Severe periprosthetic osteolytic lesions after the Ankle Evolutive System total ankle replacement

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Between 2002 and 2008, 130 consecutive ankles were replaced with an hydroxyapatite (HA) and titanium-HA-coated Ankle Evolutive System total ankle prosthesis. Plain radiographs were analysed by two independent observers. Osteolytic lesions were classified by their size and location, with cavities > 10 mm in diameter considered to be ‘marked’. CT scanning was undertaken in all patients with marked osteolysis seen on the plain radiographs.

Osteolytic lesions were seen on the plain films in 48 (37%) and marked lesions in 27 (21%) ankles. The risk for osteolysis was found to be 3.1 (95% confidence interval 1.6 to 5.9) times higher with implants with Ti-HA porous coating.

Care should be taken with ankle arthroplasty until more is known about the reasons for these severe osteolyses.

As the short- and intermediate-term results of total ankle replacement (TAR) seem to be acceptable, it is seen as a challenge to the position of arthrodesis in the treatment of arthritis of the ankle. However, there are concerns about the long-term survival of the implants. The rate of revision remains quite high, and loosening of the components has been seen.

In total hip replacement, osteolysis is regarded as a foreign-body reaction caused by wear of particles of polyethylene, cement or metal. In some series of TARs the incidence of periprosthetic lucency or osteolysis has been up to 76%.

This study describes our experience with periprosthetic osteolysis using Ankle Evolutive System TARs.

Materials and Methods

Between 2002 and 2008, 130 TARs were performed in 123 patients using the Ankle Evolutive System total ankle prosthesis (Transystème, Nîmes, distributed by Biomet, Valence, France). The demographic data of the patients are given in Table I. The mean follow-up was 31.3 months (3 to 74).

Implant characteristics. The Ankle Evolutive Surgery (AES) total ankle prosthesis is a threepiece un cemented, unconstrained design with tibial and talar components of cobalt-chromium (Co-Cr). It has a front to back mobile bearing, of tapered ultra high molecular weight polyethylene (UHMWPE) between the flat tibial component and the shallow sulcus of the talar implant. The meniscus is smaller than the metallic components to protect it from overhang. In 2004 the design was changed and the hydroxyapatite (HA) coating on metal (Co-Cr) components changed to a porous coating with pure titanium and hydroxyapatite (T40 HA). The tibial component was also changed from a modular stem to a monoblock model.

Radiographic and CT evaluation. Anteroposterior (AP) and lateral radiographs were taken, standing whenever possible. They were evaluated by two independent observers (HK and IK), who were blinded to which type of implant had been used. Angular and linear values were measured digitally with the Kodak Carestream PACS system (Carestream Health, Rochester, New York).

Coronal alignment of the ankle was assessed on the AP view or by measuring the angle formed between the long axis of the tibia and a line perpendicular to the superior surface of the talus or the talar implant. In cases of severe bony erosion, measurement relied on the sidewalls of the talus. Migration of the implant was assessed by comparing radiographs taken immediately after operation with those at follow-up. The range of movement was determined radiologically by measuring the movement between the tibial and talar implants in the lateral view in maximum dorsiflexion and plantar flexion, using lines drawn along the inferior edge of the components. Substantial medial or lateral overhang between the tibial and talar components in the AP view was considered to

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Table I. Demographic data of the patients

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of ankles (patients)</th>
<th>Mean age in yrs (range)</th>
<th>Male/female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>52 (50)</td>
<td>56.6 (26 to 80)</td>
<td>8/44</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>73 (68)</td>
<td>56.9 (18 to 86)</td>
<td>40/33</td>
</tr>
<tr>
<td>Other</td>
<td>5 (5)</td>
<td>47.2 (28 to 64)</td>
<td>2/3</td>
</tr>
<tr>
<td>All diagnoses</td>
<td>130 (123)</td>
<td>56.4 (18 to 86)</td>
<td>50/80</td>
</tr>
</tbody>
</table>

Fig. 1

Examples of osteolytic lesions in CT scans and plain radiographs, and distribution of lesions in plain radiographs (red for all lesions and blue for marked lesions).

be ≥ 3 mm, as at this extent the UHMWPE insert protrudes beyond the edge of the metallic component.

Radiolucency was defined as a complete radiolucent line < 2 mm in width, and osteolysis as discrete, well-circumscribed areas of lucency ≥ 2 mm wide in the peri-prosthetic bone. The surrounding areas divided into zones to describe the location of lucencies and lyases (Fig. 1). The osteolytic lesions were classified by size, and lesions ≥ 10 mm were considered to be ‘marked’.

In cases of marked osteolysis on standard radiographs, helical CT was undertaken using a Siemens Somatom Sensation 64-slice helical scanner (Siemens AG Medical Solutions, Erlangen, Germany) with a metal artefact-minimising protocol.

Revision surgery and samples. Of the 27 ankles with marked osteolysis, 16 have undergone revision giving a rate of revision of 15.5%. Of these, seven had a porous Ti-HA coating and nine an HA coating only. Two patients refused revision. At revision, samples were taken from the joint capsule, the joint fluid, and the contents of the cavities for microbiological and histological analysis. For histological examination the samples were fixed in formalin and stained with haema-
toxylin-eosin and van Gieson stains. Serial sections 4 μm to 10 μm were made from paraffin-embedded specimens and studied by light and polarised-light microscopy.

Back-scattered electron imaging with a scanning electron microscope (BEI-SEM) (Leo Gemini 1530; Carl Zeiss SMT AG, Jena, Germany) equipped with energy-dispersive radiographic (EDX) analysis was carried out on histological samples, showing debris particles under light microscopy and from some removed implants. The sample surface was coated with a thin layer of carbon. The EDX analysis was used for identification of the elements.

For the analysis of elements in the periprosthetic tissue, the samples were dried to constant weight and the organic material of bone samples were destroyed with a mixture of nitric, sulphuric and chloral acids (perchloric). The analyses were performed with the ICP-MS technique (Thermo XSeries2 ICP-MS, Thermo Electron Corporation, Waltham, Massachusetts, equipped with collision reaction cell). Scandium, germanium and platinum group metals were used as internal standards. This is based on the NIOSH 7000 series methods. The standards were made in acidified solutions, and for some rare elements a semi-quantified method was used. The detection limit for the elements analysed was at least < 0.0001 mg/g.

**Statistical methods.** Statistical evaluation was carried out using SPSS software (version 16.01; SPSS Inc., Chicago, Illinois). Survival curves with osteolysis as an endpoint were established using the Kaplan-Meier method, and implants were compared with the log-rank test. Cox’s proportional hazards model was used to analyse whether the type of implant or any demographic factors influenced the risk of osteolytic lesions. A p-value of < 0.05 was considered statistically significant.

**Results**

Radiolucent lines or osteolytic lesions were seen on plain radiographs in 48 (37%) ankles. Only two patients had isolated radiolucent lines; the others had osteolysis to some extent. Marked osteolytic lesions were found in 27 (21%) of the ankles (Fig. 1). The most common site of the lesions was around the tibial stem in both AP and lateral radiographs (Fig. 1). Helical CT was carried out on 26 of the 27 ankles with marked osteolysis. Examples of typical lesions are shown in Figure 1. There was an approximately similar number of lesions around the tibial stem and under the talar component. The risk for osteolysis was found to be 3.1 (95% CI 1.6 to 5.9) times higher with dual-coated implants than with implants having HA coating alone (p = 0.001). The Kaplan-Meier survival curves of implants with osteolysis as the endpoint are shown in Figure 2. Progression of the lesions was seen in sequential radiographs in 16 (33%) ankles with osteolysis. Substantial overhang was detected in nine ankles and in three with osteolysis, but this finding was not statistically significant (p = 0.21).

Male patients were found to have a 2.0 (95% CI 1.13 to 3.6) times higher risk of osteolysis (p = 0.018), but not marked osteolysis (p = 0.08). None of the other demographic factors, including age (0.47, p = 0.82), diagnosis (1.00, p = 0.92), and bisphophonate (0.68, p = 0.88) or anti-TNF therapy (0.11, p = 0.44), were found to be significant risk factors.

The talar component migrated in nine ankles (7%) and of these a shift of the tibial component was also found in two. Predisposing to migration of the talar component, there were two cases of talar necrosis, one deep infection with talar necrosis, one neuropathic arthropathy, four osteolyses and one with no specific reason. The migration of one tibial component was minimal and was associated with
migration of the talar prosthesis due to osteolysis. Another had malalignment and osteolysis around the tibial component. The relationship of the migration of components to osteolysis and required surgery is shown in Table II.

**Revisions for osteolysis.** At revision, 15 patients had marked osteolysis around the tibial and/or the talar components, and one had a large lesion in the lateral malleolus. This patient had a prosthesis with HA coating only. Revision of the lesion in the lateral malleolus included debridement and grafting with allogenic cancellous bone. This lesion healed well, but a minor osteolytic lesion has developed around the tibial stem. The bacterial samples revealed no growth and histological examination showed mainly fibrosis, with no apparent foreign-body reaction or the presence of wear particles.

At revision of the other ankles, there were large lytic cavities around the components (Fig. 3) containing brownish-grey, granulomatous necrotic material, but with no visible metallosis in the surrounding tissues. In 12 ankles both the tibial and the talar components were stable in spite of large cavities. Debridement of the lesions and grafting with allogenic cancellous bone was carried out with exchange of the polyethylene inlay. In three ankles with HA coating one of the components was loose and arthrodesis was undertaken. All the polyethylene inlays appeared intact. Bacterial cultures and staining of samples taken from the joint capsule, joint fluid and the contents of the cavities were sterile. The majority of the histological samples contained large acellular, necrotic areas in which the original tissue could not be identified, and wear debris was absent. There was an increased number of histiocytes containing small, sharp particles of foreign material, which were best seen with polarised light (Fig. 4). A few giant cells were also present in these areas. The number of osteoclasts was increased compared to normal bone tissue, and there were sporadic lines of resorption in the healthy bone. The histological findings were interpreted as a foreign-body reaction.

The BEI-SEM/EDX analysis of samples from Ti-HA ankles revealed several micrometre-sized particles of titanium and Co-Cr (Fig. 3), but particles of polyethylene could not be identified in the tissue with the methods available.

Analysis revealed measurable values of titanium, Cr, Co, aluminium and molybdenum in the Ti-HA samples. The value for titanium was 230 ± g/g of dry tissue and for Cr 18, Co 11, aluminium 1.7 and molybdenum 1.2 ± g/g of dry tissue, respectively.

**Discussion**

We describe our experience of 130 AES TARs with a high percentage of early-onset and rapidly progressing peri-prosthetic osteolysis. There have been several short-term studies of modern ankle implants, and although the survival rates are inferior to those of hip and knee replacements,
they are considered acceptable.\textsuperscript{1-13} However, there are concerns regarding the longer term. Loosening of the components is a major problem, and the rate of revision in the published series has been high (up to 26\%).\textsuperscript{1,4,8-14}

The precise pathogenesis of osteolysis remains unclear, but both biological and mechanical factors appear to contribute.\textsuperscript{15,16} In arthroplasty of the hip, osteolysis is regarded as a foreign-body reaction due to wear particles of cement, polyethylene or metal.\textsuperscript{15,16} Numerous pro-inflammatory cytokines participate in the process in response to these particles, and recent studies have shown that the receptor activator of NF-kappaB/receptor activator of NF-kappa B ligand/osteo-protegerin (RANK/RANKL/OPG) pathway might have a crucial role in osteoclastogenesis and osteolysis.\textsuperscript{15,16} Macrophages are considered to be the major source of pro-inflammatory mediators, but fibroblasts and presumably T lymphocytes are also involved in the process.\textsuperscript{15,16} Wear particles are considered the single most important factor in the development of osteolysis, but the specific nature of this process is likely to be dependent on the patterns of wear, the type of prosthesis and host factors.\textsuperscript{15}

A high incidence of osteolysis has been described with TAR.\textsuperscript{1-4,7,8} However, in some studies the bone mineral density has been shown to increase adjacent to HA-coated implants.\textsuperscript{18,19} In the study by Knecht et al,\textsuperscript{1} osteolytic lesions were detected in up to 76\% of ankles with the Agility implant (DePuy, Warsaw, Indiana). Subsidence of the tibial component was associated with a circumferential lucency. The authors defined lytic lesions in two different categories: expansile and mechanical. The latter has previously been labelled ‘ballooning’ lysis\textsuperscript{1} and is an early-onset and usually non-progressive lesion. Expansile
ysis, however, was late onset, progressive, and secondary to wear. Although the Agility implant is a second-genera
tion design, similar findings of osteolytic cavities have been reported from third-generation implants.\textsuperscript{2,4,8} In our study both types of lesion were seen.

The problem with osteolysis may be greater than previ
ously described as plain radiographs underestimate the size
of the lesions. In the study by Hanna, Haddad and Laz
arus,\textsuperscript{20} most of the osteolyses present in the talus were visible on the radiographs, whereas the CT scans showed only enormous lesions. In the series of Valderrabano et al,\textsuperscript{4} three of 68 patients with a Scandinavian Total Ankle Replacement (STAR; Waldemar Link, Hamburg, Germany) had ballooning lysis. Histological examination by light microscopy of the sample taken from the joint capsule at revision in one patient showed a mass of polyethylene particles surrounded by active foreign-body giant cells. Similar histological findings have been observed in

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**Fig. 5**
Examples of BEI/SEM micrograph and energy-dispersive radiographic analysis spectra of two histological samples showing Ti and Co-Cr particles, and BEI/SEM micrograph of one removed polyethylene inlay showing scratches filled with hydroxyapatite.
aggressive granulomatous lesions associated with hip arthroplasty. Nevertheless, most of the wear particles are presumably smaller than the resolution of the light microscope.

In hip arthroplasty the implants can be still well fixed despite large surrounding granulomatous lesions. Some authors consider that these lesions are different from aseptic loosening. Some observations in the literature and our own results support this view with ankle arthroplasty. Most of our patients with osteolysis were asymptomatic, and most implants at revision were firmly fixed.

Small, non-progressive areas of lucency around the components have been considered a benign finding due to stress shielding and remodelling of the distal tibia. In a study of the Agility implant by Pyevich et al. the amount of titanium in the analysis of elements was high compared to that of other metals, particularly Co and Cr. The BEI-SEM/EDX analysis revealed titanium and Co-Cr particles in the periprosthetic tissue. Although titanium and its alloys are widely used in total joint replacement because of their biocompatibility, high corrosion resistance and non-allergenic nature, wear debris can be formed as a result of the softness of titanium.

In one recent case report, a titanium porous coating was thought to have become detached from the humeral stem, causing osteolysis after a total shoulder replacement. In vitro, submicrometre particles of titanium have been shown to stimulate the release of pro-inflammatory mediators of macrophages even more than polyethylene particles, thereby enhancing the osteolytic potential of the monocytomacrophage cells. Titanium and soluble Co and Cr ions interfere with the function of human osteoblast-like cells and simulate fibroblasts to support osteoclastogenesis, presumably via the RANK/RANKL/OPG pathway.

We believe that particles may be detached from the surface of the AES implant by excessive shear stresses causing aggressive, granulomatous-type osteolyses. In previous studies with hip arthroplasty, implants with circumferential porous coating have been shown to have superior osseointegration and a reduced incidence of osteolysis compared to smooth-surfaced implants. With TARs there is no available information as to the effect of different coatings in non-cemented implants. Wood and Deakin described their experience with the STAR implant in 2003. Where HA was applied directly onto Co-Cr there were 7.5 times more likely to be radiolucent lines than with the dual-coating of titanium and calcium phosphate. However, only seven cases (3.5%) had osteolysis. These findings are the opposite of those seen in our study.

We do not attribute osteolysis in our patients solely to polyethylene disease, because of the early onset of the lytic lesions and the observation that the polyethylene inlays were not significantly damaged. Some authors have suggested that overhang causes osteolysis by causing excessive polyethylene wear, but this was not seen in this study. With the HA-coated prosthesis third-body wear may be a contributory factor. In BEI-SEM/EDX analysis from one removed polyethylene inlay there were scratches filled with crystallised HA, possibly capable of causing accelerated wear. The changes in component design with the use of porous pure titanium with HA coating has increased osteolysis with the AES prosthesis.

We consider that osteolyses in ankle arthroplasty can be caused by polyethylene wear, third-body wear due to HA or by the direct action of metal particles from the implants produced by stress shielding. All the current commercial ankle prostheses contain Cr, Co, HA and titanium. As the designs resemble each other, it is likely that osteolysis also occurs in these other prostheses. Few objective data on implant survival have been published apart from recent reports from national arthroplasty registries. We consider that the use of ankle arthroplasties should be avoided before the reason and extent for the problem of osteolysis has been solved.

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