Review Article

Periprosthetic Joint Infection: The Unending Journey

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Abstract

Periprosthetic joint infection (PJI) is one disaster too many and will remain a never-ending topic as long as joints are replaced all over the world. The objective was to review current literatures on the pathology, management and prevention of PJI. This is a descriptive review of the current literatures on the definition, epidemiology, risk factors, pathology, classification, diagnosis, treatment and prevention of PJI. PJI is one of the most common causes of revision arthroplasty with increasing incidence. The risk factors are patient, staff and environmental mediated, and they are grouped into modifiable and non-modifiable risk factors. The modifiable risk factors are controllable. In general, PJI can be early or late, and this provides a guide to treatment. Arriving at a diagnosis can be clinical, laboratory, radiological or a combination, with newer trends geared towards identifying the exact organism causing the infection. Preventing PJI is the goal of every arthroplasty surgeon. The diagnosis of PJI remains a problem, and the optimal method of treatment is a subject of debate. Therefore, preventive measures should be topmost on every surgeon's mind.

Keywords: Aetiopathogenesis, epidemiology, management, periprosthetic joint infection, prevention, review

Introduction

Periprosthetic joint infection (PJI) is said to be the most common reason for revision joint surgery. It is a devastating situation to the patient as well as the surgeon. With increasing life expectancy and quality of life of people outside our nation and increasing awareness of arthroplasty in our society, there is likely to be an increase in PJI as more cases are being done. Creating constant awareness of this pathology as well as dwelling on the prevention and management is needful to keep arthroplasty surgeons on their toes in a bid to reduce the incidence of PJI worldwide. With the poverty rate of our country being high and patients having to pay out of pocket for arthroplasty surgeries, it is imperative that measures to prevent this condition be highly publicised and ensured to avoid PJI as much as possible. This is because most patients may not be able to afford the cost implications for a revision surgery and more importantly the presence of psychological and emotional stress that comes with PJI for patients and surgeons. This article reviews the current literatures on the pathology, management and prevention of PJI.

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Definition

Over the past years, various definition criteria for PJI have been described by several organisations and societies. At the International Consensus Meeting (ICM) in 2013,[1] the definition of PJI was proposed as:

Major

- Two positive periprosthetic cultures with phenotypically identical organisms
- Sinus tract communicating with the joint, or
- Having three of the following minor criteria.

Minor

- Raised serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)

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- Elevated synovial fluid white blood cell count or ++ change leucocyte esterase (LE) test strip
- Elevated synovial fluid polymorphonuclear neutrophil (PMN) percentage
- Positive histological analysis of periprosthetic tissue
- A single positive culture.

The International Consensus definition of PJI is a modification of the Musculoskeletal Infection Society's (MSIS) definition of PJI.[2] The proposed diagnostic criteria by the 2018 ICM for PJI[3] have at least one of the following major criteria to be classified as infected:

- Two positive growths of the same organism using standard culture methods
- Sinus tract with evidence of communication to the joint or visualisation of the prosthesis.

It then has the following in Table 1 as minor criteria with total score reflected under decision, nevertheless a combined pre-operative and intraoperative score ≥6 is classified as infected, scores 4–5 as inconclusive and scores 3 or less as not infected.

Epidemiology

PJI is a devastating complication of joint arthroplasty, with an average 1-year incidence of 0.25%–1.0% for primary total hip replacement (THR) and 0.4%–2% for primary total knee replacement (TKR).[4] The incidence rate of infection in revision surgery is even higher, with an estimated rate of 3.2%–5.6% for both hips and knees.[4,5] Moreover, infection accounts for up to 12% of the indications for revision hip arthroplasty and 22% for revision knee arthroplasty.[6] The overall infection burden is projected to rise by 4% between 2005 and 2030 for both primary and revision hip and knee arthroplasties.[6-8]

Aetiologic/Risk factors

The causes of PJI can be single or multifactorial and can be acquired pre-operatively, intraoperatively and post-operatively. Many of the risk factors are modifiable, while some are non-modifiable, reflecting an opportunity for the surgeon to optimise the patient pre-operatively with meticulous care to reduce the risk of PJI. Risk factors for PJI can be divided into patient factor, environmental factor, surgeon factor and perioperative personnel factor.

Patient factors

Patient factors include obesity, immunosuppression, steroid ingestion, intra-articular steroid injections, protein deficiency, malnutrition, chronic diseases, diabetes mellitus, prior joint infection, remote sites of infection, prior joint surgery and invasive techniques post-arthroplasty without antibiotic coverage.

Environmental factors

Environmental factors will include the type of theatre and location; poor theatre condition such as operating room temperature particularly in tropical regions/poor resource settings where power supply is an issue and increased number of personnel in theatre as well as constant traffic in and out of theatre.

Surgeon factors

Surgeon factors include prolonged duration of surgery, breach in asepsis, poor surgical technique, allogenic blood transfusion, indiscriminate use of diathermy and prolonged tourniquet time. Too much talking in theatre particularly by the operating team can release droplets into the wound site if not properly masked or hooded.

Perioperative personnel factors

With respect to perioperative personnel factors, keeping the instruments open and exposed for a prolonged period of time can lead to contamination or colonisation by organisms; in resource-poor centres where power tools are limited, unwrapping a power tool to exchange batteries when dead or in a bid to use on another power tool and rewrapping with a sterile material can be a source of contamination.

Table 1: Minor criteria scored for definition of PJI

Preoperative diagnosis	Threshold		Score	Decision
	Acute	Chronic		
Serum CRP (mg/L)	100	1	2	
D-dimer (µg/L)	Unknown	860	2	
Elevated serum ESR (mm/hr)	No role	30	1	
Elevated synovial CRP (mg/L)	>6.9		1	
Elevated synovial WBC (cells/µL)	10,000	3,000	3	≥6 Infected
Leukocyte esterase	++	++	3	2 - 5 Possibly infected
Positive Alpha defensin (signal/cutoff >)	1.0	1.0	3	0-1 Not infected
Elevated synovial PMN(%)	90	70	2	
Intraoperative diagnosis				
Single positive culture			2	≥6 Infected
Positive histology			3	4-5 Inconclusive
Positive purulence*			3	≤3 Not infected

*No role in suspected adverse local tissue reaction. ++ refers to positive

Significant risk factors

The international consensus panel on PJIs underlined the following as significant risk factors for the development of PJI: active infection of the arthritic joint (septic arthritis), presence of septicaemia and/or presence of local cutaneous or deep tissue infection. These are absolute contraindications to undertaking total joint arthroplasty.[1,9,10]

Potential risk factors

Potential risk factors for the development of PJI as enumerated by the consensus committee are: history of previous surgery, poorly controlled diabetes mellitus (glucose >200 mg/dl or glycated haemoglobin >7%), malnutrition, morbid obesity (body mass index >40 kg/m^2), active liver disease, chronic renal disease, excessive smoking (>one pack per day), excessive alcohol consumption (>40 units per week), intravenous (IV) drug abuse, recent hospitalisation, extended stay in rehabilitation facility, male gender, diagnosis of post-traumatic arthritis, inflammatory arthropathy, prior surgical procedure in the affected joint and severe immunodeficiency.

Limited evidence suggests that intra-articular injection performed prior to total joint arthroplasty may have a time-dependent association for increased risk of PJI. The 2018 ICM panel has a table on modifiable and non-modifiable host risk factors for PJI[3] where non-modifiable risk factors include increasing age, male gender and low socioeconomic status, increasing the risk of PJI.

Pathogenesis

Microbiology

Gram-positive cocci, particularly *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS), are involved in the majority of hip and knee PJIs and contribute between 50% and 60% of the infection, whereas streptococci and enterococci together account for only 10% of cases. Aerobic Gram-negative bacilli are involved in <10% of cases of knee and hip PJI.[10,11]

S. aureus and aerobic Gram-negative bacilli together contributed more than 60% of early onset PJIs. In contrast, delayed-onset PJIs (3 months–2 years after implantation) typically involve inoculation with less virulent organisms such as CoNS and enterococci. Among the CoNS, the most frequently isolated is *Staphylococcus epidermidis,* while the real isolation rate of the other coagulase-negative species varies widely, mainly due to technical difficulties in discriminating one species from another with laboratory tests.[11,12]

Enterococci are involved in about 3%–15% of PJIs, where they are often part of early polymicrobial infections in association prevalently with staphylococci followed by *Escherichia coli* and *Pseudomonas aeruginosa*.[13]

Streptococci are the causative agents of about 10% of PJI, with most of them at delayed or late onset. A wide variety of streptococci have been identified, with Lancefield group A, B, C and G being the most prevalent.[10,14]

Gram-negative bacilli are responsible for about 5%–23% of all PJIs, especially among the elderly, but their isolation rate may increase up to 60% in early PJIs where they may be retrieved as co-pathogens in polymicrobial infections.[15,16] *E. coli* and *P. aeruginosa* are the most frequently found pathogens followed by other *Enterobacteriaceae* such as *Klebsiella* and *Salmonella* species. Acquisition of infection is generally haematogenous, and virulence of these organisms contributes to its common acute presentation.[17]

About 3%–6% of PJIs are caused by anaerobes, with *Propionibacterium* acnes being the most prominent species. PJIs caused by anaerobes often present late after surgery.[10] Among other anaerobes isolated from PJIs as part of polymicrobial infections, there are *Clostridia*, *Bacteroides fragilis*, *Peptostreptococcus* species and *Actinomyces* species. Anaerobic Gram-positive cocci (*Peptostreptococcus* species and *Finegoldia magna*) are commensal of the gastrointestinal, genitourinary tracts and skin, which have been uncommonly isolated from delayed PJIs. They usually reach the hip and knee prostheses through haematogenous, contiguous spread or direct surgery. *Actinomyces* and *B. fragilis* are responsible for a limited number of generally monomicrobial infections.[17,18]

Uncommon microorganisms, such as *Corynebacteria*, *Pasteurella multocida* and *Mycobacterium tuberculosis*, have been occasionally reported as cause of PJIs.[19] Fungi have been isolated in <1% of PJIs, and Candida spp. are responsible for 80% of these infections.[20,21]

Culture-negative (CN) infection varies from 0% to 42.1%.[22] The risk factors for CN PJIs include antecedent antimicrobial therapy, poor laboratory facilities and expertise, atypical organisms, a history of previous PJI, post-operative wound drainage and vascular insufficiency.[22,23] Hence, to reduce the incidence of CN PJI, withholding antibiotics for 2 weeks before aspiration of joint and use of molecular biology techniques based on polymerase chain reaction (PCR) have been advocated.[22]

Initiation and spread of infection

1. Direct spread: The majority of PJIs occurring within 1 year of surgery are initiated through the introduction of the microorganisms at the time of surgery.[24] A low inoculum of microorganisms is needed to establish infection in the presence of a prosthetic material.[24,25] Early infections (first 4 weeks after implantation) manifest with clear local and systemic signs of inflammation and are predominantly caused by high-virulent pathogens (e.g., *S. aureus*, streptococci and enterococci). Delayed infections (typically between 3 months and 3 years) present with more subtle symptoms such as joint pain and early loosening and are caused by low-virulent organisms (e.g., CoNS or *Cutibacterium* species)[25-27]
2. Contiguous spread of infection from an adjacent site is the secondary mechanism by which infection can be initiated, for example, from superficial surgical site infection, disruption through trauma such as periprosthetic fracture

and nearby infectious focus (soft-tissue infection and osteomyelitis)[26,27]

3. Haematogenous spread: PJI can also occur through haematogenous seeding from bacteraemia or inoculation from a remote site infection. The high vascularity of periprosthetic tissue exposes the prosthesis to the highest risk of haematogenous infection in the first years after implantation. Typically, patients present with acute onset of clinical symptoms after a painless post-operative period. The search for and the elimination of the primary focus is necessary in preventing infection relapse. The most common primary foci are skin and soft-tissue infections (e.g., *S. aureus*), respiratory tract infections (e.g., *Streptococcus pneumoniae*), gastrointestinal infections (e.g., *Salmonella, Bacteroides, Streptococcus gallolyticus*) or urinary tract infections (e.g., *E. coli, Klebsiella, Enterobacter* spp.). Haematogenous spread of infection may also occur during dental procedures, especially viridans group streptococci.

The role of biofilm

A biofilm can be described as a structured aggregation of microbial cells of one or several species, encased in a self-produced matrix and adherent to a biotic or an abiotic surface. The biofilm matrix is composed of exopolysaccharides (also called extra-polymeric substances), proteins, teichoic acids, lipids and extracellular DNA.[6,26,28] The reason why antibiotics have poor activity against biofilms is not entirely understood. It is thought that the existence of slow or non-growing cells within the biofilm, the presence of bacterial subpopulations with different phenotypic levels of resistance within biofilms, overexpression of genes and stress responses to hostile environmental conditions all contribute to the resistance of biofilms.[26] They may be monomicrobial or polymicrobial, but even monomicrobial biofilms, especially those that are long-standing, and may consist of subpopulations of the same organism with different phenotypic and/or genotypic characteristics.

The development of a biofilm on an orthopaedic implant can be described as a 4-stage process:[6] (1) cell adhesion, (2) cell aggregation, (3) biofilm maturation and (4) cellular detachment.

The ability to grow and persist and detach and spread on the implant surface and on necrotic tissue in the form of a biofilm represents a basic survival mechanism by which microorganisms resist environmental factors. Mature biofilms take 4 weeks to develop and represent complex three-dimensional-communities where microorganisms of one or several species live clustered together in a highly hydrated, self-produced extracellular matrix (slime). Depletion of metabolic substances and waste product accumulation cause microorganisms to enter a slow- or non-growing (stationary) state. Planktonic bacteria can detach at any time, activating the host immune system, causing inflammation, oedema, pain and early implant loosening.

Classification

The classification of PJI is variable in literature. Coventry and later modified by Fitzgerald defined stages of PJI where Stage I is an acute infection that occurred within 3 months of the index procedure. Stage II is a delayed infection that occurred between 3 months and 2 years after the index procedure where there was no pain-free interval. Stage III is a haematogenous infection where there is pain-free stage.[29-31] The Zimmerli/Trampuz classification defines an early infection as one that occurs within 3 months of index surgery. Infections with onset between 3 and 24 months are delayed infections and those occurring >24 months after index arthroplasty are classified as late.[27,32]

Tsukayama *et al*. in their classification scheme divided PJIs into four categories, based partly on the time since operation and also on the presumed mode of infection.[33,34] The first category is positive intraoperative cultures, in which a patient undergoing revision for presumed aseptic failure is found to have positive intraoperative cultures. The second category is the early post-operative infection that occurs within the first month after surgery. The third category is late chronic PJI which occurs >1 month after the index operation and is typically associated with an indolent course. The final category of infection is acute haematogenous. This classification system is useful in determining medical and surgical management of PJIs.

McPherson *et al*. proposed a staging system for PJI that categorises not only the type of infection but also the systemic and local host status with some similarity to the Cierny–Mader staging systems for osteomyelitis.[35] This system includes three of the four types of infection in the system of Tsukayama *et al*. Early post-operative infection, haematogenous infection and late chronic infection, which are graded as Type I, II or III. The systemic host status is graded as A (uncompromised), B (compromised) or C (significant compromise), corresponding to a number of factors, including the presence of neutropenia, low CD4 T-cell count or age >80 years. Finally, the local extremity is graded as 1 (uncompromised), 2 (compromised) or 3 (significantly compromised), corresponding to the presence of local chronic active infection, soft-tissue loss or the presence of a fistula or subcutaneous abscess among other factors. This system allows more individualised treatment decisions and prognostic information.

Diagnosis

The diagnosis of PJI is based on a combination of clinical findings, laboratory results from peripheral blood and synovial fluid, microbiological and histological evaluation of periprosthetic tissues, intraoperative inspection and in some cases, radiographic results.

Clinical Features

The clinical manifestations of PJI vary depending on the virulence of the organism, the mode of initiation of infection,

the host immune response, the soft tissue surrounding the joint and the joint involved. Commonly reported signs or symptoms of PJI include pain, joint swelling or effusion, erythema or warmth around the joint, fever, drainage or the presence of a sinus tract communicating with the joint.[26,27]

Pain is said to be less frequent with chronic infections.[36] Open wounds, sinus tract or abscess has been reported to be more common in patients with contiguous or perioperatively acquired *S. aureus* PJI than in those with haematogenously acquired *S. aureus* infection. In contrast, systemic signs or symptoms such as fever or chills were significantly more common in patients with haematogenous PJI.[26]

Other symptoms of joint dysfunction such as stiffness and reduced range of motion maybe reported.[26,27,37]

Investigations

Imaging studies

Plain radiographs

Examination of serial conventional radiographs may be helpful to detect early loosening. A rapid development of a continuous radiolucent line of >2 mm or focal osteolysis within the first 3 years after implantation or subperiosteal elevation is suggestive of an infection but are neither sensitive nor specific enough to distinguish between septic and aseptic failure. Plain radiographs also assist the surgeon with pre-operative planning.[10,26]

Computed tomography

Computed tomography (CT) gives good contrast resolution of bone and surrounding soft tissue and can be useful in the pre-operative evaluation of excessive bone defects.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) displays greater resolution for soft-tissue abnormalities than CT. In particular, metal artefact reduction sequence MRI is useful for differential diagnosis with metallosis.[26]

Bone scintigraphy

Bone scintigraphy with ^{99}mTc has an excellent sensitivity, but its specificity to diagnose PJI is low. Positive uptake detected by delayed-phase imaging due to increased bone remodelling around the prosthesis is normally present in the first 2 years after implantation and even later, aseptic loosening cannot be differentiated from infection.[26] The use of antigranulocyte scintigraphy with ^{99}mTc-labelled monoclonal antibodies demonstrates a sensitivity of 83% and a specificity of 79% to detect PJI. Scintigraphy with Indium-111-labeled leucocytes in combination with marrow imaging shows about 90% accuracy for diagnosing PJI. Indium-111-labelled leucocytes do not accumulate in normally healing surgical wounds, and preliminary data indicate a comparable accuracy even in the early post-operative period. ^{18}F-fluorodeoxyglucose positron emission tomography is a fast, safe, high-quality imaging for the detection of PJI with a reported sensitivity of 82.1% and a specificity of 86.6%, however expensive and not readily available.[1,26]

Ultrasound

It can be useful in evaluating soft-tissue infections, particularly when there is concern for fluid collections or effusions. It can be useful as a tool for image-guided aspiration.[10,26]

Laboratory studies

Serum markers of inflammation

The American Academy of Orthopaedic Surgeons and the ICM on PJI currently recommend the assessment of patients' serum ESR and CRP as the first line of diagnostic evaluation in patients with suspected PJI.[1,10,26] However, there are issues with these serum markers of inflammation as they are elevated with any type of inflammation and infection, compromising their specificity for the diagnosis of PJI. Recent evidence suggests that PJI with some slow-growing organism may not result in a florid physiological response and hence may not result in the elevation of ESR and CRP in the serum, raising a concern regarding the sensitivity of the tests in some settings. It is also imperative for clinicians to consider the timing of infection prior to assessing patients' ESR and CRP results, as they are usually elevated in the early post-operative period. ESR can be elevated for up to 6 weeks after surgery and CRP by up to 2 weeks post-surgery. Therefore, the use of ESR and CRP for diagnosis of PJI is only meaningful when the other MSIS diagnostic criteria are present.[1,10,12,26]

Recently, numerous serum biomarkers have been studied for the diagnosis of PJI. These mainly include inflammatory biomarkers such as interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α), soluble intercellular adhesion molecule-1, immunoglobulin G antibodies to short chain exo-cellular lipoteicholic acid and procalcitonin.[38]

Synovial fluid analysis and culture

Pre-operative joint aspiration is the most valuable diagnostic tool and should be performed for every painful prosthetic joint prior to the surgical revision.[10,39] Determination of synovial fluid leucocyte count and percentage of granulocytes represents a simple, rapid and accurate test for differentiating between PJI and aseptic failure.

As a general principle, three to five intraoperative tissue samples should be submitted for the culture. The sensitivity ranges from 65% to 94%. It must be noted that the sensitivity of intraoperative swabs is low, and that swabs of superficial wounds or sinus tracts can mislead by detecting the colonising rather than the infecting microorganisms and should therefore be avoided. The sensitivity of synovial fluid culture is 45%–75% with a specificity of 95%. The sensitivity can be diminished by long transportation time in inadequate transport media. This can be prevented by the inoculation of aspirated synovial fluid into paediatric blood culture bottles. An incubation time of 14 days is necessary to detect low-virulent and difficult-to-detect pathogens, such as *Cutibacterium* species.[26,27,39]

Sonication of removed implants

Sonication is a method using low-frequency ultrasound waves that pass through a liquid surrounding the prosthesis and detach biofilm microorganisms from the surface. The sonicate fluid can then be submitted for culture and plated onto aerobic and anaerobic plates. Inoculation in the blood culture bottles improves the sensitivity and may reduce the cultivation time by up to 5 days. A cut-off of 50 colony-forming units/ml of sonication fluid yields a sensitivity of 79% and a specificity of 99% for the diagnosis of PJI. The culture of sonication fluid shows superior sensitivity compared with the standard culture of the periprosthetic tissue (79% vs. 54%), and can be especially useful in chronic infections or for patients on previous antimicrobial treatment.[27,39]

In acute post-operative infections, sonicating parts of the implants that are covered with antibiotic-loaded bone cement may inhibit bacterial growth and lead to false-negative results caused by increased antibiotic elution during sonication.[12,26,27]

Leucocyte esterase test

LE is an enzyme that is secreted by the activated neutrophils and detected using colorimetric strip tests. LE is a simple, readily available test, requiring application of synovial fluid to a urine test strip. It is now part of the minor criteria of the MSIS/International Consensus Diagnostic Criteria for PJI.[1,24,26] The accuracy of the LE test reported a sensitivity between 92.9% and 100% and a specificity between 77.0% and 88.8%. Bloody aspiration can potentially interfere with the colourimetric changes of the test strip, so centrifugation is found not to alter the accuracy of the LE test.[26]

Alpha defensin

Alpha defensin is an antimicrobial peptide released by activated neutrophils as a response to bacterial infection that has been used as a biomarker for the detection of PJI.[26,27,40] The alpha defensin lateral flow (ADLF) test is a qualitative test that determines the presence of alpha defensin in synovial fluid and can be performed in the operation theatre or immediately after the joint aspiration within 10 min. In the early post-operative period when synovial fluid leucocyte count is not readable (specificity of only 60% in the first 6 weeks post-operatively), the ADLF test may still be applied with a specificity of 99%.[24,40]

Synovial C-reactive protein

Although serum CRP (secreted by the liver) is elevated as part of the systemic response to PJI, recent studies show that the synovial CRP is also increased in PJI patients and is actually more accurate than serum CRP.[24,41,42] A recent publication demonstrated that combined CRP and α-defensin in the synovial fluid with the use of enzyme-linked immunosorbent assay provides sensitivity and specificity of 97% and 100%, respectively, based on the MSIS criteria as the standard definition for PJI.[42]

Histopathological examination

Histopathology of periprosthetic tissue should be considered a standard procedure in the diagnosis of PJI. Neutrophil granulocytes can be detected through immuno-histochemical techniques and validated using histopathological scores. The presence of PJI can be determined by the count of neutrophils per high-power field (HPF) at a magnification of 400.[1,10,12,24,26,41]

Peri-implant tissue sampling can be an effective diagnostic tool; the turnaround time for interpreting a single frozen section is approximately 20 min from the time it is received. Frozen sections have the advantage of being available relatively quickly, but the freezing process induces artefacts not seen in formalin-fixed tissue.[24,26]

Many studies have attempted to define an optimum cut-off threshold for the tissue concentration of neutrophils to support the diagnosis of infection and so a maximum tissue concentration between 5 and 10 PMN/HPF in each of the five 400 HPFs seems to carry the best diagnostic performance.

Molecular diagnosis

PCR can identify pathogens in synovial fluid with a sensitivity and specificity of 84% and 89%, respectively. The current limitations of this sensitive technique are its high costs and its susceptibility to contamination leading to false-positive findings.[1,10,24]

Fluorescent *in situ* hybridisation techniques are also used in identifying organisms involved in PJI.[10,24]

The high cost, heavy reliance on expertise, susceptibility to sample contamination and the lack of primers relevant to the diagnosis of PJI currently limit the routine use of molecular techniques in medical microbiology. At present, they are probably best reserved for CN cases.[10]

Treatment

There are different options of treatment for PJI, and they include debridement antibiotic and implant retention (DAIR), single-stage revision arthroplasty, two-stage revision arthroplasty, three or more stage revision arthroplasty, suppression antibiotic therapy (SAT), excision arthroplasty, arthrodesis and amputation. The goals of treatment are to eradicate infection, restore pain-free function of the infected joint and minimise PJI-related morbidity and mortality for the patient.[10] The goal of each surgical strategy is to remove all the infected tissue and hardware or to decrease the burden of biofilm if any prosthetic material is retained, such that post-operative antimicrobial therapy can eradicate the remaining infection.[10] Many factors such as duration of symptoms, joint age (early, delayed or late), infecting pathogen and its susceptibility pattern, prosthesis stability and the patient's pre-existing medical comorbidities influence the surgical choice of management.[43] Other factors, such as the quality of the periprosthetic soft tissue, the options available for successful reconstructive surgery after resection arthroplasty, the expertise of the clinician(s) and the patient's preferences, also influence the surgical management.[43]

Debridement antibiotic and implant retention

This involves opening into the joint, thorough debridement of necrotic tissue, haematoma and copious joint irrigation with saline and antiseptic solutions. The modular implants like polyethylene liner, insert and modular heads are removed and replaced with new ones. The removal allows for easy reach to the back and inside of the joint to clear all infected materials as well as those between the modular components. The wound is usually closed over a closed drainage system. It is indicated in early infections where patients diagnosed with a PJI have a well-fixed prosthesis without a sinus tract and are within approximately 30 days of prosthesis implantation or fewer than 3 weeks of onset of infectious symptoms.[10,43] Inability to close a wound is an absolute contraindication to DAIR. Arthroscopic DAIR can be done but is not advised as not only is it difficult to reach all the corners of the joint arthroscopically, but it has also been fraught with high failure rates.[44] Duration of antimicrobial therapy after DAIR is unsolved, but most authors consider 2–6 weeks of specific IV treatment followed by 3 months of specific oral antibiotics in THR or 6 months in TKR necessary.[43]

Single-stage revision arthroplasty

This was described in 1981 by Buchholz *et al*.[45] for the treatment of deep infections involving THR. One-stage revision arthroplasty is also known as direct exchange arthroplasty, and it is less common in the United States of America,[10] appearing more common in the United Kingdom. This involves resection of the prostheses with reimplantation of new prostheses at the same sitting. Here, there is a total removal of all the prostheses, cement for thorough debridement, wash out of joint and at the same sitting after redraping and removing contaminated instruments and materials, the replacement prostheses for revision arthroplasty are inserted with antibiotic bone cement. Samples are taken for tissue culture, and antibiotics are commenced based on pre-operative culture sensitivities or started empirically and then changed after intraoperative culture results are out. The indications for single-stage revision are for a selected group which include an absence of concurrent sepsis, host immunocompromise and soft-tissue or bony compromise.[46] For a good outcome following single-stage revision, knowledge of microbiological profile in the perioperative period is important.[46] Factors associated with failure include polymicrobial infection and Gram-negative organisms, especially pseudomonas species, methicillin-resistant *S. epidermidis*, Group D streptococcus.[47] Single-stage revision may be considered the first-line treatment for all PJIs unless the organism is unknown, the patient is systemically septic or there is a poor tissue envelope.[48] In addition, excellent cure rates and function have been reported by some studies of single stage in hip revision and infected knee surgeries, respectively.[49,50] The main advantage of single-stage exchange for PJI is that explantation and reimplantation are performed with one procedure, reduction in overall cost and operative time.[48] Other advantages are one anaesthesia, less demanding financially, emotionally and physically for the patient.

Two-stage revision arthroplasty

From 1983 till 2019, it has been severally reported as the gold standard for managing infected hip and knee arthroplasty.[51-54] It appears to be the safest, most effective and by far the most reported mode of treating infected revision arthroplasty, going by the papers studied in their reviews.[50,55] It has been reported with success rates ranging from 70% to 100%[55-57] and is the treatment of choice for chronic periprosthetic infection in North America.[58]

Here, the infected prostheses are all removed, joint is thoroughly debrided, necrotic tissues and inflamed synovium are excised, purulent cavities are cleared, joints are copiously irrigated, antibiotic spacer is inserted and wound is closed over a closed drain. The joint is revisited after an interval with antibiotic therapy for insertion of new prostheses once infection has been eradicated. Specimens collected during the procedure are analysed to determine the infecting organism and sensitive antibiotic is given for a period of 2–6 weeks while monitoring clinical and laboratory evidence of infection clearance/control. A second surgery is done after infection control for insertion of definitive prostheses. During the second surgery, thorough debridement is done after the removal of antibiotic spacer and collection of multiple tissue specimens for microbiology and histopathology. The definitive prosthesis is then inserted, and empiric antibiotic is given and stopped if cultures come out negative and continued for about 12 weeks if positive.

When there is no contraindication to surgery, the indications for two-stage revision arthroplasty include chronic PJI; acute PJI with failure of DAIR; failure of one-stage exchange procedure; acute infection in an immunocompromised host; infections with resistant organisms, highly virulent organisms[59] and methicillin-resistant *S. aureus* infection;[59] significant bone loss; soft-tissue compromise particularly if time is required for flap development;[60] patients with polymicrobial infection; atypical and CN organisms;[61] multidrug-resistant organisms;[46,61] unhealthy patients (systemic infection); those with wound complications; inability to identify an organism preoperatively; sinus tract; methicillin-resistant organisms; those with Gram-negative organisms such as *Pseudomonas* spp. and organisms not susceptible to antibiotics.[47] In all these and more, it is safer having a two-stage surgery than otherwise. Some studies[22,62] have reported that up to 41% of infected revision cases are CN and so would be wise to stage their surgeries. CoNS are difficult to treat due to biofilm formation/antibiotic resistant, and some works have alluded to successful treatment using a two-stage revision.[63] The optimal interval between the two stages is not defined, but mostly from 2 weeks to several months. Some give an antibiotic holiday of about 2–8 weeks before reimplantation[43] while monitoring clinically and with laboratory investigations.

Suppression antibiotic therapy

Indications for SAT include a very sick patient unfit for surgery or patient refusal for surgical intervention. The sensitive antibiotic to the infecting organism is given to the patient for

a long period or indefinitely depending on the patient's status or decision to go for recommended surgical treatment. SAT helps to reduce the load of microorganisms, thereby reducing pain, swelling and discharge.

Excision arthroplasty

This appears to be very common in Nigeria probably because our patients pay out of pocket for arthroplasty services, which is unaffordable to most. It is commonly done in the hip where the diseased head of femur is excised and no replacement is done. The aim of the procedure is to reduce joint pain though the resultant effect is an unstable hip. Thus, rehabilitation of the glutei and lower limb muscles is needed to enhance mobilisation albeit with support. It is usually done as a salvage procedure in recalcitrant infections.

Arthrodesis

This is the surgical fusion of the joint involved. It is indicated in salvage cases where other options have failed and patient would want a pain-free joint in addition to stability. The major concern with arthrodesis is inability to move the joint and hence, sitting with a joint that cannot bend is an issue. For the knee, the concern of tripping someone passing by with the extended limb is a problem and the difficulty entering and staying in a public transport with the limb extended. Indications for knee arthrodesis may include failed multiple attempts at reconstruction, repeated arthroplasty procedures with risk of infection and deficient extensor mechanism.[1]

Amputation

This is another salvage procedure indicated when the infection is repeated and extensive with no hope of eradication or the life of the patient is at stake. It is an option that should be avoided as much as possible.

Prevention

A meticulous review of all the plausible risk factors and causes of PJI is needful to carefully eliminate or correct the risk factors of PJI. Patients need to be thoroughly investigated and optimised prior to surgery and maybe *S. aureus* screening and decolonisation can be considered.[64] Strategies to prevent infection intraoperatively will look at timing of shaving, skin preparation, staff gowning and draping, prophylactic antibiotic use, traffic control, reducing operating time, surgical efficiency, blood management, intraoperative irrigation, use of drains, use of anticoagulants to prevent venous thromboembolism, long hospital stay and use of prophylactic antibiotics prior to invasive procedures post-arthroplasty.[64]

Conclusion

Specific diagnostic measures are needed to identify the organism(s) present in PJI. Treatment should be individualized, while ultimate pursuit remains preventing periprosthetic joint infections.

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Conflicts of interest

There are no conflicts of interest.

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