

CURRENT CONCEPTS REVIEW

Late Acute Hematogenous Infections after Total Knee Arthroplasty: Results of Debridement, Antibiotics, and Implant Retention

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Abstract

The frequency of late acute hematogenous infection (LAHI) following total knee arthroplasty (TKA) is between 0.2% and 0.5%. There is controversy over the results of patients treated for LAHIs by surgical debridement, antibiotics, and implant retention (DAIR). This narrative review of the literature aims to establish the role of DAIR in LAHIs after TKA. The published success rate (retention of the prosthesis) after DAIR is between 50% and 100%. The success rate is associated with a shorter duration of symptoms (5–14 days from the onset of symptoms). Factors associated with failure are an accompanying infection and the diagnosis of rheumatoid arthritis before the TKA is performed. It is not recommended to indicate a DAIR in patients with atrial fibrillation, chronic obstructive pulmonary disease, the presence of >15 cells per high-powered field, preoperative C-reactive protein >500 mg/L or methicillin-resistant *S. aureus*. In such patients, a two-stage revision arthroplasty should be recommended. Arthroscopic DAIR has a limited effect. It is most efficacious in the very early stage of acute presentations of infected TKA. It can be useful in patients with extreme frailty as an adjunct to suppressive antibiotic therapy. If carried out, high volumes of fluid should be utilized. The indications for an open DAIR are the following: duration of clinical signs and symptoms is less than 3 weeks; patients with a well-fixed implant; no abscess or sinus tract; low-virulence bacteria; elderly patients with multiple comorbidities; and nonimmunocompromised patients. Open DAIR should not be advised in cases with chronic infection (>4 weeks postoperatively, insidious beginning of symptoms).

Level of evidence: III**Keywords:** Acute hematogenous infection, Antibiotics, Debridement, Implant retention, Total knee arthroplasty**Introduction**

New technologies have made it possible to gradually reduce the mechanical causes of failure in total knee arthroplasty (TKA). However, periprosthetic joint infection (PJI) continues to occur and is currently the most worrisome complication in patients who have undergone TKA surgery (1-7). PJI is a serious complication involving high costs and high morbidity. The rates of deep, superficial, and hematogenous infection published by Renaud et al. in TKA were 1.6%, 0.7%, and 0.2%, respectively (8).

Late acute hematogenous infection (LAHI) is a devastating complication of TKA, and the best strategies

for its management remain controversial. Two-stage revision arthroplasty is considered the gold standard for the treatment of late chronic infections. However, there is currently little knowledge on the treatment and results of people treated for LAHIs (9).

In 2007, Cook et al. analysed the incidence of LAHIs in a series of 3013 primary TKAs. After a mean of 10 years, they found 14 LAHIs in 14 patients (a rate of 0.5%) (1). In an infected TKA, antibiotic prophylaxis is usually employed until the causal bacterium is detected by culture and antibiogram (10). In 2018, Westberg et al. had found that the incidence of late acute hematogenous

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PJI following TKA was 3%, 2% and 14%) after primary complicated TKA, non-infected revisions, and infected revisions, apiece (11).

Arthroscopic debridement, antibiotics, and implant retention (DAIR) and open DAIR and liner exchange, have been considered reasonable therapeutic options for PJI after TKA. However, multiple recent studies have challenged this claim (12). It is also unclear whether in an infected TKA revision, DAIR can eradicate the infection (13).

The value of C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) are well known in the diagnosis of TKA infection. However, the value of preoperative CRP and ESR in terms of predicting outcomes after DAIR for late acute hematogenous TKA infection is not entirely clear (14).

The purpose of this narrative review of the literature is to analyze the above-mentioned aspects, primarily the results of DAIR, in LAHIs after TKA.

Arthroscopic DAIR (debridement, antibiotics, and implant retention)

According to Miles and Parrat, arthroscopic DAIR can be advised in cases of acute infections of well-fixed prostheses (15). Curation of infection is far from guaranteed and is only probable in patients with streptococcal infection. Arthroscopic surgical treatment is only the beginning of management, and prolonged antibiotic therapy is mandatory. Arthroscopic DAIR of infected TKA is almost never utilized. Today, arthroscopic DAIR plays a small role because full biofilm clearance is in theory implausible. It is most efficacious in the very early stage of acute presentations of infected TKA. Arthroscopic DAIR can be useful in patients in which the bacteria is not associated with a strong biofilm; in people with extreme frailty, as an adjunct to suppressive antibiotic therapy; or as piece of a diagnostic workup. If carried out, accessory portals and high volumes of liquid must be utilized (15).

Open DAIR and liner exchange

According to Encinas-Ullán et al, the indications for an open DAIR and polyethylene exchange are the following: the duration of clinical signs and symptoms has been less than 3 weeks; patients have a well-fixed implant and healthy local soft tissues (no abscess or sinus tract); low-virulence bacteria; elderly people with osteoporosis and many comorbidities, for whom anesthesia and more invasive surgical procedures could be hazardous; and nonimmunocompromised patients (16). Open DAIR and polyethylene exchange must not be advised in cases of chronic infection (>4 weeks after surgery, treacherous onset of symptoms). Arthroscopic DAIR has inferior results compared with open DAIR (16).

Results of open DAIR and liner exchange

Table 1 shows the main data and results of surgical DAIR in LAHIs after TKA in the literature (9, 10, 13, 14, 17-22).

In 2007, Chiu and Chen had studied 40 infected revision TKAs. No implants were loose or misaligned

(13). Utilizing the classification reported by Tsukayama et al., 10 of the individuals experienced type I (acute postoperative), 20 type II (chronic late), and 10 type III (acute hematogenous) infection. All the patients were treated by DAIR. The minimum follow-up was 3 years (range, 36–143 months). A successful outcome (prosthesis retention) was accomplished in 12 (30%) of the 40 patients. Nevertheless, the probability of success was determined by the category of infection: individuals with type I infection (7 of 10) and those with type III infection (5 of 10) were able to retain their implants more frequently than individuals with type II infection (0 of 20). Therefore, in a TKA review, these authors recommended DAIR when the infection is type I or type III (50% success rate); however, when the infection is type II, they advised primary removal of the implant (13).

In 2007, Debarge et al. had analyzed 923 primary TKAs. Their aim was to determine the PJI rate, including infections diagnosed during the first year, and their risk factors (22). The minimum follow-up was 12 months. The sex was predominantly female (72%), the mean patient age was 71 years (range 26–93), and the etiologies were osteoarthritis (87.5%) and rheumatoid arthritis (RA) (6.9%). Cefazolin was utilized as antibiotic prophylaxis. Vancomycin was utilized in individuals with a contraindication to cefazolin. Over a 10-year period, 20 PJIs were identified after TKA (2.1% rate). The mean follow-up was 43 months (range 12–123 months, median 37 months). The rate of PJI during the first postoperative year was 1.4%, with 80 per cent of the infections (n = 16) occurring within the first 2 postoperative months. Due to hematogenous contamination, there were 4 infections: 2 between 2 and 5 years after the surgical procedure, and another 2 more than 5 years after the surgical procedure. All infections were caused by a single bacterium. The causing bacteria were the following: Gram+ (90%) and Gram- (10%), with a clear prevalence of *Staphylococcus aureus* (*S. aureus*) (n = 9). Infection was 2.1 times more frequent in individuals with RA. Age and body mass index (BMI) was not different between individuals with and without PJI (22).

In 2010, Burnett et al. had conducted an investigation to establish whether preoperative prophylactic intravenous antibiotics affected culture results attained intraoperatively (10). They analyzed 25 individuals with 26 infected TKAs, with identified preoperative bacteria, and no recent antibiotic therapy. After anesthesia and sterile preparation, joint re-aspiration of the infected TKA was performed. After administering intravenous antibiotic prophylaxis, the tourniquet was inflated. Intraoperative culture swabs and tissue were attained at arthrotomy. Data from pre- and post-antibiotic cultures were analyzed to establish the effect of preoperative intravenous prophylactic antibiotics on the intraoperative cultures attained. Four infections were acute postoperative, nineteen were chronic and three were acute hematogenous. The most usual bacterium was cloxacillin-sensitive *S. aureus* (9 joints [35%]). The conclusion was that preoperative

Table 1. Main data and results of open debridement, antibiotics and implant retention open (DAIR) in late acute hematogenous infections (LAHIs) after total knee arthroplasty (TKA) in the literature

Authors	Year	N ^a of cases	Healing rate (implant retention)	Comments from the original publications
Chiu and Chen (9)	2007	10	50%	These authors recommended DAIR in LAHIs.
Debarge et al (18)	2007	4	NA	Infection was 2.1 times more frequent in patients with RA.
Burnett et al (6)	2010	3	NA	Preoperative prophylactic antibiotics do not affect the results of intra-operative cultures and therefore should not be discontinued before the surgery of an infected TKA, provided that the bacterium has been identified by preoperative aspiration and a test has not been performed. Recent antibiotic therapy (4 weeks).
Stryker et al (10)	2013	69	72%	CRP and ESR are not valid for the prediction of DAIR results in the treatment of late acute hematogenous TKA infection.
Konigsberg et al (13)	2014	42	76%	Non-staphylococcal infections had a particularly low failure rate (96% survival at 2 years).
Koh et al (8)	2015	52	55%	The success rate was associated with a shorter duration of symptoms. The rapidity in performing the DAIR, more than the type of causal organism or its virulence, is of paramount importance for therapeutic success.
He et al (5)	2016	11	0% in patients with staphylococcal infection and 100% in patients with non-staphylococcal infection	The duration of symptoms before the operation and the type of bacteria affected the result ($P = 0.00$).
Son et al (14)	2017	25	88%	Factors associated with the failure were accompanying infection before the TKA and the diagnosis of RA. Useful treatment for TKA infection if it is performed within the first 5 days or less of the onset of symptoms, in patients who do not have an accompanying infection and in those whose indication for TKA is not RA.
Song et al (15)	2018	24	73.3%	The failure of the DAIR had a significant correlation with sinusitis and the duration of infection symptoms over 14 days ($P < 0.05$). The results of the multivariate logistic regression analysis showed that sinusitis was an independent risk factor for failure ($P < 0.05$). The conclusion was that DAIR plays an important role in the treatment of PJI after TKA.
Bene et al (16)	2018	76	NA	The conclusions of this study were that reoperation-free survival after DAIR in late acute infected primary TKA improves with the increased duration of postoperative antibiotic therapy, so chronic antibiotic suppression after DAIR should be considered; worsens with atrial fibrillation, COPD, > 15 cells / HPF, a CRP protein > 500 mg / L or a S. aureus MRSA, so in these patients two-stage revision arthroplasty should be recommended; and it is similar in acute postoperative infections and in LAHIs.
Calanna et al (17)	2019	NA	NA	These authors have reported a new technique: debridement antibiotic pearls and retention of the implant (DAPRI). The DAPRI technique could represent a safe treatment in early acute hematogenous PJI.

NA = Non-available; RA = rheumatoid arthritis; CRP = C-reactive protein; ESR = Erythrocyte sedimentation rate; PJI = Periprosthetic joint infection; COPD = chronic obstructive pulmonary disease; HPF = high powered field; MRSA = Methicillin resistant S. aureus.

prophylactic antibiotics do not influence the results of intraoperative cultures and consequently should not be discontinued prior to surgery for an infected TKA, provided that the bacterium has been identified by preoperative aspiration and recent (4 weeks) antibiotic therapy has not been performed (10).

Stryker et al. had analyzed 70 patients (44 men, 26 women) (14). Their mean age was 72 years (range, 51-91 years), and the mean follow-up was 54 months (range, 12-176 months). Seventy-two procedures (69 patients) met the inclusion criteria. Of these, 20 (28%) further procedures were performed for the infection and were considered as management failures. The mean CRP was 173.7 mg/L in the successful group and 159 mg/L in the unsuccessful group ($P=0.31$). The mean ESR at the time of DAIR was 61.3 mm/h in both groups ($P=0.49$). The conclusion was that CRP and ESR are not valid for predicting DAIR outcomes in the treatment of LAHI after TKA (14).

Forty patients (42 joints: 22 TKA, 20 total hip arthroplasties) treated for LAHIs were reviewed by Konigsberg et al. in 2014 (17). All patients underwent DAIR. After a mean of 4.6 years, repetitive infection needing surgery appeared in 9 (21%) of 42 joints; 8 of the 9 repetitive infections were in individuals with staphylococcal infection ($P=0.0004$). Ten (25%) of the 40 individuals passed away within 24 months of infection. DAIR for the management of a LAHI was successful in the majority of patients (76% survival at 24 months). Nonstaphylococcal infections had a low failure percentage (96% 2-year survival) (17).

In 2015, Koh et al. had attempted to establish the success percentage of DAIR and whether this success percentage was influenced by the timing of DAIR or by the bacteria causing the infection (12). They analyzed 52 cases of DAIR for acute PJI that met the definition of PJI from the International Consensus Group on PJI. The overall success percentage of DAIR was 71%, and early postoperative infection and LAHI had a success percentage of 82% and 55%, apiece. The success percentage was associated with a shorter duration of symptoms in patients with LAHI ($P=0.040$). Nevertheless, success was not affected by the type ($P=0.992$) or virulence of the causative bacteria ($P=0.706$). DAIR should be considered a viable therapeutic alternative for acute PJI following TKA. The speed with which the DAIR is performed, rather than the type of causative bacterium or its virulence, is of crucial significance for therapeutic success (12).

In 2016, He et al. had investigated the results of 11 acute hematogenous TKA infections treated with DAIR (9). The mean age of the 11 patients was 56.3 years, with 2 men (18.2%) and 9 women (81.8%). The diagnosis at the primary surgical procedure was osteoarthritis in 3 patients, RA in 7, and osteoarthritis subsequent to fracture in one. Patients had acute pain and inflammation after a beforehand well-functioning TKA. Failure was defined as the following: (i) passing away prior to completion of antibiotic therapy; (ii) additional surgery required to treat the infection; and (iii) lifelong antibiotic therapy or chronic infection. The most common bacteria

were staphylococci and streptococci. The 2 cases of staph infection were *Staphylococcus epidermidis* (one) and *S. aureus* (one); The seven cases of *Streptococcus* infection were *Streptococcus agalactiae* (one), *Streptococcus β haemolyticus* (one), *Streptococcus pneumoniae* (three), *Streptococcus dysgalactiae* (one), viridans streptococci (one), and *Enterobacter cloacae* (one). After 2 years of follow-up, 9 TKAs had survived. The survival percentage for individuals with staphylococcal infection was 0%, whereas survival was 100% for individuals infected with nonstaphylococcal species. The duration of symptoms before the surgery and the type of bacteria influenced the result ($P=0.00$). Individuals with LAHI by nonstaphylococcal bacteria had satisfactory results after DAIR, but individuals infected with staphylococci had poor outcomes. To ameliorate the success percentage of DAIR, individuals should be managed as soon as possible according to the result of the bacterial culture (9).

In 2018, Bene et al. had attempted to determine whether survival without reoperation after DAIR in acute infected primary TKA is influenced by the duration of postoperative antibiotics; by the characteristics of the patient or surgical factors; by the causative bacteria; or whether the infection was acute postoperative or hematogenous (20). Of 1735 cases of revision TKA, 76 underwent DAIR, with an average follow-up of 3.5 years. Twenty-one individuals who needed reoperation due to infection were compared with fifty-five who did not need it. The augmented duration of postoperative antibiotic therapy diminished the need for reoperation due to infection. Atrial fibrillation, chronic obstructive pulmonary disease (COPD), the presence of more than 15 cells per high-powered field (HPF) or a higher preoperative CRP augmented the necessity for reoperation due to infection. The frequency of infection repetition was higher with methicillin-resistant *S. aureus* (MRSA) and lower with Gram-negative bacteria. There were no differences between acute and hematogenous postoperative infections in terms of survival without reoperation. The conclusions were that reoperation-free survival after DAIR in acute infected primary TKA ameliorates with increases in the duration of postoperative antibiotic therapy, so chronic suppression of antibiotics after DAIR should be considered; worsens with atrial fibrillation, COPD, >15 cells/HPF, preoperative CRP >500 mg/L or *S. aureus* MRSA, so for these patients, two-stage revision arthroplasty should be recommended; and is similar in acute postoperative infections and in LAHIs (20).

In 2019, Calanna et al. had described a modified surgical DAIR technique to improve the chances of retaining an infected TKA (21). This technique, debridement antibiotic pearls and retention of the implant (DAPRI), aims to eliminate the intra-articular biofilm, leading to a higher and more prolonged local antibiotic concentration due to the use of calcium sulphate beads. The combination of 3 surgical techniques (staining with methylene blue, argon beam electrical stimulation, and brushing with chlorhexidine gluconate) could improve the identification, interruption, and ultimately elimination

of the bacterial biofilm, which is primarily responsible for antibiotic resistance. The DAPRI technique could represent a safe treatment for early acute hematogenous PJI (21).

This narrative review of the literature shows that open DAIR liner exchange seems to be a useful treatment method for late acute hematogenous TKA infection when it is carried out within the first 5–14 days from the beginning of symptoms, in patients without another

accompanying infection and in those whose indication of TKA has not been rheumatoid arthritis.

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