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Infections associated with percutaneous osseointegrated titanium implants for limb prostheses

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i föreläsningssal Järneken, Kvinnokliniken, Sahlgrenska Universitetssjukhuset/Östra

Torsdagen 16 november 2017, klockan 09.00.

av Jonatan Tillander

Fakultetsopponent:
Bo Söderquist, Professor
Örebro Universitet

Avhandlingen baseras på följande delarbeten:

I. Tillander J, Hagberg K, Hagberg L, Brånemark R. **Osseointegrated Titanium Implants for Limb Prostheses Attachments: Infectious Complications.** *Clin Orthop Relat Res (2010) 468: 2781. DOI 10,1007/s11999-010-1370-0*

II. Zaborowska, M, Tillander, J, Brånemark, R, Hagberg, L, Thomsen, P, Trobos, M 2016. **Biofilm formation and antimicrobial susceptibility of staphylococci and enterococci from osteomyelitis associated with percutaneous orthopaedic implants.** *J Biomed Mater Res Part B 2016:00B:000–000.*

III. Tillander J, Hagberg K, Berlin Ö, Hagberg L, Brånemark R. **Osteomyelitis Risk in Patients with Transfemoral Amputations Treated with Osseointegration Prostheses.** *Clin Orthop Relat Res DOI 10,1007/s11999-017-5507-2*

IV. Tillander J, Hagberg L, Brånemark R. **Possible to cure osteomyelitis with retention of osseointegrated femoral implants.** *Submitted 2017.*

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Abstract

Femoral amputation is a devastating event. Percutaneous, bone anchored prosthetic systems reduce problems associated with socket suspended prostheses, but the design is inherently vulnerable to infection. The aims of this thesis were to determine the risk of implant-associated infection, bacterial biofilm properties and the functional impact using this implant treatment regime. Definition of implant related osteomyelitis was based on clinical signs, radiography and positive tissue cultures. In 3-year prospective study 39 patients were evaluated twice for infectious frequency, clinical presentation, and its relation to bacterial flora at the skin-implant interface (*Paper I*). The frequency of implant infection was 5% at inclusion and 18% at follow-up. The most common bacteria in superficial, and deep cultures were *S. aureus* and coagulase-negative staphylococci. Despite frequent colonization by potentially virulent bacteria, limited disability, and only one implant removal was found. Phenotypical and genotypical biofilm formation was determined in 13 (7 staphylococcal, 6 enterococcal) osteomyelitis strains (*Paper II*). Antimicrobial resistance was tested with a novel combination of the Calgary biofilm MBEC device, and a custom-made susceptibility MIC plate. The majority of the strains produced biofilm with increased antimicrobial resistance, compared to their planktonic counterparts. Slime producing strains tolerated higher antimicrobial concentrations compared to non-producers. All staphylococcal strains carried *ica* genes. The long-term risk of implant-associated infection, and its relation to patient and method specific factors was determined in a 20-year retrospective analysis of the first 96 femoral implant patients (102 implants) (*Paper III*). A 10-year cumulative risk of 20% for developing osteomyelitis (16 patients), and a 10-year cumulative risk of 9 % for implant extraction due to osteomyelitis (10 patients) was found. Antibiotic treatment (median 3.5 months) and selective minor debridement, with retained implants, cured 7 out of 18 patients at the 24-month follow-up (*Paper IV*). Six patients were cured after implant extraction, and 5 had chronic low-grade infections with stable implants, but variable use of the external prosthetic leg. The most common pathogens were *S. aureus* and *E. faecalis*. C-reactive protein serum levels were significantly higher in patients with osteomyelitis caused by *S. aureus* than other pathogens.

It is concluded that the finding of an increased risk of osteomyelitis with time using this implant system calls for; i) careful patient selection and information of long term risks, ii) further studies on infection control, iii) consideration of biofilm in treatment, and iv) improved diagnostics, and antibiotic delivery.

Keywords: *amputation, osseointegration, osteomyelitis, clinical presentation, long-term risk, biofilm*

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