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REVIEW ARTICLE

Therapeutic Efficacy and Clinical Advances in Debridement, Antibiotics, and Implant Retention for Acute Periprosthetic Joint Infection Following Total Knee Arthroplasty

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Abstract: Periprosthetic joint infection (PJI) is a primary cause of failure in total knee arthroplasty (TKA), requiring careful management techniques to preserve joint function and mitigate surgical morbidity. Debridement, Antibiotics, and Implant Retention (DAIR) serves as a critical, joint-preserving intervention for early postoperative and acute hematogenous infections. Clinical success with the DAIR protocol ranges between 41% and 92%, a variance heavily influenced by the timing of intervention, the virulence of causative pathogens, and the physiological status of the host. Optimal outcomes are typically achieved when surgical intervention occurs within a narrow window of 4 to 6 weeks following the onset of symptoms, particularly when combined with the exchange of modular components. Conversely, infections involving highly virulent strains such as Staphylococcus aureus or those occurring in elderly patients with significant systemic comorbidities often result in higher rates of treatment failure. The integration of modern diagnostic guidelines, such as the 2021 European Bone and Joint Infection Society (EBJIS) criteria, has refined the precision of diagnostic staging and therapeutic planning. While targeted antibiotic regimens specifically those utilizing rifampin for staphylococcal biofilms are essential components of the protocol, the ideal duration of therapy remains a subject of active investigation. Emerging surgical techniques, including the use of antibiotic pearls and specialized antiseptic irrigation solutions, show promise in enhancing biofilm eradication. Although chronic infections remain a relative contraindication, the application of DAIR in acute care offers superior functional recovery and patient satisfaction compared to more invasive multi-stage revision procedures.

Keywords: Periprosthetic Joint Infection; DAIR Technique; Total Knee Arthroplasty; Biofilm Management; Orthopedic Surgical Outcomes.

1. Introduction

The clinical demand for prosthetic knee implants has escalated globally, driven by an aging population and an increased emphasis on maintaining active lifestyles among older individuals [1]. While primary total knee arthroplasty (TKA) is recognized as a safe and highly effective procedure for restoring mobility and alleviating pain, the rising volume of surgeries has led to a proportional increase in the incidence of periprosthetic joint infections (PJI) [2]. Current data indicates that the incidence of PJI following primary TKA is approximately 1.08%, but this figure rises significantly to between 5.6% and 35.0% following revision surgeries [2, 3]. These infections represent a catastrophic complication, often resulting in prolonged hospitalization, multiple surgical interventions, and substantial economic burdens on healthcare systems.

The management of PJI is complicated by the formation of bacterial biofilms on the surface of the implant, which render pathogens highly resistant to both systemic antibiotic therapy and the host's immune response [1, 3]. Traditionally, the gold standard for treating established PJI has been a two-stage revision, involving implant removal, the placement of an antibiotic spacer, and subsequent reimplantation. However, this approach is associated with significant morbidity and functional decline. In response, Debridement, Antibiotics, and Implant Retention (DAIR) has gained prominence as a less invasive, joint-preserving alternative for early postoperative and acute hematogenous infections [4]. The success of DAIR is contingent upon a multitude of factors, including the timing of debridement, the antimicrobial susceptibility of the infecting organism, and the stability of the prosthetic components [5]. Recent advances in diagnostic criteria and surgical techniques continue to refine the application of DAIR, aiming to maximize success rates while minimizing the need for radical component removal.

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2. Diagnostic Criteria

The absence of a singular, universally accepted definition for PJI has historically impeded the comparison of clinical data and the standardization of treatment protocols [4, 6]. To address this, various organizations have developed diagnostic guidelines that rely on a combination of clinical, microbiological, and biochemical markers.

2.1. The EBJIS 2021 Consensus

The European Bone and Joint Infection Society (EBJIS) introduced a revised diagnostic definition in 2021, developed in collaboration with nuclear medicine and infectious disease specialists [7, 8]. This protocol is designed to be more sensitive than previous criteria, particularly in identifying low-grade or biofilm-mediated infections that might otherwise be overlooked. The EBJIS criteria utilize a three-tier system: "Infection Unlikely," "Infection Likely," and "Infection Confirmed" [8, 9]. This graded approach acknowledges the diagnostic uncertainty inherent in PJI management.

Table 1. EBJIS 2021 Diagnostic Criteria for Periprosthetic Joint Infection

Diagnostic Tier	Clinical & Laboratory Findings
Infection Confirmed	Presence of a sinus tract, gross intraoperative pus, or ≥ 2 positive cultures with the same organism.
Infection Likely	Synovial WBC > 3000/μL or PMN > 80\%; positive alpha-defensin test; single positive culture of a virulent organism.
Infection Unlikely	Synovial WBC < 1500/μL and PMN < 65\%; negative cultures; CRP < 10 mg/L without clinical suspicion.

Confirmed infection is defined by the presence of a sinus tract, gross intraoperative pus, or positive histopathology [10]. In the absence of these definitive signs, the diagnosis relies on synovial fluid analysis, including white blood cell (WBC) counts and polymorphonuclear (PMN) percentages, as well as advanced microbiological techniques like implant sonication [11]. The criteria emphasize that no single test possesses perfect accuracy, advocating for a holistic interpretation of serum markers such as C-reactive protein (CRP) and D-dimer alongside synovial biomarkers like alpha-defensin [12].

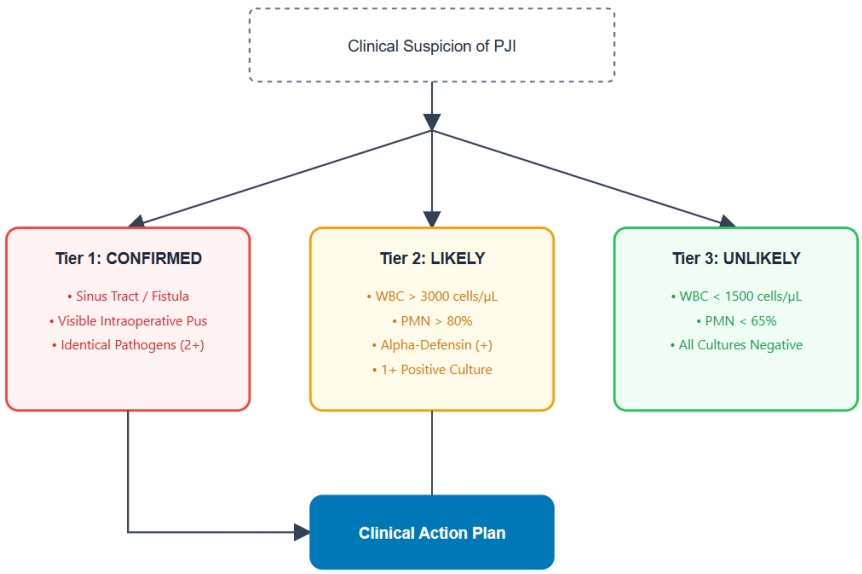

Figure 1. The EBJIS 2021 Three-Tier Diagnostic Pathway

2.2. Role of Advanced Diagnostics

Modern diagnostic protocols have moved beyond simple culture techniques. Prolonged incubation of periprosthetic tissue samples often up to 14 days is now recommended to capture slow-growing organisms [13]. The application of metagenomic next-generation sequencing (mNGS) and sonication of the explanted components has improved the detection of pathogens in culture-negative cases

[14]. These tools are particularly relevant when contemplating a DAIR procedure, as identifying the pathogen and its resistance profile is fundamental to selecting appropriate postoperative antibiotic therapy.

3. Classification of Infection

Classification systems for PJI are primarily based on the temporal relationship between the index surgery and the onset of symptoms, which serves as a surrogate for the maturity of the bacterial biofilm.

3.1. Temporal Classification Systems

The Coventry system remains a foundational guideline, categorizing infections into early (within 30 days of surgery), intermediate (1 to 24 months), and late (beyond 24 months) [1, 14]. This system helps surgeons decide between DAIR and revision, as early infections are generally more amenable to implant retention. In contrast, the International Consensus Meeting (ICM) criteria utilize a 90-day threshold to distinguish between early and late infections, reflecting a different perspective on the window of opportunity for effective debridement [15].

Table 2. Comparison of PJI Classification Systems

Classification System	Categories	Timing/Criteria
Coventry	Early / Intermediate / Late	< 1 month / 1–24 months / > 24 months
ICM (2018)	Early / Late	< 90 days / > 90 days
Tsukayama	Early Postoperative	Within 4 weeks of index surgery
	Acute Hematogenous	< 4 weeks symptoms, previously stable joint
	Chronic	> 4 weeks symptoms or late presentation

3.2. Clinical Presentation Systems

The Tsukayama classification offers a more nuanced approach by considering the mechanism of infection alongside the timing [14]. It identifies four distinct categories: early postoperative infections (occurring within one month), acute hematogenous infections (characterized by a sudden onset of symptoms in a previously well-functioning joint), chronic infections (symptoms persisting for more than one month), and positive intraoperative cultures (where infection is discovered incidentally during revision for presumed aseptic loosening) [16, 17]. This classification is particularly useful for DAIR indications, as both early postoperative and acute hematogenous cases are the primary candidates for this joint-preserving technique. Other systems, such as the Auckland classification, use a one-year cutoff, further illustrating the lack of global consensus on the precise timing that defines "early" infection [14, 15].

4. Clinical Indications for the DAIR Procedure

The selection of candidates for Debridement, Antibiotics, and Implant Retention (DAIR) requires a meticulous assessment of the infection's chronicity and the host's physiological resilience. Since its recognition by the International Consensus on Periprosthetic Joint Infection in 2013, DAIR has been established as a frontline intervention for specific subsets of PJI [18].

4.1. Acute Postoperative and Hematogenous Infections

The primary indication for DAIR is early postoperative infection, typically occurring within four weeks of the index arthroplasty [10, 19]. During this initial phase, bacterial biofilms are relatively immature and lack the complex extracellular matrix that characterizes chronic infections, making them more susceptible to surgical irrigation and systemic antimicrobial agents [20]. DAIR is indicated for acute hematogenous infections, where a previously stable and asymptomatic joint becomes infected via the bloodstream from a distant source [21, 22]. In these cases, the criteria for retention include a stable prosthesis, the absence of radiographic evidence of loosening, and a healthy soft tissue envelope [23, 24].

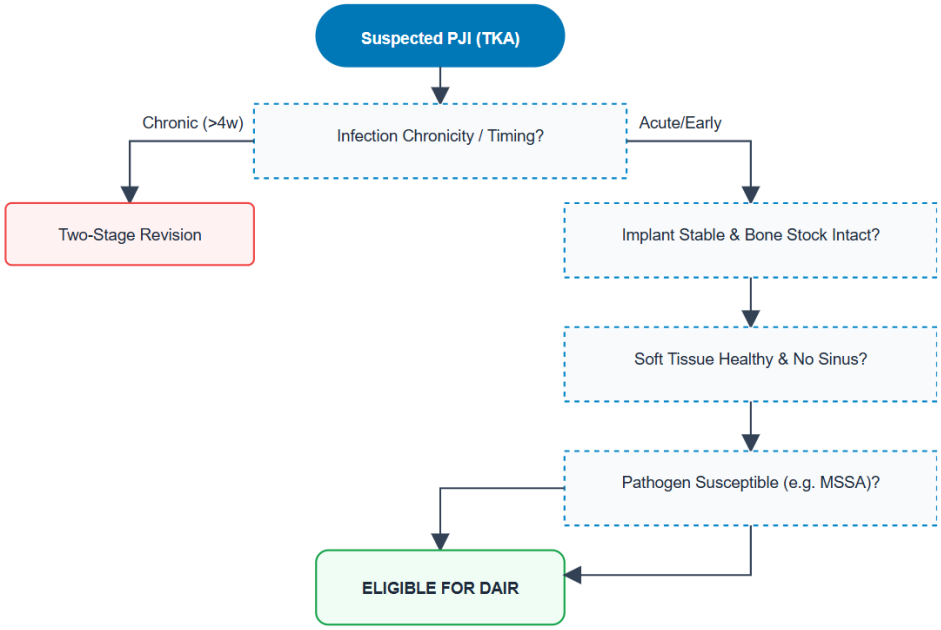

Figure 2. Clinical Decision Flow for DAIR Eligibility

4.2. Constraints in Chronic Presentations

The application of DAIR in chronic PJI defined by symptoms persisting beyond the acute window is generally associated with high failure rates [14, 15]. When a biofilm has matured on the implant surface, mechanical debridement alone is often insufficient for total eradication. In such scenarios, radical component removal through staged revision remains the standard of care to ensure the complete elimination of the infectious nidus [14, 16].

5. Prognostic Determinants of Therapeutic Success

Identifying the factors that influence the outcome of DAIR is essential for surgical decision-making and patient counseling. Success rates are highly variable, necessitating a multifactorial analysis of clinical variables [15, 25].

5.1. Temporal and Surgical Factors

The interval between the onset of symptoms and the surgical intervention is perhaps the most critical determinant of success. Interventions performed within a 4-to-6-week window postoperatively or within days of acute hematogenous symptoms demonstrate significantly higher retention rates [26]. Beyond timing, the thoroughness of the surgical debridement is paramount. The exchange of modular components, such as polyethylene liners and modular heads, is strongly advocated [27]. This practice allows for a more comprehensive irrigation of the posterior joint space and removes the biofilm that inevitably colonizes the undersurface of modular elements [28]. The involvement of fellowship-trained arthroplasty surgeons has been linked to improved outcomes, likely due to more meticulous tissue handling and radical debridement techniques [29].

Table 3. Prognostic Determinants for DAIR Outcome

Favorable Prognostic Factors	Unfavorable Prognostic Factors
Surgical intervention < 4 weeks post-op	Symptoms persisting > 3 weeks before DAIR
Exchange of modular components	Presence of sinus tract or skin fistula
Low-virulence pathogens (e.g., *Streptococci*)	Highly virulent strains (MRSA, Poly-microbial)
High synovial fluid glucose levels	Elevated CRP (> 150 mg/L)
Stable implant (no radiographic loosening)	Systemic host frailty (ASA Class III/IV)

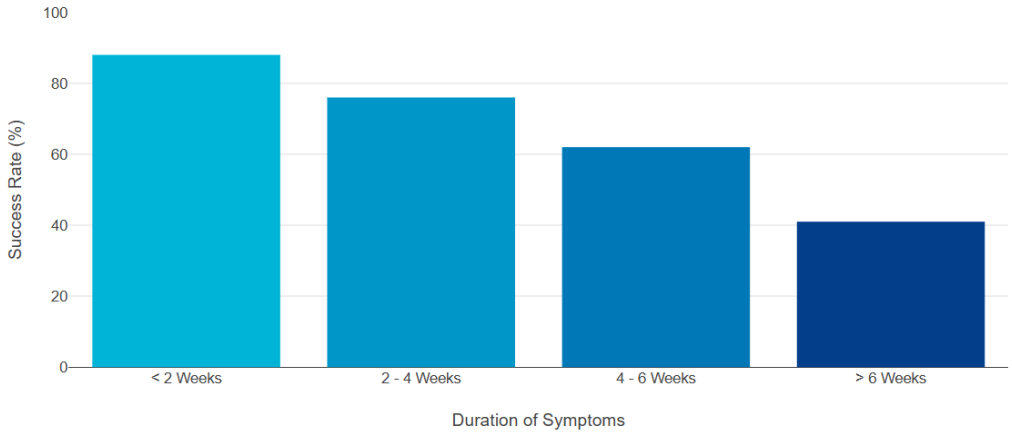

Figure 3. Impact of surgical timing on clinical success

5.2. Host-Related and Pathogen-Specific Variables

The physiological status of the patient plays a significant role in the body's ability to clear an infection. Younger patients with fewer systemic comorbidities, such as controlled diabetes and healthy renal function, typically experience better outcomes [9, 29]. Conversely, advanced age (specifically over 80 years), malnutrition, and systemic conditions like liver cirrhosis, rheumatoid arthritis, or chronic obstructive pulmonary disease (COPD) are associated with an increased risk of DAIR failure [30, 31].

The virulence and resistance profile of the causative pathogen are equally influential. Infections involving Staphylococcus aureus, particularly methicillin-resistant strains (MRSA), are notoriously difficult to treat with implant retention due to their aggressive biofilm production [32, 33]. Conversely, infections caused by less virulent organisms, such as certain streptococcal species, often yield higher success rates with the DAIR protocol [34].

5.3. Predictive Scoring Systems

To assist in risk stratification, scoring systems like the KLIC score (Kidney, Liver, Index surgery, Cloacae, CRP) have been developed. These tools integrate patient health markers and local infection characteristics to provide a quantifiable probability of success [35]. Additionally, local biomarkers, such as low synovial fluid glucose levels, have emerged as predictive indicators for the failure of the DAIR procedure [36].

Table 4. KLIC Score for Predicting DAIR Failure

Component	Definition	Points
Kidney	Chronic Kidney Disease	+2
Liver	Liver Cirrhosis	+1.5
Index Surgery	Revision Surgery (vs. Primary)	+1.5
Cloacae	Infection with *Enterobacter* species	+1
CRP	Serum CRP > 115 mg/L	+2
Total Score	**Probability of Failure**	
0–2 Points	~15–20% failure risk	
> 7 Points	~90–100% failure risk	

6. Antimicrobial Management

Pharmacotherapy is a cornerstone of the DAIR protocol, acting in synergy with surgical debridement to eliminate residual pathogens and prevent the maturation of remaining biofilms.

6.1. Antibiotic Selection and Biofilm Eradication

Once intraoperative cultures identify the pathogen, targeted antimicrobial therapy is initiated. For staphylococcal infections, the inclusion of rifampin is considered essential due to its unique ability to penetrate bacterial biofilms [37]. Evidence suggests that

combining rifampin with a fluoroquinolone significantly enhances treatment efficacy compared to monotherapy or combinations with other antibiotic classes [38]. This synergy is particularly effective in knee infections, where it has been shown to improve long-term retention rates [39].

Table 4. Common Antibiotic Regimens in DAIR Management

Pathogen	Initial IV Therapy (2–6 weeks)	Oral Step-down (3–6 months)
Staph. aureus (MSSA)	Cefazolin or Flucloxacillin	Rifampin + Levofloxacin
Staph. aureus (MRSA)	Vancomycin or Daptomycin	Rifampin + Linezolid or Cotrimoxazole
Streptococcus spp.	Penicillin G or Ceftriaxone	Amoxicillin or Clindamycin
Gram-Negative Bacilli	Ciprofloxacin or Ceftazidime	Ciprofloxacin or Levofloxacin

6.2. Duration and Delivery of Therapy

The traditional regimen involves 2 to 6 weeks of intravenous (IV) pathogen-specific therapy followed by a transition to oral antibiotics [40]. However, the total duration of therapy remains a point of debate. Some studies suggest that extending the course of oral antibiotics up to one year can reduce the incidence of late failure, particularly in high-risk patients [40, 41]. Conversely, other research indicates that a standard 6-to-12-week course may be sufficient for lower-risk cases, as the benefits of long-term suppressive antibiotic therapy (SAT) must be balanced against the risks of drug toxicity and the development of antimicrobial resistance [42, 43]. The decision to continue or discontinue SAT often depends on the stability of inflammatory markers and the clinical appearance of the joint during follow-up [44].

7. Surgical Refinements and Technical Advancements

As the limitations of standard DAIR become better understood, surgical modifications have been introduced to enhance the mechanical and chemical eradication of biofilms from prosthetic surfaces.

7.1. The DAPRI Technique

In 2019, the Debridement, Antibiotic Pearls, and Retention of the Implant (DAPRI) technique was proposed as a sophisticated modification of the traditional DAIR protocol [45]. This approach involves a more aggressive surgical debridement of all accessible intra-articular surfaces, followed by the application of calcium sulfate antibiotic-impregnated beads (pearls) directly into the joint space [46, 47]. The localized, high-concentration release of antibiotics from these pearls aims to eliminate residual planktonic bacteria and prevent the recolonization of the implant surface. Preliminary evidence suggests that DAPRI may provide a higher success rate in early acute infections compared to standard debridement, offering a potentially more robust joint-preserving strategy [48].

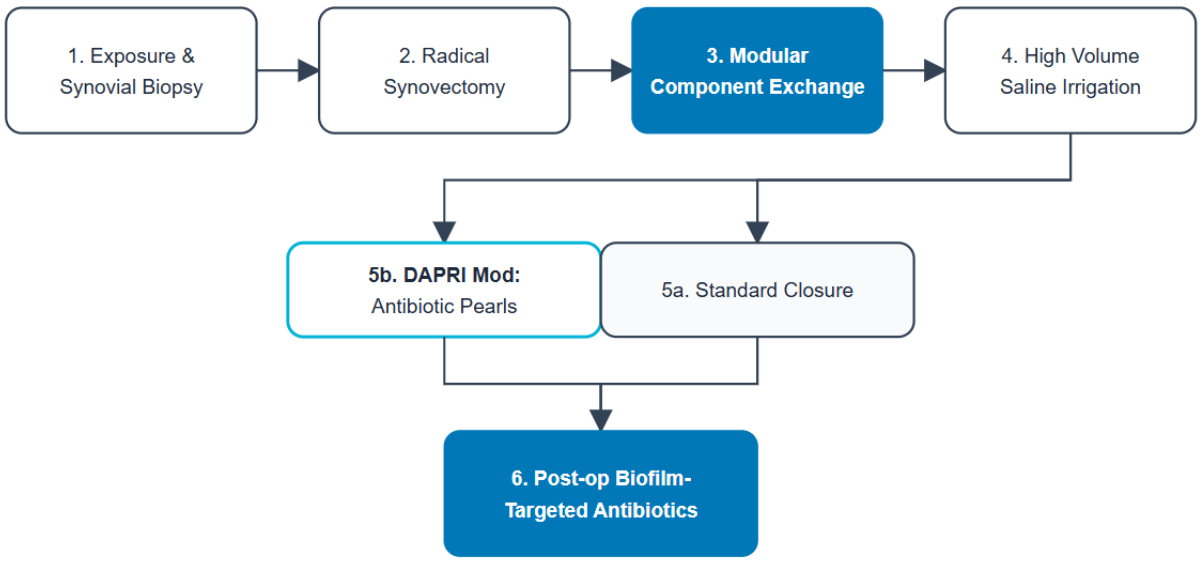

Figure 4. The DAIR vs. DAPRI Surgical Flow

7.2. Antiseptic Irrigation and Novel Solutions

The choice of irrigation solution is another area of active clinical investigation. Beyond standard saline irrigation, the use of dilute povidone-iodine and specialized antiseptic washes, such as acetic acid or commercially formulated surfactants, has been explored for their ability to disrupt the biofilm matrix [46, 47]. Recent studies indicate that these novel solutions may significantly lower the bacterial load intraoperatively, though standardized protocols for their application are still being refined through randomized controlled trials [48].

8. Clinical Implications of Treatment Failure

A critical concern for surgeons is whether a failed DAIR procedure negatively impacts the success rate of subsequent salvage operations, such as a two-stage revision.

8.1. Impact on Subsequent Revisions

The consensus on this issue remains divided. Some retrospective analyses suggest that a failed attempt at implant retention can compromise the soft tissue envelope and lead to poorer outcomes during a later two-stage reimplantation [49]. This "failed DAIR" cohort may face higher rates of persistent infection compared to patients who undergo a two-stage revision as their primary intervention. However, other longitudinal studies have found no statistically significant difference in infection eradication rates for subsequent revisions after a failed DAIR, suggesting that the initial attempt at retention does not necessarily preclude a successful outcome if the failure is recognized and managed promptly [50].

8.2. Economic and Biological Costs

While DAIR is initially less invasive and more cost-effective than component replacement, the cumulative economic burden of a failed procedure followed by a two-stage revision can be substantial. Surgeons must therefore weigh the potential benefits of joint preservation against the biological "cost" of additional surgeries and prolonged antibiotic exposure [51].

9. Functional Outcomes and Patient-Reported Metrics

Beyond the primary goal of infection eradication, the success of any PJI treatment is measured by the patient's eventual quality of life and joint function.

9.1. Mobility and Satisfaction

A successful DAIR procedure offers significant advantages in terms of functional recovery. Patients typically achieve quicker rehabilitation and better range of motion compared to those undergoing revision surgery by preserving the original prosthetic joint and avoiding the extensive bone loss associated with component removal [52, 53]. Comparative studies have shown that patients managed with modified DAIR or DAPRI report higher satisfaction scores and improved knee flexion compared to the two-stage revision cohorts [54].

9.2. Quality of Life Post-Infection

Successful implant retention allows patients to return to their baseline activities of daily living more rapidly. The psychological benefit of avoiding a "staged" process which often involves months of limited mobility while a spacer is in place cannot be overstated. However, these superior functional outcomes are strictly contingent upon the complete eradication of the infection; a persistent, low-grade infection following a "successful" DAIR can lead to chronic pain and long-term dissatisfaction [55].

10. Conclusion

The management of periprosthetic joint infection following total knee arthroplasty has evolved significantly with the refinement of the DAIR technique. Current evidence supports the use of DAIR as a primary intervention for acute postoperative and hematogenous infections, provided that patients are carefully selected based on the timing of symptoms, pathogen virulence, and host comorbidities. The integration of modern diagnostic criteria, such as the EBJIS 2021 guidelines, and the utilization of predictive tools like the KLIC score are essential for optimizing patient selection and predicting therapeutic success. While surgical advancements like the DAPRI method and targeted antibiotic regimens involving rifampin-fluoroquinolone combinations show

great promise in enhancing biofilm management, the variability in success rates underscores the need for standardized global guidelines. When executed correctly within the appropriate clinical window, DAIR not only eliminates infection but also preserves joint integrity and improves the overall quality of life for the patient.

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