Orthopaedic Infection: Prevention and Diagnosis

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Abstract

Host optimization, reduction of bacteria, and establishing proper wound environment in the preoperative, intraoperative, and postoperative periods are the traditional cornerstones of infection prevention. Most institutions have standardized a systems approach to reduce the incidence of surgical site infections. Typically, these systems-based approaches promote protocols for hand and environmental hygiene, patients risk assessment and screening, surgical delays for identifiable and modifiable risk factors, infection surveillance, antibiotic stewardship programs, communication/coordination of care, physician 360° reporting, and unit-based safety programs. Despite the institution of these prevention efforts, there remains controversy about the efficacy and cost-effectiveness of a number of these approaches.

Reduction of Bacteria

Methicillin-resistant *Staphylococcus aureus* Decolonization Protocols

Staphylococcus aureus is one of the most commonly isolated organisms in periprosthetic joint infection (PJI). Because resistant strains are becoming more prevalent, many institutions have instituted decolonization protocols based on generalized data including many surgical subspecialties.[1,2] There are limited data on the success of *S aureus* nasal decolonization programs and their effectiveness in preventing PJI. A recent prospective study of 1,305 arthroplasties suggested no clear benefit in screening/decolonizing carriers before total joint arthroplasty.[3] A recent historic control study of 3,434 patients revealed that 20% of patients remained colonized despite undergoing the decolonization protocol and that compared with controls, no decrease in surgical site infection could be demonstrated.[4] These authors postulated that the power to demonstrate effectiveness of decolonization at 80% power, based on their study data which achieved only 41% power, would require a total of 72,033 study patients.

One of the problems associated with decolonization protocols is establishing patient compliance which may contribute to persistent colonization.[5] A novel technique of intranasal antimicrobial photodisinfection therapy combined with chlorhexidine gluconate body wipes in 3,068 patients compared with 12,593 control subjects revealed a significant reduction in the surgical site infection rate.[6] The benefits from this approach also included excellent compliance and easy integration into the usual preoperative work routine. Unfortunately, this technology is unavailable in the United States because it does not yet have FDA approval. It has been suggested to perform a large multicenter study to determine whether or not decolonization is an effective strategy in prevention of PJI, and if so, whether it can be determined using prioritized study arms and how compliance can be improved. Finally, almost all decolonization protocols incorporate preoperative showers and chlorhexidine body wipes as an additional method of bacterial reduction.

Prophylactic Antibiotics

The use of perioperative prophylactic antibiotics (primarily the use of cephalosporins) remains as one of the cornerstones of bacterial reduction and PJI prevention.[7,8] Because of the emergence of resistant organisms associated with PJI, there are recent reports on the use of optimal antibiotic regimens and, in some cases, the use of dual antimicrobial therapy.[9] Because of the number of patients required to achieve appropriate power, however, it remains unclear whether these alternative strategies are effective. The role of antibiotic-loaded bone cement in prophylaxis of primary hip and knee arthroplasty still remains controversial.[10,11] It is important to note that this use of antibiotic-loaded bone cement is not FDA approved, and because of the number of patients required, this controversy will require a large multicenter prospective randomized trial. The final remaining and long-standing controversy is when and in whom prophylactic antibiotics should be given for invasive procedures, the most notable being dental, genitourinary, and gastrointestinal procedures.[12]

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Novel Prosthetic Coatings

The development of novel prosthetic coatings to obtain antibacterial activity on implant surfaces has been under intense investigation for many years.[13] In general, the strategies have been centered around the release of antimicrobial drugs or use of novel bacteriocidal metallic nanocrystalline coatings.[14–16] A wide spectrum of substances and technological approaches has been proposed and tested for antibacterial features with the following specific aims: (1) prevention of bacterial adhesion (antiadhesive polymers, albumin, superhydrophobic surfaces, nanopatterned surfaces, and hydrogels) and (2) bactericidal activity (inorganic: silver, titanium dioxide, copper, selenium, and zinc; organic: coated or covalent antibiotics, antimicrobial peptides, cytokines, and enzymes; multilayered coatings, positive-charged polymer, and multifunctional smart coatings with nanocontainers).[13]

Surgical Environment

There is a long list of traditional procedures and technologies used in the operating room to reduce bacterial counts. These include the use of laminar airflow ventilation, ultraviolet lights, reduction of operating room personnel and room traffic, bacteriocidal skin preparations, bacteriocidal wound irrigation, sterile draping, hoods, masks, helmet exhaust suits, and terminal room cleaning.[7,8] Despite widespread acceptance of many of these practices, there is still controversy regarding their effectiveness. New technologies such as a pulsed-xenon ultraviolet room disinfection device provide the potential for improved terminal cleaning of operating room suites, but need further study before widespread acceptance.[17]

Host Optimization

The categories of host factors that can potentially be optimized in perioperative prevention protocols are currently identified as "modifiable risk factors."[18,19] These modifiable factors include obesity, diabetes, rheumatoid arthritis, depression, immunosuppressive medications, nicotine use, malnutrition, anemia of chronic disease, alcohol abuse, intravenous drug abuse, HIV infection, operating time, allogeneic blood transfusion, operative normothermia, and *S aureus* colonization. This topic of host modification is covered within a subsequent section of this consensus symposium and will not be discussed here.

Proper Wound Environment

Although there are numerous variables that help promote successful wound healing and avoidance of PJI, many of these are very difficult to quantify and study (eg, meticulous surgical technique, accurate wound closure, and the effectiveness of deep drains). Nevertheless, one factor, the increased surgical time, has been clearly demonstrated to correlate with increased incidence of PJI.[19] Additionally, there is emerging evidence that the use of antimicrobial dressings may reduce the incidence of PJI.[20]

Diagnosis of Infection

Definition

In the diagnosis of infection, one of the primary problems has been how to exactly define a deep periprosthetic infection and what variables constitute or contribute to the diagnosis. The definition proposed by the Musculoskeletal Infection Society (MSIS) is currently the most favored definition in orthopaedic study publications.[21] The MSIS definition of infection is as follows: (1) There is a sinus tract communicating with the prosthesis; or (2) A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or (3) Three of the following five criteria exist: (i) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration; (ii) Elevated synovial leukocyte count or a ++ result on leukocyte esterase test strip; (iii) Elevated synovial neutrophil percentage (polymorphonuclear leukocyte %); (iv) Isolation of a microorganism in one culture of periprosthetic tissue or fluid; or (v) Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at 9,400 magnification.

One of the problems with this definition is that many clinicians have abandoned the use of intraoperative pathology in their daily practice, and therefore, one of the minor criteria in the MSIS classification is often not available for evaluation. Furthermore, other medical specialties have established slightly different definitions of PJI.[22] Finally, there are many emerging diagnostic technologies being used for the facilitation of diagnosis that are not considered in these definitions. Despite these shortcomings, it should be recognized that the use of an accepted definition should be encouraged for publication and study comparisons, and the use of a common definition actually facilitates evaluation of new technologies as they emerge.

Clinical Practice Guideline

The American Academy of Orthopaedic Surgeons has proposed a clinical practice guideline to facilitate the diagnosis of PJI.[23] This guideline recommends initial screening of patients with ESR and CRP and whether either is elevated to proceed with arthrocentesis. Fortunately, these two serum biomarkers are easy to obtain and facilitate the process of determining whether or not the clinician should proceed with arthrocentesis. Unfortunately, these biomarkers are relatively poor determinants of PJI in the first 3 weeks postoperatively. Furthermore, in the setting of chronic infection, approximately 4% of PJIs in the hip and knee have a normal ESR and CRP at the time of presentation.[24] For these reasons, continued investigations are underway to identify other more sensitive screening serum biomarkers (such as interleukin-6 or procalcitonin) to facilitate the diagnosis in both the acute and chronic settings.[25,26]

Arthrocentesis

Arthrocentesis of the affected joint remains the cornerstone of the diagnosis of infection and microorganism identification. Currently, clinicians are performing arthrocenteses more frequently than in the past years for different reasons. This practice has facilitated consistent synovial fluid analysis for leukocyte counts and differentials, and is an invaluable tool to aid in the diagnosis of infection when using techniques that evaluate synovial biomarkers.

Synovial Biomarkers

The emergence of synovial biomarkers, such as alpha defensin, leukocyte esterase, interleukin-6, CRP, and lactate, has demonstrated very promising results in identifying infection, but there is room for considerable investigation to determine the best synovial biomarker (or panel of synovial biomarkers) to improve diagnostic accuracy.[25–31] Despite the potential to improve the diagnosis of PJI with these emerging synovial biomarkers, traditional culture techniques to identify micro-organisms and determine antimicrobial sensitivities are still required to guide appropriate treatment. Development of alternative techniques to identify micro-organisms is worthy of investigation.

Culture-negative Infection

Despite best efforts to identify a microorganism in the setting of active infection, occasionally none can be identified.[32] This is the problem of the so-called culture-negative infection.[33] This is frequently associated with the use of antibiotics before intervention or slow specimen transportation and delayed culture techniques.[32] Fortunately, for clinicians and patients alike, however, a 94% successful treatment rate has been demonstrated in these patients at 5-year follow-up. [33,34]

Biofilms and Ultrasonication

It is well known that most PJIs have associated biofilms and that the use of recent antibiotics affects the accuracy of traditional culture techniques. There is some evidence that use of

ultrasonication fluids obtained from explanted devices can improve the accuracy of intraoperative cultures and thereby facilitate effective postoperative antibiotic regimens.[35] This practice has become routine at many institutions when no microorganism has been identified preoperatively.

Areas Requiring Further Study

There are several areas of investigation that may facilitate a more accurate diagnosis of infection but require further study. These include the following: (1) new serum biomarkers to improve screening in chronic PJI and consider preoperative panels to facilitate diagnosis of the immediate postoperative PJI, (2) identification of best synovial biomarkers for diagnosis with a multicenter study, and (3) a study of the ultrasonication fluid for infected prosthesis in multiple centers to validate an expanded role for this technique.

Conclusion

An institution-based systems approach is critical to implementing standardized, reproducible practices to reduce infection. Nevertheless, the single most important factor in the prevention of PJI is the use of perioperative prophylactic antibiotics. The precise diagnosis of infection remains elusive and controversial, but the MSIS definition provides a reproducible, objective measure that is encouraged for future study comparison and technological evaluation. Arthrocentesis of the affected joint remains the cornerstone of infection diagnosis, but the future study of serum and synovial biomarkers will undoubtedly aid in more reliable, accurate, and prompt diagnoses.

Still, there are many areas related to the prevention and diagnosis of PJI that require further investigation. Because of the relatively low rate of PJI and the multifactorial nature of risk factors associated with PJI, large numbers of study patients are required to achieve the power necessary to provide statistical certainty of study conclusions, and as such, most studies surrounding the topic of infection will require large multicenter, prospective, randomized trials.

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