One stage uncemented revision of infected total hip replacement using cancellous allograft bone impregnated with antibiotics

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Infection of a total hip replacement (THR) requires component removal and thorough local debridement. Usually, long-term antibiotic treatment in conjunction with a two-stage revision is required. This may take several months. One-stage revision using antibiotic-loaded cement has not gained widespread use, although the clinical and economic advantages are obvious. Allograft bone may be impregnated with high levels of antibiotics, and in revision of infected THR, act as a carrier providing a sustained high local concentration.

We performed 37 one-stage revision of infected THRs, without the use of cement. There were three hips which required further revision because of recurrent infection, the remaining 34 hips (92%) stayed free from infection and stable at a mean follow-up of 4.4 years (2 to 8). No adverse effects were identified. Incorporation of bone graft was comparable with unimpregnated grafts.

Antibiotic-impregnated allograft bone may enable reconstruction of bone stock, insertion of an uncemented implant and control of infection in a single operation in revision THR for infection.

The treatment of an infected total hip replacement (THR) commonly requires removal of the implant, radical debridement, and long-term antimicrobial treatment. Eradication of infection is difficult because of the high resistance of bacteria to antibiotics, adhering to foreign bodies within biofilms1,2 and the poor penetration of antibiotics into infected bone.3,4 Local administration of high-dose antibiotics has been used to overcome the problems with systemic antibiotic delivery. In order to optimise local antibiotic administration a carrier with good biocompatibility and storage capacity is needed. Buchholz and Engelbrecht5 have used polymethylmethacrylate (PMMA) cement impregnated with various antibiotics since 1970 and subsequently developed a technique of cemented one-stage revision of infected THRs.6 However, this technique had several disadvantages and acceptance was low among the orthopaedic community, but the principles of local antimicrobial delivery gained widespread use, in the form of spacers in two-stage revisions. Unfortunately, even antibiotic-loaded PMMA may act as a bed for colonisation with selected bacteria7 and a novel approach is necessary.

At revision of an infected THR, after removal of implants and debridement of necrotic bone, bony defects remain. Impacted cancellous allograft bone is commonly used to restore bone stock and give mechanical support, but only after a period of systemic antibiotic therapy, while signs of infection decline and blood indices return to normal. Otherwise, the allograft is likely to become re-colonised with any remaining bacteria. Allograft bone has previously been used as a delivery vehicle for antibiotics. Witso et al8 used netilmicin-impregnated allografts for reconstruction in revision hip or knee surgery and found no adverse effects. Buttaro, Russo and Piccaluga9 and Buttaro et al10 favourably used vancomycin-supplemented cancellous grafts for reconstruction after infected THR. Michalak et al11 and Khoo et al12 impregnated segmental allografts with gentamicin and flucloxacillin, respectively. However, all those groups have used antibiotic-impregnated grafts only in the second stage of a two-stage revision, after resolution of clinical and laboratory evidence of infection. Uncemented reconstruction of failed THR has been recommended by several authors.13-15 However, all of them have excluded its use in cases with florid infection. Our own studies, using a proprietary impregnation technique, revealed markedly higher concentrations of antibiotics inside processed bone grafts with a further prolonged release for
several weeks compared with the unprocessed grafts used by
and Lawrence18 on the acetabular side (Fig. 1) and any
defects not exceeding type 2 according to Paprosky, Perona
revision THR with culture-proven deep-infection. Bone
(hematogenous) in 16 hips, respectively.

Patients and Methods
Between 1998 and 2004 we treated 37 patients with an
infected THR. Operations were performed in the index
clinic (Weinviertelklinikum Mistelbach) (20 hips) and vari-
ous other hospitals (17 hips) by the senior author (HW).
Follow-up of these 17 hips was in our Osteitis Center
(Vienna, Austria).

There were 17 men and 20 women with a mean age at
revision of 68.5 years (42 to 83). Infections were classified
according to the Mayo Clinic classification17 as early
(acute) in 12, low-grade (chronic) in nine and late
(hematogenous) in 16 hips, respectively.

This study included all patients undergoing one-stage
revision THR with culture-proven deep-infection. Bone
defects not exceeding type 2 according to Paprosky, Perona
and Lawrence18 on the acetabular side (Fig. 1) and any
defects on the femoral side were included. In all hips a
lateral transfugate approach was used. All the acetabular
implants were removed, even when they were well fixed,
but five uncemented femoral implants were retained as they
were completely integrated. The remainder were removed
with minimal damage to the remaining bone. Meticulos
excision of all cement, granulation and necrotic tissue was
performed. Debridement was completed using saline pulsed
lavage. The extent of the bone defects was evaluated and
the defect then filled with antibiotic-impregnated allograft.
The allograft was from tibial and femoral metaphyses of
cadaver donors, procured according to the standards of the
European Association of Tissue Banks.19 The retrieved can-
cellous bone was morsellised to granules with a diameter of
between 2 mm and 8 mm and lavaged with ether and
alcohol to remove fat, marrow and adhering soft tissue.
After lyophilisation and packaging, sterilisation was per-
formed by gamma irradiation. The allograft was stored at
room temperature. Immediately preceding surgery, the
allograft was impregnated with antibiotic, using a specific
incubation technique.16 The choice of antibiotic, vanco-
mycin or tobramycin, depended upon the causative patho-
gen. Vancomycin was used in all cases, but tobramycin was
added in cases of mixed infections. The impregnation pro-
cedure produced an antibiotic-bone compound with high
levels of antibiotic inside the graft; vancomycin levels were in
the range of 100 mg/cc of bone and; tobramycin levels were in
the range of 75 mg/cc of bone. The mean amount of anti-
biotic-bone compound used per case was 75 cc (30 to 150).
On the acetabular side, this was impacted into the defects
using a modification of the technique described by Schreurs
et al.20 The choice of implant depended upon the size of the
bony defects; in cases with minor defects (Paprosky type 2)
a threaded conical acetabular component (Alloclassic
Zweymueller; Zimmer, Warsaw, Indiana) was used, while
larger defects (Paprosky type 2) required a hemispherical
acetabular component with or without additional screw
fixation (Allofit, Zimmer). On the femoral side we rou-
tinely used a rectangular-diameter titanium stem (Alloclas-
L component where there was good femoral bone stock, and the oblong
SLL component where there was marked metaphyseal bone
loss. If a lateral osteotomy was required, it was secured
with one or two titanium cerclage bands. All components
were inserted using a press-fit technique without the use of
cement. Fixation intra-operatively was regarded as stable in
all cases. Additional antibiotic-bone compound was placed
around any uncovered parts of the implants and impacted
for stability. In general, this was implanted on the medial
wall of the acetabulum, in the femoral medullary cavity and
around the proximal half of the Zweymueller component
(dorsally and ventrally) (Fig. 2). It was important that the
fixation of the implant mainly relied on the original bone,
around the distal third of the component and the rim of the
acetabulum. Wounds were drained and closed and rehabil-
itation was commenced as per a routine revision opera-
tion.21 Peri-operative intravenous antibiotic treatment was
according to susceptibility testing for two weeks, usually
with second-generation cephalosporins or, in cases with
methicillin resistant Staphylococcus aureus (MRSA), with
fusidic acid. Post-operatively, levels of vancomycin were
monitored both in the drainage fluid and in serum for two
to three days.
Intra-operative cultures grew coagulase-negative staphylococci in 19 hips, *Staph. aureus* in 11, MRSA in five, enterococci in eight, and other gram-positive pathogens in six. In eight hips gram-negative organisms were also identified. All organisms were susceptible to vancomycin, tobramycin, or both. Patients were reviewed at two weeks, six weeks, three months, six months and one year after surgery. Follow-up included clinical and radiological examination, and blood tests including C-reactive protein, erythrocyte sedimentation rate, white blood cell count, urea and creatinine. A successful outcome was defined as a stable implant without clinical, radiological or laboratory evidence of infection.

**Results**

Post-operative rehabilitation in patients with a short history of infection (up to three months) was similar to rehabilitation after an uncomplicated primary THR. However, lengthy rehabilitation was required in cases of prolonged infection.

The mean follow-up was 4.4 years (2 to 8). There was recurrence of infection in three hips, two of which were diagnosed between six and 12 weeks after operation. In one hip the well-fixed femoral component had not been exchanged, in the other a technical error during impregnation of the bone graft was noted. Both patients underwent successful revision using the same technique with complete removal of components and use of appropriately impregnated bone graft, and remain free of infection at the latest follow-up. In the third hip, infection recurred after six months; *Staph. aureus* was cultured as in the previous revision. This patient underwent resection arthroplasty in another hospital.

At latest follow-up 34 hips (92%) showed no signs of infection. C-reactive protein values remained normal and were not significantly different when compared with the findings after an uncomplicated THR.

Radiological examination revealed partial resorption of allograft bone in non-weight-bearing areas, while in weight-bearing areas, increased density was observed. Parts of the allografts, especially in the femoral diaphysis remained unchanged at latest follow-up. In general, the allografts appeared to follow the established patterns of incorporation compared with normal allograft with uncemented implants.15,23 There were no signs of loosening in any of the components during the period of follow-up (Fig. 3).

**Discussion**

One-stage revision of an infected THR is attractive because of reduced burden for the patient and economic advantages. However, this technique is rarely used and only ever with cemented components (with cement as the antibiotic carrier). Bone cement can provide local antibiotic levels which exceed levels achieved by parenteral delivery,24 but the mechanical properties of cement are diminished, and *in vivo* levels are still estimated to be insufficient by many surgeons, leaving two-stage revision as the present technique of choice.25-28 Antibiotic-bone compound is a powerful carrier, likely to outperform the properties of PMMA in most aspects. The mechanical properties of cement are not of relevance since fixation relies on press fit with original bone and as the local antibiotic concentration is increased both immediately after implantation and in the following weeks,29 there should be less risk of the development bacterial resistance due to subinhibitory concentrations originating from old PMMA,30 and there is a good chance of allograft integration into osseous defects. Uncemented implants, both on the femoral and the acetabular side, are likely to provide better long-term results in revision cases than cemented systems.31 The technique of using antibiotic-bone compound in combination with uncemented implants...
techniques and concentrations were used by Witso et al.32,33
sent a volume equivalent to 50 cc of cancellous bone. Similar
immediate post-operative drainage fluid, as we did in our
Both groups found comparable levels of antibiotic in the
improved long-term results, all within a single revision pro-
procedure. It must be emphasised that antibiotic-bone com-
ound can only be considered one tool within a complex
treatment protocol, which follows the established princi-
pies of revision surgery for infection.
To date, impregnated bone grafts have been used by other
groups as a prophylactic measure in patients with a high risk
of infection but without any florid signs of infection. But-
taro’s group added 500 mg of vancomycin powder to one
morsellised femoral head,9 which may be estimated to repre-
sent a volume equivalent to 50 cc of cancellous bone. Similar
techniques and concentrations were used by Witos et al.32,33
Both groups found comparable levels of antibiotic in the
immediate post-operative drainage fluid, as we did in our
series. However, we could show that with our impregnation
technique, 5 g of vancomycin may be incorporated into the
same volume of cancellous bone graft, which represents a
tenfold concentration. We conclude that our impregnation
technique is likely to provide a biphasic antibiotic release: the
superficially-adhered antibiotic seems to be active immedi-
ately but this only represents approximately 10% of the total
implanted dose. The additional nine times greater dose,
bound to the osseous structures of the graft, is presumed to
be released slowly between two and eight weeks after opera-
tion. The sustained release of antibiotic may protect both the
graft and the implant from recolonisation, even in markedly
contaminated areas, and simultaneously may eradicate the
remaining bacterial colonies. We consider these kinetics to be
a fundamental prerequisite for a one-stage revision.
Although extremely high concentrations of antibiotic
were present at the operative site we did not see any adverse
effects, confirming the results of similar studies.34 The local
wound healing and remodelling of the graft seem not to be
impaired by these high concentrations of antibiotic. This
may be because of the low cytotoxic property of vancomycin
and tobramycin, respectively.35-37 We did not observe any
differences in the biological behaviour between our impreg-
nated allografts and existing allograft described in the
literature.23 Both are well incorporated in regions where a
physiological stress is present and are resorbed or remain
static in unloaded areas.
Studies investigating the diffusion rates of vancomycin
into biofilms were suggested that the minimum bactericidal
concentration of vancomycin required to eliminate staphy-
lcocci embedded in biofilms is 200- to 600-fold greater
than the minimum bactericidal concentration for freely
floating planktonic cultures.38,39 Such concentrations can
ever be reached by parenteral administration or by estab-
lished carriers like PMMA. Therefore it has been consid-
ered mandatory to remove all implants for eradication of
infection. Since antibiotic-bone compound can create and
maintain local antibiotic concentrations more than 1000
times the minimum bactericidal concentration of relevant
pathogens for several days,16 it is possible that closely-
adjacent antibiotic-bone compound might be sufficient to
eliminate even biofilm-embedded bacteria. Such a possibil-
ity potentially avoids the need to remove well-incorporated
implants. However, leaving an implant in situ makes it
impossible to examine its whole surface. Hidden, or more
distant colonies may be isolated from sufficient antibiotic
diffusion and be the origin of later recurrence. In our series,
five femoral components had been well fixed and were left
in place, surrounded by antibiotic-bone compound. While
four of the hips did not show any sign of recurrence, one re-
infection occurred 12 weeks after operation. We believe
that undetected colonies may explain the failure in this case
and, therefore, still recommend removing well-
incorporated implants. If removal is only feasible with
destruction of original bone it is the surgeon who should
calculate the risks of retention versus removal.
Deep infection with MRSA is considered a particular
threat in THR surgery. Published treatment protocols
include repeated surgery and markedly prolonged hospital
stays39 Positive results are infrequent with a success rate of
approximately 50%. One reason for the poor outcome is
the limited availability of effective antibiotics, most of
which show unfavourable kinetics when administered sys-
temically. Local application of vancomycin in sustained
high concentrations may be a solution to this problem. In
our series, five deep infections caused by MRSA were
treated successfully with a one-stage revision.
To the best of our knowledge this is the first report in literature describing one-stage THR without the use of cement. Although numbers are small, it seems that one-stage uncemented revision, in combination with antibiotic-bone compound, provides an excellent tool in the treatment of infected THR. Further studies are needed to answer questions like possible retention of implants and the long-term behaviour of the reconstructions. The prescribed technique of uncemented reconstruction is applicable to all defects on the femoral side but restricted to acellular defects of Paprosky type 1 and 2. In our opinion, infection-related type-3 defects still require the use of cement.

In conclusion, antibiotic-impregnated bone grafts may provide increased local antibiotic concentrations at the site of infection as well as simultaneous repair of osseous defects. Uncemented one-stage revisions for infection appear feasible. A success rate of 92% may be achieved, which is comparable with the results of two-stage exchange procedures but without the obvious disadvantages of two operations and the period of disability between them. For the treating team there is a markedly reduced burden of operations and the period of disability between them. For the patient there is a marked reduction of disability and pain with improvement of post-operative function; while for the treating team there is a markedly reduced burden of peri-operative care, and for society a significant cost-saving may be expected.

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References