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QUESTION 3: Do antibiotic coatings on implants reduce the rates of surgical site infections/ periprosthetic joint infections (SSIs/PJIs)?

RECOMMENDATION: The use of antibacterial coatings on implants has been shown to reduce SSIs and/or PJIs based on in vitro and pre-clinical animal model studies. The use of antibiotic-coated implants in small series of patients appears to be encouraging. Larger-scale studies to prove the value of these technologies are needed.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 90%, Disagree: 6%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

Implanted biomaterials continue to play a key role in orthopaedic surgery. However, infections surrounding these implanted biomaterials remain a leading cause of failure, especially in total hip and knee arthroplasties [1–3]. The biofilm theory and its role in the propagation of bacterial growth is postulated to play a quintessential role in the etiology and pathogenesis of PJIs in modern-day total joint arthroplasties (TJAs) [4–8]. Surface roughness, hydrophobicity and electrostatic charge are important characteristics of implanted biomaterials that are exploited by bacteria to promote adherence [9,10]. Strategies proposed to reduce the rates of these complications have included the use of implants coated with antiseptic materials or antibiotic agents. Antibacterial coatings engineered for the surfaces of implanted biomaterials have been an evolving technology over the last three decades [11]. Romano et al. described ideal characteristics of future antibacterial coatings, namely that they would be proven in vivo by demonstrating acceptable antibacterial properties towards a large spectrum of organisms, easy handling, cost-effectiveness and lack of local or systemic toxicity while ensuring bone healing, on-growth or in-growth [9].

Antibacterial coatings can be categorized into three groups: (1) perioperative antibacterial local carriers or coatings (LCC), (2) passive surface finishing/modification (PSM) and (3) active surface finishing/modification (ASM) [9].

The first group, LCC, are antibacterial carriers or coatings that are applied to implants at the time of surgery. The most popular and well-studied vectors in this category include antibiotic-laden bone cement, used when coating intramedullary nails or total joint components [12]. Antibiotic-laden hydrogel that may be applied to the implant by the surgeon has been shown to reduce surgical site infections in a multicenter randomized controlled trial of 380 patients undergoing primary and revision total hip and total knee arthroplasties [13]. Similarly, a pilot study of second-stage implantation for prosthetic joint infections utilized implants coated with a resorbable calcium based bone substitute mixed with gentamycin or vancomycin [14]. At a minimum follow-up of one year, 95% of patients did not show any clinical signs of infections. However, no control group was used in this pilot study [14]. Furthermore, these studies, as well as other smaller cohorts that have been reported, are underpowered to make definitive recommendations for its widespread use.

The second group, PSM, revolves around the premise that chemical and/or physical modifications to the surface of an implanted biomaterial may reduce bacterial capabilities of adherence, and thus, prevent biofilm formations. These modifications are made without the planned release of bacteriostatic or bacteriocidal agents into the surrounding tissues. Such technology includes treatment of the surface layer of an implant with ultraviolet (UV) light irradiation to increase the hydrophilicity of the implant, which decreases bacterial adherence [15]. Changing the morphology of the surface layer of implants without decreasing the reliability of osseointegration has been proven capable of decreasing bacterial adherences in in vitro studies [16–19]. Polymer coatings (hydrophilic polymethacrylic acid or polyethylene oxide) or hydrogel coatings can also be applied to titanium implants, which helps deter bacterial adhesions [18,20–24]. PSM has great potential for future use on implanted biomaterials, however, there is concern regarding the osseointegration with coatings or surface modifications with strong anti-adhesive capabilities. Future in vitro and in vivo studies are needed prior to widespread clinical application.

The third group, ASM, includes modifications to the surface of the implant that impart pharmacologically-active antibacterial agents such as antibiotics, antiseptics, metal ions and/or organic compounds [9]. Antibacterial surface innovation largely revolves around metal ions such as magnesium, gold or silver [25–31], as well as non-metal elements such as chlorohexidine [32]. Antibiotics may be sprayed on or covalently bonded to the implant surface [33], applied via hydrogel or coating [13,34] or contained in and released via nanotubes [35,36]. While there is a myriad of vectors to deliver antibiotics to the surrounding tissue, there is a paucity of conclusive in vitro studies, and a relative lack of in vivo studies demonstrating safety and efficacy with this technology. Further confounding ASM is the wide variability of coatings studied. This makes it tremendously difficult to draw conclusions from the current literature regarding ASM. While studies have shown that antibiotic coatings do not affect bone healing in animal models [37,38], this technology has not been studied clinically.

Perhaps the most well-studied antibacterial coating are antiseptics, such as metal ions impregnated into the implant or applied via coating. Both in vitro and in vivo animal models have demonstrated significant antibacterial effects [23,25,26,28,31,36,39–41]. Additionally, clinical studies of silver-coated endoprostheses have demonstrated the efficacious antiseptic effects of the metal-ion coating in reducing infection [42–44]. However, these studies are largely retrospective in nature, and underpowered to render conclusive evidence supporting the widespread application of such technologies. While there are concerns of metal-ion toxicity that may result from such coatings, several studies have demonstrated little to no evidence of toxicity or side-effects [30,40,45]. Metal-ion coatings appear to the most promising in terms of efficacy and near-future implementation based on review of the present literature surrounding antibacterial coatings.

Despite the promise of these individual reports, the paucity of high-level controlled trials in the setting of arthroplasty, suggests that it is too early to conclude that antibiotic coatings will reduce the rates of SSIs/PJIs following primary or revision procedures. However, these strategies could prove to be beneficial in high-risk primary or revision cases. Further high-quality studies are needed to address these questions.

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