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REVIEW ARTICLE

PERIPROSTHETIC JOINT INFECTIONS: RISK FACTORS, DIAGNOSIS AND ITS MANAGEMENT

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ABSTRACT

Periprosthetic joint infection (PJI) affects 1% to 2% of primary arthroplasties and in 4% of revision arthroplasties.The frequency of PJI cases continues to climb in tandem with the increasing number of implantations. Complex treatment options, including numerous surgical modifications and long-term antibiotic treatment, arerequired to manage PJI. It's crucial to have a correct diagnosis, which includes identifying the infecting microorganisms and their antibiotic susceptibility, before deciding on the best treatment method to get rid of the infection. When PJI is ignored or undertreated, it causes infection to persist and repeated surgical revisions, resulting in poor function or impairment and a significant reduction in quality of life. [1] This review article provide an insight about the risk factors, diagnostic methods, treatment options for Periprosthetic infection.

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INTRODUCTION

Prosthetic Joint Infection (PJI), also known as Periprosthetic Infection, is an infection that affects the joint prosthesis as well as the surrounding tissue (Aaron, 2014). Periprosthetic Joint Infections after joint replacement are a difficult and severe complication of arthroplasty, with incidence ranging from 1% to 2% in native joints and up to 7% in patients requiring joint revision at 2 years postoperatively (Ron, 2018). One of the most damaging and costly consequences of total joint arthroplasty (TJA) is Periprosthetic joint infection. The diagnosis and treatment of PJI might be difficult for surgeons (Vinay, 2013).

RISK FACTORS

Patients with body mass index higher than 40,Diabetes mellitus, Kidneyand liver disease,vascular disease of the lower extremities, Positive drain tip culture are significantly at risk of developing periprosthetic joint infection (Jozef Breznicky, 2020).

The main risk factors for PJI are coagulopathy, congestive heart failure, obesity,systemic neoplasia male gender, chronic lung disease, and hypertension. The following are some of the behavioural risk factors: Alcohol abuse, immunosuppressive therapy, steroid therapies,tobacco and the infectious risk factors includessurgical site infections, postoperative urinary tract infections, and prior joint infections (Vera, 2021). PJI after primary replacement was caused by Gram positive bacteria. Staphylococcus epidermidis was the most common cause of infection after hip joint replacement (38.10 percent),while Staphylococcus aureus was the most common cause of infection after knee joint replacement (40.74 percent) (Vera, 2021). Long surgical time, large postoperative drainage volume, long hospitalization stay, history of surgery at incisions, preoperative hypoproteinaemia and superficial infectionwere most vulnerable (Heng Guo, 2020). Avascular necrosis, femoral neck fracture, rheumatoid arthritis, neurological disease, opioid use, iron-deficiency anemia were also significantly correlated with higher rate of PJI (Xiaolei Ren *et al*., 2021).

DIAGNOSIS

•**HISTORY AND PHYSICAL:** PJI's background will frequently reveal vital clues and raise suspicions. First and foremost, any known risk factors that may put the patient at a higher risk of developing PJI should be recognised. It's crucial to know when the patient's suffering or pain started (Springer, 2015).

•**LABORATORYTESTFOR DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION:** In the early evaluation of a patient with suspected PJI, blood testing is a useful screening tool. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) should be acquired as an initial screening technique in all patients of suspected PJI. [9]ESR and CRP are currently recommended as first-line screening tests for PJI and are included in the diagnostic criteria proposed by the MSIS of the 2013 ICM.

•**ERYTHROCYTE SEDIMENTATION RATE AND C-REACTIVE PROTEIN:** In joint arthroplasty patients who come with pain, the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level should be assessed, and preoperative screening can assist identify the presence of infection. They are the most often used inflammatory indicators, and they are determined in most laboratories using inexpensive, widely available, non-invasive procedures with quick turnaround times (Seung-Ju Kim, 2021).

•**INTERLEUKIN – 6:** Monocytes and macrophages create IL-6 to boost the immune response, which results in the creation of major acute phase proteins such as CRP. IL-6 levels in the blood peak two days after total joint arthroplasty and quickly return to normal. Furthermore, serum IL-6 has been found to be a helpful and accurate diagnostic for the identification of chronic PJI (Seung-Ju Kim, 2021).

•**D-DIMER:** D-dimers are fibrin degradation products that occur when the fibrin clot is dissolved by plasmin. Multiple investigations have demonstrated that both systemic and local infections can result in elevated D-dimer levels due to fibrinolytic activity. D-dimer has recently been shown to be a promising diagnostic serological marker for PJI, with sensitivity and specificity of 89 percent and 93 percent, respectively. Though D-dimer testing has certain limitations due to non- specificity and observations that high D-dimer levels can suggest the existences of an inflammatory state unrelated to infection, it may be useful in recognising early postoperative infection (Seung-Ju Kim, 2021).

•**PROCALCITONIN:** In the presence of bacteria, serum procalcitonin levels rise more quickly than CRP levels, peaking within a 6 – 24 hours window. Procalcitonin levels also return to normal faster than CRP levels due to its shorter half- life of 25 -30 hours. The accuracy of procalcitonin in detecting PJI, on the other hand, appears to be very low, as the procalcitonin threshold in patients with local infection overlaps greatly with its normal range (Seung-Ju Kim, 2021).

•**ALPHA-DEFENSIN:** Alpha-defensin appears to be the most promising synovial fluid biomarker for PJIin terms of sensitivity and specificity. Human neutrophils release alpha-defensin, an antimicrobial peptide, in response to the presence of pathogens. Alpha-defensin can be identified using an alpha-defensin test kit or laboratory- based alpha-defensin enzyme-linked immunosorbent assay (ELISA). Although alpha-defensin has a higher sensitivity and specificity than other synovial fluid markers, some authors advise against using it routinely and only when traditional testing is inconclusive, because the laboratory-based synovial alpha-defensin immunoassay does not help diagnose or rule out PJI when combine with routine serologies and synovial fluid analysis (Seung-Ju Kim, 2021).

•**LEUKOCYTE ESTERASE:** LE is an enzyme generated at the infection site by activated neutrophils. The presence of LE in synovial fluid is determined using low-cost colorimetric strip assays that generate an immediate and easily identifiable colour shift. According to the International Consensus Group the use of LE test has recently been validated and adopted as a minor factor in the definition of PJI (Seung-Ju Kim, 2021).

•**ALBUMIN AND GLOBULIN:** Albumin is commonly used to assess nutritional status; however, recent research has revealed that albumin is a negative phase reactant, meaning that its synthesis reduces during inflammation. During inflammation process, serum globulin (GLB), which includes complement components (interleukin-6, immunoglobulins.) and ceruloplasmin, rises. Because both decreased albumin and increased globulin play important roles in inflammation, the AGR, which considers both albumin and globulin at the same time, may be a more accurate indicator of the body's inflammatory state (Huhu Wang, 2021).

•**HISTOPATHOLOGICAL STUDIES:** For the diagnosis of PJI, histopathological investigation shows a high sensitivity (95%) and specificity (92%). Wear particle-induced, infectious, mixed, and indeterminate forms of periprosthetic membranes have been described based on histomorphological parameters. Unfortunately, despite its high efficacy in diagnosing PJI, the histopathology examination does not identify the causative bacteria.

MICROBIOLOGICAL STUDIES

- **PREOPERATIVE ASPIRATION:** The sensitivity of synovial fluid culture ranges from 50% to 70%, and it should be done before revision procedures (together with the determination of leukocyte count in the synovial fluid).[10]

- **INTRAOPERATIVE SPECIMENS:** Intraoperative tissue samples give precise specimens for detecting the infecting microorganisms, with a sensitivity of 45% to 78% and specificity of 91% to 96%. For culture, at least three to five intraoperative tissue samples from various anatomical areas should be taken. Because it is instructive, samples should always be taken from a zone where the tissue structure is obviously inflamed. Any antibiotic regimen should be stopped for two weeks before collecting microbiological samples to allow the disease to proceed (Cheng, 2018).

- SONICATION FOR REMOVED IMPLANT: Sonication is utilised to remove adhering bacteria from the prosthetic joint's surface. Sonication fluid culture has higher sensitivity and specificity than periprosthetic tissue culture, and it is also applicable to patients who have had antibiotic treatment prior to surgery (Cheng, 2018).

- **FROZEN SECTION:** The use of frozen section is still debatable, and it is highly dependent on a number of factors. The key concern is the number of neutrophils per high-magnification field (400 magnification) and the minimum number of fields carrying that concentration of inflammatory cells (Springer, 2015).

- **IMAGING STUDIES:** In the first step of the imaging diagnosis of PJI, conventional radiography is most commonly use.However,plain X- Ray film has low sensitivity and specificity in the diagnosis of infection. (12)Every patient with a painful total joint replacement should have a plain radiograph taken. Early indicators of failure, such as unexpected bone loose (osteolysis) or component loosening, should prompt suspicion of the PJI in the clinician (9). The contrast resolution of computed tomography (CT) imaging of bone and surrounding soft tissue is excellent.Patients with non – ferrimagnetic implants can safely undergo magnetic resonance imaging (MRI). The patients musthowever, remain in an enclosed machine, which may be difficult for claustrophobic people. The most significant drawback of Imaging interference in the region of metallic orthopaedic implants is seen on CT and MRI scans. PET with fluorine 18-fluorodeoxyglucose (FDG) is a fast, safe, and high-quality imaging technique for detecting PJI.

- **MOLECULAR DIAGNOSTIC METHODS:** Theoretically, using molecular technology to improve diagnostic accuracy, such as multiplex polymerase chain reaction, appears promising. Novel tests are continually being developed to help with diagnostic accuracy, but there isn't enough high-level data to support their use. Furthermore, when compared to culture, next-generation sequencing did not yield higher sensitivity or specificity results. As a result, molecular testing is unreliable and, given its low sensitivity, has limited utility as a single test for PJI diagnosis. Furthermore, the cost-effectiveness of molecular testing is still unknown (Seung-Ju Kim, 2021)

- **NEW DIAGNOSTIC METHODS:** Polymerase chain reaction is a new diagnostic method. Techniques can be used to identify an isolated bacterium as well as some bacteria that are difficult to culture. When the patient is given antibiotics, multiplex PCR has a high sensitivity and specificity for diagnosing PJI and distinguishing aseptic loosening. According to a meta-analysis of 14 investigations, PCR in synovial fluid samples had a sensitivity and specificity of 84 percent and 89 percent, respectively, and PCR in sonication fluid culture had a sensitivity and specificity of 81 percent and 96 percent for the detection of PJI. Fresh samples performed better than frozen samples in terms of sensitivity. Microcalorimetry can be used to quickly detect the presence of microorganisms by measuring the heat generated by microbial growth and metabolism. Microcalorimetry of sonication fluid has a sensitivity of 100 percent and a specificity of 97 percent, according to a study.

TREATMENT: The treatment for PJI is to relieve pain, restore normal joint infection and remove the infection. Individualized treatment decision should be made with the help of multidisciplinary team in order to tender the best approach for each patient based on a rigorous analysis of current data. For a successful therapy, an appropriate procedure in combination with an antibacterial idea is essential. New scientific evidence and clinical experience have enhanced the previous recommendation or PJI treatment, which have been optimized and summarized in a surgical and antibiotic treatment regimen13.

- **SURGICAL TREATMENT:** Debridement and implant retention, one stage or two stage implant replacement are some of the major surgical strategies for the treatment of PJI. Debridement in conjunction with retention technique has been studied in the past. Prosthetic joint infection aredifficult to cure and have a failure rate. when the following conditions are met: (1) the prosthesis is stable; (2) a pathogen susceptible to antimicrobial agents is active against surface – adhering microorganisms; (3) there is no sinus tract or compromised soft tissue and (4) the symptoms duration of infection is less than 3 weeks, success rate can be greater than 80%. According to a recent study, 90 percent of orthopaedic device related infection can be treated with surgical debridement and implant retention, as well as antimicrobial therapy, only if patients meet the above selection criteria and that the pathogen is susceptible to rifampin (or gram – positive pathogen) or ciprofloxacin (for gram - negative pathogens) (or gram – negative pathogens).

- Implant replacement in a single stage exchange- Is a single process that involves the removalof the old devices and the installation of the new one. patients with good bone and soft tissue conditions without recognized bacteria with no difficult – to – treat (DTT) infections caused by pathogens resistant to biofilm – active antimicrobials, can benefit from one stage exchange.
- Implant replacement in two stages exchange– Is the removal of the prosthesis and the subsequent reimplantation of a second prosthesis at a later date. The short interval (2 -4 weeks) method is appropriate for the patients with a known and readily curable pathogen, impaired soft tissues, or a disturbed sinus tract. The strategy of a long interval (8weeks) is appropriate for organisms that are unknown or have DTT and soft tissue that is severely weakened. Two stage exchange has been regarded as the standard for treating patients, particularly in DTT microorganism Like enterococci and fungus. The success rate of a two-stage procedure is usually greater than 90 %. Before reimplantation,if there are more than three morbidities and a high ESR or CRP, the chance of reinfection is significant 14

- ANTIMICROBIAL TREATMENT: A total of two weeks of antibiotics treatment is suggested or all surgical operations. Antibiotic treatment without surgery is not recommended and should only be used I the patient oppose surgery or I the surgical procedure poses a significant risk to the patient'slife. rifampin is effective against staphylococci and Propionibacterium implant – associated infections, but ciprofloxacin has biofilm action against gram negative bacteria 14.

- **ORAL ANTIMICROBIAL SUPPRESSION FOR A LONG TREATMENT:** The majority of the patients in the study received at least 6 months of treatment, according to the report. Recommending prolonged to young patients is very contentious an should be done on a case-by-casebasis. patients on long term oral antimicrobial suppression should be closely evaluated for both clinical failure and antimicrobial toxicity. 15

- **DAIR:** Debridement, Antibiotics and implant retention are all abbreviated as DAIR. DAIR entails the retention of the implant secured to the bone, with the removal of only the polyethylene (PPE) insert \ liner and aremaining modular element, followed by a thorough radicle debridement, and re insertion of a new insert \ liner. When compared to implant exchange revisions, this method is straight forward,retains bonestock, lowers expenses and lowers morbidity. The success rate, however, is low. The PJI setting is changeable. The timing of the infection and the infections causative organisms appear to have an impact on the DAIR results. In the case of early and sensitive Staphylococcal infections, DAIR is preferred.However, in the instances of PJI, where the casual organism is methicillin – resistant Staphylococcus aureus, this treatment strategy has been demonstrated to fail in 84 percent of cases. while DAIR should not be used or PJI with pathogen like MRSA. 16

CONCLUSION

Periprosthetic joint infections are a serious after-arthroplasty complication that leads to significant patient morbidity. The gold-standard approach for clearing chronic infection is currently two-stage exchange arthroplasty, however the more conservative surgery of one-stage exchange is gaining fresh interest in specific subsets of patients. PJI study will tell surgeons whether to focus on genuine eradication of pathogenic organisms from an infected joint or on enhancing patient function and pleasure after this terrible consequence, regardless of the therapeutic strategy chosen. This review assessed risk factors, diagnosis, and treatment options for prosthetic joint infection. Thus, the information provided in the review helps to gain better understanding about the disease and provide better attention and care in patients with periprosthetic infections.

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