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2022 American Association of Hip and Knee Surgeons Symposium: Periprosthetic Joint Infection

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ABSTRACT

Periprosthetic joint infection (PJI) is the leading cause of failure in patients undergoing total joint arthroplasty. This article is a brief summary of a symposium on PJI that was presented at the annual AAHKS meeting. It will provide an overview of current technqiues in the prevention, diagnosis, and management of PJI. It will also highlight emerging technologies in this setting.

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Periprosthetic joint infection (PJI) is one of the leading causes of failure following primary and revision total joint arthroplasty (TJA) [1]. Furthermore, as the number of TJA procedures performed annually is expected to increase over the next few years, so will the rate of subsequent PJI [2]. Concurrently, the per annum cost of PJI is at an all-time high and will reach $1.85 billion by 2030 [3].

Despite efforts to the contrary, PJI continues to cause major morbidity and mortality following TJA [4]. Notwithstanding, a number of recent developments have helped standardize how the orthopaedic community approaches this complex disease process. The availability of practical and effective methods for the prevention of PJI has increased substantially in the last decade [5]. Also, the introduction of several criteria for the identification of PJI has tremendously improved diagnostic confidence in this setting [6,7]. In addition, the implementation of evidence-based treatment algorithms and risk calculators has resulted in treatment individualization and the selection of more appropriate management options for patients who have PJI [8].

This article will review current techniques employed in the prevention, diagnosis, and management of PJI. In addition to this, it will also highlight emerging technologies in this setting.

Prevention

Preoperative

A number of modifiable host risk factors such as diabetes, malnutrition, obesity, and smoking have all been shown to increase

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the risk of infection in patients undergoing TJA [9]. In particular, hyperglycemia at the time of admission is increasingly common in this patient population [10,11]. Although HbA1c remains the "gold standard" test for identifying patients who have poor glycemic control, a recent multicenter study found that fructosamine, a glucose intermediate, outperformed HbA1c at predicting 90-day outcomes [12–14]. In addition to this, it is well-established that obesity increases the risk for postoperative medical and surgical complications [15]. However, there have been data to suggest that the implementation of a body mass index threshold may not be effective at reducing acute PJI rates [16].

Intraoperative

Administration of perioperative antibiotic prophylaxis prior to skin incision has become part of the standard-of-care [17]. Due to a growing body of evidence, the use of first or second generation cephalosporins as the primary mode of antibiotic prophylaxis in this setting is increasingly popular [18]. In addition to this, concerns over cross reactivity between penicillin and cephalosporins in patients who have self-reported penicillin allergies have now been largely dispelled [19,20]. Notwithstanding, additional antibiotic coverage may be warranted in certain high-risk patients. Of note, the administration of dual antibiotic coverage, consisting of a cephalosporin and vancomycin, has become common practice in patients deemed at an increased risk of developing methicillin-resistant *Staphylococcus aureus* infection [21]. Another important method of PJI prevention is the chemical and mechanical debridement of soft tissues at regular intervals throughout the procedure [22]. While the ideal choice of an antiseptic agent remains up to individual surgeon preference, a growing body of evidence on the efficacy of povidone-iodine irrigation solution has resulted in its use at the majority of institutions [23].

Postoperative

Proper wound closure with subarticular sutures and silver-impregnated occlusive dressing has been shown to be effective at reducing rates of superficial infections and postoperative drainage [24,25]. In addition to this, the administration of more potent anticoagulation agents, such as warfarin, can result in major wound drainage and increase the risk of surgical site infection [26]. More recently, there has been extensive data showing that less aggressive anticoagulation agents, such as aspirin, may be appropriate for venous thromboembolism prevention in patients undergoing TJA [27,28].

Diagnosis

Stepwise Algorithmic Approach

Serological Markers

Serological markers such as c-reactive protein (CRP) and erythrocyte sedimentation rate have been universally adopted as the first-line screening tests to help rule out PJI in patients presenting with a painful prosthesis (Fig. 1) [9]. Notwithstanding, several studies have shown that CRP and erythrocyte sedimentation rate are poorly specific and often miss PJI caused by "low-virulence" organisms [29]. More recently, there have been data to support the use of D-dimer for the screening of patients with suspected PJI [30].

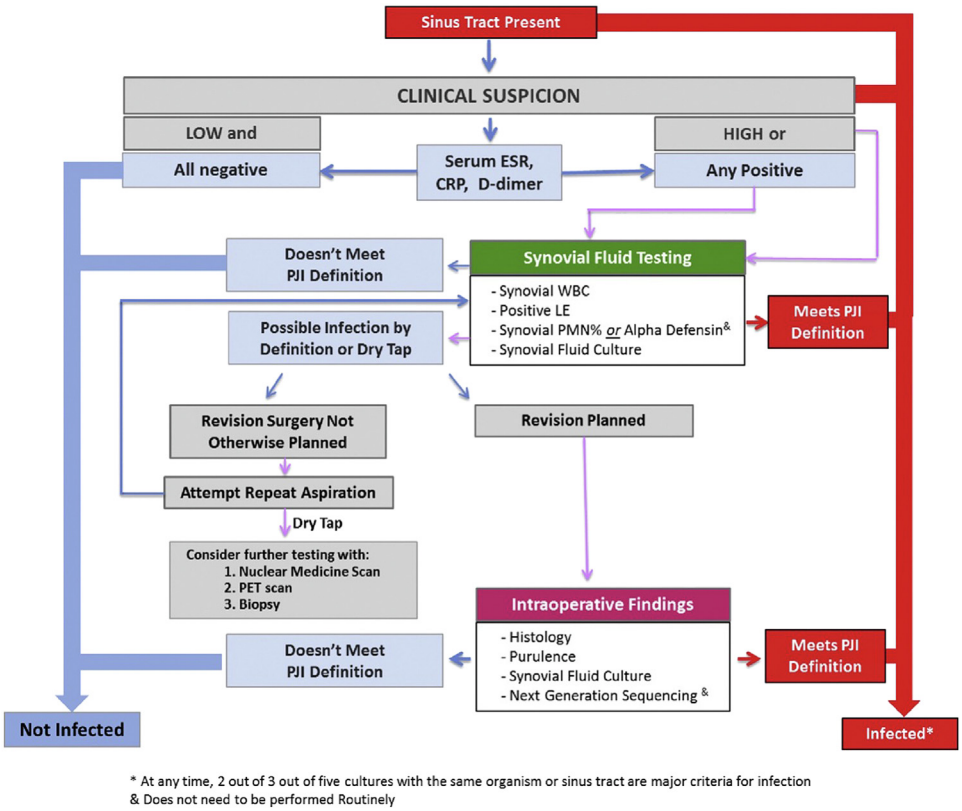

Fig. 1. Stepwise algorithmic approach reproduced with permission from Shohat N, Tan TL, Della Valle CJ, Calkins TE, George J, Higuera C, Parvizi J. Development and Validation of an Evidence-Based Algorithm for Diagnosing Periprosthetic Joint Infection. J Arthroplasty. 2019 Nov; 34(11):2730-2736.e1.

Synovial Markers

The next step in the workup of patients who have suspected PJI is aspiration of the affected joint and subsequent analysis of synovial fluid biomarkers [31]. Based on data spanning several years, it is now evident that conventional synovial fluid markers, such as white blood cell count and polymorphonuclear leukocyte percentage, have excellent utility in the diagnosis of PJI [32,33]. Another synovial marker that has garnered interest in this setting is the alpha defensin [34]. Despite initial reports of its superior accuracy, recent studies have demonstrated that alpha defensin has comparable diagnostic utility to conventional synovial fluid markers such as white blood cell count and polymorphonuclear leukocyte percentage [35,36].

Pathogen Identification

Even with the advent of more sophisticated techniques, traditional culture remains the "gold standard" for pathogen identification in patients with PJI [37]. Notwithstanding, the incidence of culture negative PJI is on the rise [38]. Current clinical practice guidelines recommend that at least 3-5 intraoperative samples be taken in order to maximize the chances of culture isolating a pathogen [39]. More recently, molecular techniques, such as polymerase chain reaction and next generation sequencing, have garnered interest in this setting [40–42]. In a recent study, next generation sequencing was capable of identifying at least one or more organism(s) in 65.9% of culture negative PJI patients [43].

Diagnostic Criteria

In 2018, the International Consensus Meeting (ICM) on musculoskeletal infection introduced the first evidence based and validated definition of PJI [7]. Using random forest analyses, the diagnostic utility of different serological and synovial markers were assessed. Subsequently, each variable was assigned a score and weight based on its performance (Fig. 2). After application of the criteria, patients are placed into one of 3 groups based on their ICM scores: (1) infected (≥6); (2) inconclusive (4-5); or (3) aseptic (0-3). Of note, the 2018 ICM criteria have been shown to have a sensitivity of 97.7% and specificity of 99.5% for the diagnosis of PJI [7].

Management

Acute PJI

Debridement, antibiotics, and implant retention (DAIR) is a popular treatment option for patients presenting with acute PJI [44]. However, it is important to note that several factors have been shown to influence the success of a DAIR procedure. In a recent study, elevated serum CRP levels, presence of positive blood cultures, older age, and PJI due to methicillin-resistant *Staphylococcus aureus* were all found to be associated with higher rates of failure following a DAIR procedure [8]. Furthermore, there have been data to suggest that there is no role for subsequent irrigation and debridement in patients that fail an initial DAIR procedure [45].

Chronic PJI

Two-stage exchange arthroplasty remains the "gold standard" for the treatment of chronic PJI in North America [46]. Notwithstanding, the use of one-stage exchange arthroplasty has increased substantially in recent years following several promising reports [47]. However, it is important to note that there are downsides to both of the aforementioned surgical techniques. To date, we are yet to identify a single marker that can help determine infection control and optimal timing of reimplantation [48]. As a result, the

Major criteria (at least one of the following)	Decision
Two positive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

Preoperative Diagnosis		Minor Criteria	Score	Decision
	Serum	Elevated CRP *or* D-Dimer	2	≥ 6 infected
		Elevated ESR	1	
	Synovial	Elevated Synovial *WBC or LE* (++)	3	2-5 possibly infected*
		Positive Alpha-defensin	3	
		Elevated Synovial PMN %	2	0-1 Not infected
		Elevated Synovial CRP	1	

Preoperative Diagnosis	*Inconclusive pre-op score *or* dry tap	Score	Decision
	Preoperative score	-	≥ 6 infected
	Positive Histology	3	4-5 Inconclusive**
	Positive Purulence	3	
	Positive Single Culture	2	≤ 3 Not infected

* For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI.
**Consider further molecular diagnostics such as Next-generation sequencing

Fig. 2. 2018 International Consensus Meeting criteria reproduced with permission from Shohat N, Tan TL, Della Valle CJ, Calkins TE, George J, Higuera C, Parvizi J. Development and Validation of an Evidence-Based Algorithm for Diagnosing Periprosthetic Joint Infection. J Arthroplasty. 2019 Nov; 34(11):2730-2736.e1.

decision whether to proceed with reimplantation relies on a number of factors and can be difficult to make [49]. On the other hand, the success of a one-stage exchange procedure is dependent on a number of host and pathogen-related factors. For example, patients who have increased comorbidities and those who have PJI due to resistant organisms are not suitable for a one-stage exchange arthroplasty and may benefit more from an extended course of therapy [50].

Emerging Technologies

Prevention

Recently, there have been data to suggest that drug-eluting implants may play a role in the future of PJI prevention. Of note, a recent study demonstrated that the use of antibiotic-eluting polyethylene materials in a rabbit model resulted in absolute eradication of infection caused by *Staphylococcus aureus* [51]. In addition to this, silver-coated hip implants have garnered interest in this setting following several promising reports in the literature. In contrast to antimicrobial therapy, silver possesses several mechanisms of action against bacteria and is therefore less likely to be susceptible to conventional methods of antibiotic resistance [52].

Diagnosis

Over the years, advancements in technology have resulted in the identification of several novel biomarkers for the diagnosis of PJI [53]. In a recent study, a point of care synovial calprotectin test demonstrated near perfect accuracy in the diagnosis of PJI [54]. Furthermore, the widespread availability of genomic testing has resulted in an increased utilization of techniques such as shotgun metagenomics [55–57]. Notwithstanding, it is important to note that there remain valid concerns over the specificity of this technology.

Treatment

To our knowledge, there are no accurate metrics to determine infection eradication in patients who have PJI [48]. In addition to this, PJI has been shown to induce an immunosuppressive state through a mechanism that remains unknown [58]. In one study, the authors found that overexpression of programmed cell death receptor, a protein that downregulates the immune system, is common in infected tissues and may be a risk factor for failure in this patient population [59]. Furthermore, there have been data to suggest that monoclonal antibodies, cationic peptides, bacteriophage therapy, and lysins are all effective at eradicating infection and may allow for greater individualization of PJI management plans in the near future [60–63].

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