DATA SOURCES AND SEARCH STRATEGY

This systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.[14] Electronic databases, namely MEDLINE, Scopus, and Scholar, were reviewed for studies investigating DAIR treatment in hematogenous (late acute) knee periprosthetic infections. A combination

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of the following keywords was used for article search: "PJI OR periprosthetic joint infection OR Prosthetic infection" AND "acute hematogenous infection" AND "debridement OR implant retention OR DAIR" AND "knee OR knee joint" AND "treatment outcome".

ELIGIBILITY CRITERIA

The inclusion criteria were not limited to English literature and specific publication dates. Reference lists of selected articles were searched for additional pieces that were not identified in the database search. In addition, longitudinal studies (retrospective and prospective) evaluated DAIR's treatment outcome in hematogenous knee PJI were included. The exclusion criteria included: case reports, expert opinions, previous systematic reviews, letters to the editor.

Furthermore, we excluded: (I) studies that do not perform only open debridement (II) and studies that included different joints involved in which knee data could not be extrapolated (III) papers which did not report joint age, and within these, patient with a joint age inferior to 3 months.

STUDY ASSESSMENT AND DATA EXTRACTION

Initially, the titles and abstracts of the studies were screened by two independent reviewers (RdG, EF). Next, the full text was obtained for all the abstracts that appeared to meet the inclusion criteria or those with any uncertainty. Then, each study was assessed based on the inclusion criteria by two independent reviewers. Finally, any disagreement regarding the inclusion of any study was resolved by evaluating the article by the senior Author (GB).

The flow diagram of our search strategy is presented in Figure 1. A total of 693 potentially relevant studies were found through computer search and manual screening of reference lists. Having removed all duplicates, 494 articles remained for evaluation. After screening the titles and abstracts, 416 studies were excluded, and full texts of 78 articles were evaluated and screened for relevance to the review's topic. In total, 478 studies were excluded after a detailed assessment. The remaining 16 articles were included in our systematic review.

Relevant data were extracted from each included study. In addition, data describing participants' demographics, follow-up, microbiology, diagnosis classification, treatment options, and outcomes were collected and recorded.

RESULTS

Sixteen papers met the inclusion criteria for a total of 430 infected knee implants (Table 1). Based on reported data in 13 of the included studies,[1,2,10,15-25] hematogenous knee infections have occurred in patients with a mean age at diagnosis ranging from 56 years old,8 to 74 years old.[24,25] Only six studies described the percentage of males among the patients treated,[15,17,18,21,24,25] ranging from 18%,8 to 66%.[18] The mean follow-up varied from 27 months,[19] to 98 months.[20]

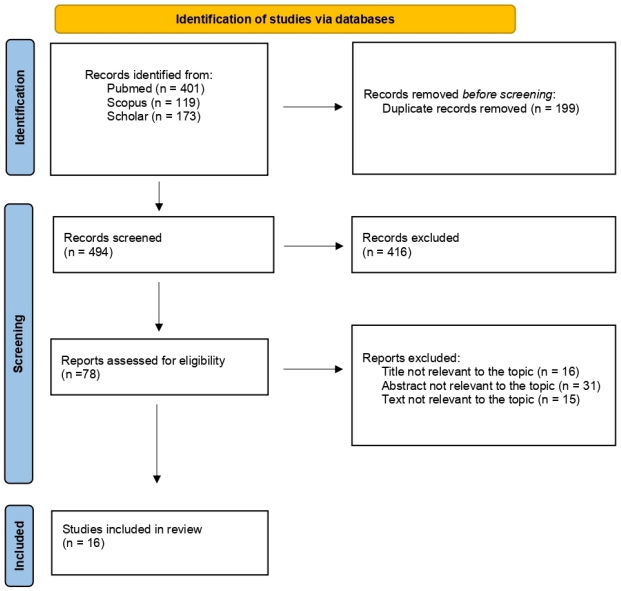

Figure 1.

In stratifying the diagnosis of infection, the most used classifications were the one proposed by Tsukayama et al.,[26] in 10 out of 16 (62,5%), followed by Zimmerli-Trampputz et al.,[27] in 3 out of 16 (18,75%) (Table 1). Fever was reported as the first symptom by Vilchez et al. in up to 83.3% of patients.[25]

All studies in our systematic review reported the causative microorganisms involved in the septic process (Table 2). Gram-positive species (spp.) were the most represented (86% of the total), with Gram-negative spp. Representing only 8% of the causes of acute hematogenous infections, and other microorganisms such as fungi accounted for less than 1%; culture-negative diseases were reported in 5% of the total analyzed cases.

In all the selected papers, an open debridement as a surgical procedure has been performed. The replacement of mobile parts of the knee implants was described to be completed in a percentage of patients varying from 29%,[21] to 100%.[1,15,17,22-25,28] Two papers did not mention modular component exchange.[2,18]

Mean interval time from onset of symptoms to DAIR was reported in all papers, but two,[18,22], ranged from 1 to 60 days. Twelve of the included documents treated patients within 28 days from the onset of symptoms.[10,15,17,19-21,23-25,28-30] Reported joint age, defined as the time interval between index procedure and DAIR, ranged from 2 weeks to over 20 years (Table 3).[29]

In ten out of sixteen papers, intravenous (iv) antibiotic therapy for six weeks, followed by a variable therapy per os, was the antibiotic regimen applied.[1,10,15,17,18,21,22,24,29,30] The rest of the papers reported to have practiced an iv therapy for between 1,5 to 4 weeks (Table 3).[2,19,20,23,25,28] The use of rifampin as antibiotic treatment for staphylococcal PJI was described in only six papers (Table 3).[10,15,19,23,25,28]

The definition of failure was specified in all papers included. Failure to eradicate infection, a wound fistula,

drainage, intolerable pain, or infection recurrence caused by the same organism strain; subsequent removal of any component for disorder; unplanned second wound debridement for the ongoing deep condition; and occurrence of periprosthetic joint infection-related mortality were considered failures of DAIR procedure.[31] Conversely, success was defined as retention of implant, with no signs and symptoms of infection and regular laboratory markers after a minimum of 12 months from DAIR.

The percentage of failures ranged from 0%,20 to 69%.[29]

The main microorganism responsible for the failure was *S. aureus*, accounting for 36 of the 23 failures in which the involved bacteria were described (Table 3). In case of failure of DAIR treatment, patients generally repeated open debridement (8 on 12 papers)[1,17,20,21,23,25,29,30]: other options were two-stage revision,[2,15,21,23,24,30]or suppression antibiotic therapy (SAT).[1,2,22]

DISCUSSION

The treatment of periprosthetic joint infection represents a challenge for orthopedic surgeons. While the management of chronic diseases has been well described,[4-7,16,32] there is a lack of information on the management and outcomes of patients treated for an acute hematogenous infection. To the best of our knowledge, there are no systematic reviews that describe the effectiveness of the DAIR procedure in infection eradication in patients affected by a hematogenous periprosthetic knee infection. Our study shows an average success rate of 41% (31% to 100%), at mean follow-up; this outcome is slightly worse than the moderate DAIR success reported for acute infection by Maillet et al. (51,7%),[33] Romanò et al. (45.9%),[34] and Vilchez et al. (75% early infection VS 45% hematogenous infections).[25] One possible reason for this result may be the lack of a clear definition of acute hematogenous PJI. Two classifications have been proposed to better distinguish acute postoperative and hematogenous infections. Zimmerli and Tramputz, back in 2004, defined as hematogenous PJI any infection that occurs after 24 months from index procedure.[27] Instead, Tsukayama et al. defined as hematogenous PJI any deep infection characterized by acute presentation in a previously well-functioning joint arthroplasty.[26] In our systematic review, the Tsukayama and Zimmerli-Tramputz definitions are applied in 10 and 3 of included studies.[26,27] Another possible reason is the period from symptoms onset to DAIR procedure instead of the time from index procedure (joint age). Our data suggest that the best outcomes are described by authors reporting the shorter period from diagnosis to surgical procedure, with an average of 6,4 days.[(1-60)]

These results are by the Second International Consensus Meeting (ICM) on PJI,[13] that advice to perform a DAIR when the onset of symptoms is <4 weeks (good < 7 days). In addition, according to the Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA),[35] patients who have a well-fixed, functioning prosthesis without a sinus tract, infection occurring within 30 days of index arthroplasty or < 3 weeks of the onset of infectious symptoms, and an organism susceptible to oral antimicrobial agents should be candidates for debridement antibiotics and implant retention (DAIR). In our systematic review, the reported joint age, defined as the time interval between index procedure and DAIR, ranged from 2 weeks to 20 years. Health status, such as nicotine abuse, the ASA status, and the number of previous operations represent the leading causes of increased risk to a hematogenous infection even after different years from prosthetic implantation.[2,18,28]

In the end, how the DAIR is performed and the management of modular prosthetic components may influence the outcome. As reported, 100% of the selected papers have conducted an open debridement. Still, in some cases, the modular part was not exchanged–whereas the ICM stated that exchanging modular components reduces the recurrence of infection.[13] Specifically, Choi et al. did not remove the liner in all cases,[29] and Estes et al. reused the mobile parts after a sterilization process[10]; it is remarkable that the worst results were found in the group who did not perform routinely polyethylene exchange.[10,29] It has been stated at that same consensus meeting that DAIR may prove a solid therapeutic option in treating acute infections in unicompartmental knee arthroplasties and mega prosthesis alike,[13] widening its indication to more than just primary or revision TKA.

Other factors have been confirmed to be associated with treatment failure in acute PJIs treated with DAIR, including the type and virulence of the microorganisms involved and the consequent duration of prescribed antibiotic treatment.[30] Polymicrobial infections were the most difficult to treat, showing up to 75% failures. Whenever coagulase-positive staphylococcal spp. has been isolated, cases failed an average of 55%, staphylococcus Epidermidis (50%) followed by Enterococcus spp. (38%) and Streptococcus spp. (37%). Gram-negative bacteria have reported a success rate of nearly 90%, as well as fungi (Table 3). Furthermore, high failure rates were reported in those case series that provided an IV antibiotic duration of fewer than six weeks.[2,25]

In case of failure of DAIR, many Authors repeated debridement[1,17,20,21,23,25,29,30]; other options were two-stage revision or lifelong antibiotic suppression therapy. Salvage procedures were performed in selected cases.[17,29,30] A repeated DAIR with an interval of 7 days was not reputed a failure. To this matter, the ICM in 2018 relevantly stated that after a failed DAIR procedure, one and two-stage revisions should be considered rather than attempting a second time.[13]

To the best of our knowledge, ours is the first study focused on DAIR treatment in acute hematogenous periprosthetic infection of the knee, with a mean follow-up of two years and a high number of patients enrolled. Selection criteria resulted in decent uniformity of surgical treatment.

Like every publication, our work has some limitations: despite the strict selection criteria of the surgical treatment, conclusive studies lack homogeneity of medical treatment. The antibiotic treatment scheme was not uniform in duration and molecules used. Furthermore, the database search retrieved no RCT studies.

In conclusion, debridement, antibiotics, and implant retention has been demonstrated to be a safe, economical,

Table 1. Basic information of the studies included in the systematic review

Lead author, publication date	Study design	Journal	Classification of PJI used	Definition of hematogenous infection	Number of PJI/ patients	Male (%)	Age (years)	Follow-up (months)
Chiu et al. 2007,[24]	Retrospective 1992-2003	Clinical Orthopaedics and Related Research	Tsukayama	Type III	10	40	74 (62-85)	80 (39-136)
Choi et al. 2011,[29]	Retrospective 2002-2007	Clinical Orthopaedics and Related research	Tsukayama	Type III	29	NA	NA	36 (12-84)
Estes et al. 2010,[10]	Retrospective	Clinical Orthopaedics and related research	Mc pherson	Acute onset in a previously well-functioning joint arthroplasty	15	NA	65 (28-91)	32 (14-85)
Fink et al. 2017,[28]	Retrospective 2004-2013	The Journal of Arthroplasty	Tsukayama	Type III	20	NA	NA	> 24
He et al. 2016,[15]	Retrospective 2002-2012	Orthopaedic Surgery	Trampuz-Zimmerli 2004	> 6 months at least	11	18	56 (35-73)	60 (26-98)
In jun Koh et al. 2015,[30]	Retrospective 2005 - 2012	Archives of Orthopaedic Trauma Surgery	Tsukayama	Type III	20	NA	NA	35 (24-94)
Konigsberg et al. 2014,[17]	Retrospective 1995-2006	The Journal Of Arthroplasty	NA	NA	20	55	60 (25-86)	56 (25-124)
Koyonos et al. 2011,[18]	Retrospective 1996-2007	Clinical Orthopaedics and related research	Tsukayama	Type III	34	66	63 (61-66)	54 (12-115)
Lora-Tamayo et al. 2017,[19]	Retrospective 2003-2012	Clinical Infectious Diseases	Zimmerli-Tramputz 2004	Acute onset after an uneventful postoperative course	156	NA	72 (65-78)	27 (17-44)
Meehan et al. 2003,[20]	Retrospective 1969-1998	Clinical Infectious Diseases	Tsukayama	Type III	10	NA	72 (60-80)	98 (22-133)
Mont et al. 1997,[21]	Prospective	The Journal of Arthroplasty	NA	NA	13	46	67 (46-80)	35 (24-76)
Segawa et al. 1999,[22]	Retrospective 1980-1995	The Journal of Bone and Joint Surgery	Tsukayama	Type III	7	NA	67 (32-87)	40 (36-66)
Son et al. 2017,[23]	Prospective 2010-2014	Knee Surgery & Related Research	Tsukayama	Type III	15	NA	71 (35-86)	29 (24-35)
Triantafyllopoulos et al. 2014,[1]	Retrospective 2000-2013	The Journal of Arthroplasty	Tsukayama	Type III	43	NA	64 (38-90)	80 (12-172)
Vilchez et al. 2011,[25]	Prospective	The International Journal of Artificial Organs	Zimmerli Tramputz 2004	>24 months	10	50	74	32
Zhang et al. 2016,[2]	Retrospective 1998-2013	The Journal of Knee Surgery	Tsukayama	Type III	17	NA	71 (55-81)	54 (10-184)

and effective technique but have to be performed in a very narrow temporal window; modular component exchange is strongly advised. In addition, further studies are needed concerning the antibiotic treatment (antibiotic choice, duration, and regimen) to reach an effective standardization.

AUTHORS' CONTRIBUTIONS

EF, VdM, and ML screened the studies and selected the data. MA, RdG, and TA wrote the manuscript. Finally, GB and MM corrected the whole paper.

COMPETING INTERESTS

No author is involved in a conflict of interest. No author has received any funding.

FUNDING

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Table 2. Microorganisms involved in the systematic review

Lead Author, Publication Date	Infective organisms reported (%)
Chiu et al. 2007,[24]	*Coagulase negative staphylococcus* (40%) MRSA (30%) *S. beta haemoliticus* (10%) *S. aureus* (10%) *Candida parapsilosis* (10%)
Choi et al. 2011,[29]	*S. aureus* (33%) *Coagulase-negative Staphylococcus* (26%) *Streptococcus* spp. (10%) Others (17%) Polybacterial (10%)
Estes et al. 2010,[10]	MSSA (27%) MRSA (9%) Coagulase Negative Staphylococcus (9%) *Streptococcus* spp (36%) Polymicrobial (1%) *E. coli* (18%)
Fink et al. 2017,[28]	*S. aureus* (25 %) MSSE (14%) MRSE (4%) *Streptococcus* spp. (14%) Others (22%)
He et al. 2016,[15]	*Staphylococcus spp.* (18%) *Streptococcus spp.* (63%) *Others* (18%)
In jun Koh et al. 2015,[30]	Culture negative (19%) *Staphyloccus* spp. (42%) Others (39%)
Konigsberg et al. 2014,[17]	*Streptococcus* spp. (75%) *Staphylococcus* spp. (40%) Others (12%) Polymicrobial (5%) No growth (5%)
Koyonos et al. 2011,[18]	MRSA (12%) Culture-negative (16%) *Staphylococcus* spp. (40%)
Lora-Tamayo et al. 2017,[19]	*Streptococcus* spp. 100%
Meehan et al. 2003,[20]	*Streptococcus* spp. 100%
Mont et al. 1997,[21]	*S. aureus* (64%) *S. epidermidis* ((21%) *E. coli* (14%)
Segawa et al. 1999,[22]	Coagulase-positive staphylococci (22%) Coagulase-negative staphylococci (22%) *Streptococcus* spp. (44%) *Enterococcus* spp. (11%)
Son et al. 2017,[23]	MRSA MRSE Imipenem resistant *Acinetobacter baumanii* MSSA *Streptococcus* spp. Polymicrobial
Triantafyllopoulos et al. 2014,[1]	MRSA (27%) MSSA (41%) Other gram-positive bacteria (10%) Gram negative bacteria (7%) Negative cultures (11%)
Vilchez et al. 2011,[25]	MRSA (20%) Staphylococcus aureus resistant to fluoroquinolones (80%)

Zhang et al. 2016,[2]	*Staphylococcus* spp. (64%) Nonstaphylococcal spp (36%): *S. enteriditis*; *S. dysgalactiae*; *P. acnes*; *P. aeruginosa*; *E. coli*

Table 3. Timing, procedures, outcomes and other strategies

Lead Author, publication date	Mean time intervals from onset of symptoms (days) to DAIR	Time interval from index procedure. and DAIR (joint age)	Debridement Type	Exchange modular components N (%)	Use of rifampicin	Duration of antibiotic therapy (weeks)	Patient failed N (%)	Bacteria involved in failed cases	Surgical option for failed patients
Chiu et al. 2007,[24]	Within 28 days	28 – 72 months	Open	100%	NA	6 weeks IV at least	5 (50%)	NA	Fusion or two-stage reimplantation.
Choi et al. 2011,[29]	Within 28 days	0,5 – 240 months	Open	With or without PE exchange	NA	6 weeks IV	16 (69%)	*S. aureus* 16 (100%)	Staged revision operation or repeated DAIR or fusion or amputation or resection.
Estes et al. 2010,[10]	Within 28 days	NA	Open (two debridements + beads)	0% (all modular components were removed and sterilized by flash autoclave or in a betadine soak)	26,6%	6 weeks IV + 36 weeks OS	2 (11%)	MRSA 1 (50%) *S. agalactiae* 1 (50%)	None
Fink et al. 2017,[28]	1 - 21	NA	Open	100%	100%	2 weeks IV + variabile OS	NA	NA	NA
He et al. 2016,[15]	2–7	7 – 61 months	Open	100%	100%	6 weeks IV + 12 weeks OS	2 (19%)	*S. epidermidis* 1 (50%) *S. aureus* 1 (50%)	1 Two-stage. 1 second implant removal prior to a second revision.
In jun Koh et al. 2015,[30]	4–26	5 – 144 months	Open	94%	NA	6 weeks or less IV and then OS	9 (45%)	NA	Multiple irrigation and debridement 1 (5%) Suppression antibiotic therapy 1 (5%) Two-stage revision 6 (30%) Fusion or amputation 2 (10%)
Konigsberg et al. 2014,[17]	1-28	6 – 186 months	Open	100%	NA	6 weeks IV	NA	*Staphylococcus* spp.	Second debridement or following implant removal and II stage reconstruction including a medial gastrocnemius flap in one knee or knee fusion or above knee amputation.
Koyonos et al. 2011,[18]	NA	NA	Open	NA	NA	6 weeks IV	NA	NA	NA
Lora-Tamayo et al. 2017,[19]	2–12	NA	Open	55%	37%	3 weeks IV	NA	NA	NA
Meehan et al. 2003,[20]	1 – 9	1,8 – 138 months	Open	40%	NA	4 weeks IV + NA oral therapy. 42% of cases received long-term oral antimicrobial therapy	0 (0%)	None	Patients underwent a median of one surgical debridement (range, 1–3).
Mont et al. 1997,[21]	3 - 28	6 – 71 months	Open	29%	NA	6 weeks IV	4 (29%)	*S. aureus* 1 (25%) *S. epidermidis* 2 (50%) *E. coli* 1 (25%)	Two-stage reimplantation or second DAIR or knee fusion.
Segawa et al.	NA	NA	Open	100%	NA	6 weeks IV	2	NA	1 Arthrodesis.

1999,[22]							(29%)		1 Suppressive antibiotic. Both failed
Son et al. 2017,[23]	1 - 5	NA	Open	100%	Used when *S. aureus* was detected	4 weeks IV	3 (20%)	MSSA 1 (33%) *Enterobacter* 1 (33%) *Streptococcus* spp. 1 (33%)	Second DAIR or two-stage revisions.
Triantafyllopoulos et al. 2014,[1]	2 – 60	95.3% occurred within the first 365 days after index surgery	Open plus arthroscopy	100%	NA	6 IV weeks + 6 weeks OS	NA	*Staphylococcal* spp (38%) Other gram-positive bacteria (4%) Gram negative bacteria (1%) Negative cultures (1%)	II stage or second/third DAIR or long-term suppression treatment with antibiotics.
Vilchez et al. 2011,[25]	4,7	9 – 88 months	Open	100%	100%	1,5 week IV + 16 weeks OS	7 (59%)	*Staphylococcus aureus* resistant to fluoroquinolones 3	Second DAIR
Zhang et al. 2016,[2]	1 – 60	0 – 230 months	Open	NA	NA	4/6 weeks IV + 12/24 weeks OS	11 (65%)	*Staphylococcus* spp. and nonstaphylococcal spp.	Two-stage revisions or lifelong antibiotics suppression.

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