Gene therapy and cement injection for the treatment of hip prosthesis loosening in elderly patients

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Percutaneous periprosthetic cement injection as an alternative treatment for aseptic hip prosthesis loosening in elderly patients with significant comorbidity. A report of seven cases.

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Abstract

Background

Elderly patients are sometimes not eligible for revision arthroplasty due to high mortality risks. Previously, a minimal invasive approach was developed to percutaneously inject bone cement periprosthetically after removal of interface tissue using a suicide gene therapy approach. This case series was performed to investigate the possibility of injecting bone cement around the loosened prosthesis without previous removal of the interface.

Methods

Seven patients with high morbidity risks due to high age, serious comorbidity or low bone stock were treated with percutaneous, periprosthetic cement injection. Patients had spinal anaesthesia and bone cement was injected after CT-guided placement of vertebroplasty needles. The amount of cement that could be injected and the distribution in the periprosthetic space was recorded. Patients were followed up in the outpatient clinic.

Results

A mean volume of 16 ml of cement could be injected around the stem and 5.5 ml around the cup. All seven patients reported improvement in walking distance and pain.

Interpretation

This small case series shows that bone cement can be injected periprosthetically in patients with loosened hip prostheses, as an alternative for revision surgery in high risk patients. Due to small patient numbers no conclusions can be drawn on the necessity to remove interface tissue before injecting bone cement to stabilise aseptically loosened prostheses.

Introduction

Revision surgery for hip prosthesis loosening has a high complication rate in elderly patients with comorbidity.[6,92,99,114] Revision hip arthroplasty is associated with a higher number of complications and less improvement in social outcome compared to primary hip arthroplasty.[103] Due to the tendency to insert orthopaedic implants in younger patients and their longer life expectancy, the number of revision surgeries in elderly patients is likely to increase considerably in the next decades. Kessler *et al*.[64] concluded that duration of surgery, which is about 3 times longer in revision than in primary surgery, is the main indicator for the severity of the operation. Elderly patients with ASA-category 3 and more (American Society of Anaesthesiologists)[121] are at higher risk for developing major and moderate complications after revision hip arthroplasty.[6]

One of the major difficulties in revision surgery is the removal of cement from the femoral shaft, without fracturing the femur. Biomechanical studies showed that recementing can give a good interface strength with the old cement.[49] Lieberman *et al.*[73] showed this in practice in 19 patients where a new prosthesis was cemented in an old cement mantle. In a previous study we showed that bone cement can be injected percutaneously in the periprosthetic space of loosened hip prostheses after the interface tissue was removed with a suicide gene-directed enzyme-prodrug therapy (GDEPT).[28] Some of these patients had to be recemented after 6 months, with successful relief of symptoms. Therefore, and to bypass the more complicated GDEPT-approach, we refixated prostheses in patients that were at high risk for perioperative morbidity. In a small case series of percutaneous peri-prosthetic cement injections, the results for this increase of stabilisation of loosened hip prostheses were evaluated.

Materials and methods

Patients

Goal was the evaluation of CT-guided periprosthetic percutaneous cement injection to increase stabilisation of aseptically loosened total hip prostheses. Patients with debilitating pain from a loosened hip prosthesis and a high perioperative morbidity and mortality risk if revision total hip arthroplasty was performed, were included. Risks were advanced age, serious comorbidity, and low bone stock. Before the procedure, laboratory tests (ESR, CRP) were done, and a routinely performed arthrogram was made with aspiration of joint fluid to exclude the presence of a (low-grade) infection and to verify loosening of the prosthesis. Furthermore, marcainisation of the hip joint was performed to confirm that the pain experienced by the patient was due to

a loosend hip prosthesis. Patients who had undergone previous peri-prosthetic percutaneous cement injections combined with gene therapy[28] were excluded from the case series. Patients undergoing the cement injection were admitted to the hospital for 1 or 2 days. On the first day bone cement was injected peri-prosthetically in a predefined space as described below. Depending on post-procedural pain and / or travelling distance patients stayed overnight before returning home. Patients were then once seen for follow-up in the outpatient's clinic, or at a later time point whenever patients were capable.

Cementing technique

On previously performed routine radiographs and a CT-scan of the hip and pelvis the areas most suitable for cement injection were identified. These were the areas with the widest periprosthetic radiolucency. All patients were screened by the anaesthesiologist prior to the procedure and underwent spinal anaesthesia preferably. Patients were positioned supine on the CT-table with a marker grid fixed to the patient's hip region and a planning CT-scan was performed. The markers and planning CT were used to exactly define the positions for introduction of the needles through the skin and the angle by which the needle needed to be introduced to reach the designated periprosthetic radiolucent zone. In this way 3 to 5 points were marked on the skin for introduction of the needles. All patients received prophylactic antibiotics (cephalosporin) intravenously as is routinely used for any arthroplasty procedure. The hip and groin region were then disinfected and sterilely covered, and 3 to 5 vertebroplasty needles of 1.8 or 3.2 x 100 mm (Biomet, Dordrecht, The Netherlands) were introduced with soft blows into the periprosthetic space where the cortex was thinnest (usually <2mm), using a hammer, advancing 1-2 mm per blow and controlling the position with CT-scan (Figure 1). If the cortex was too thick (i.e. >3mm) a needle with a drill bit was used first, after which the cement needle was used. The areas where the radiolucent zones were widest were preferrably chosen as entrance points. The position of the needles and the depth of the insertion were then controlled by CT guidance (Figure 2). The needles were turned in such a way that the opening faced the prosthesis to minimise leakage of the cement. After placement of the needles the fluoroscopy C-arm was positioned over the patient (Figure 3). Polymethylmethacrylate (PMMA) cement (Osteopal [Biomet] or Disc-OTech [Disc-O-Tech Medical Technologies, Herzeliya, Israel]) was injected into the periprosthetic space under high pressure with a Cementoset (Biomet). During injection, the flow of the PMMA cement was continuously monitored by fluoroscopy, and intermittantly with CT-scan. Injection was continued until the periprosthetic space was filled or until the cement

Figure 1. CT-guided placement of vertebroplasty needles in the periprosthetic space around stem and cup a) and cement injection under fluoroscopic guidance (b).

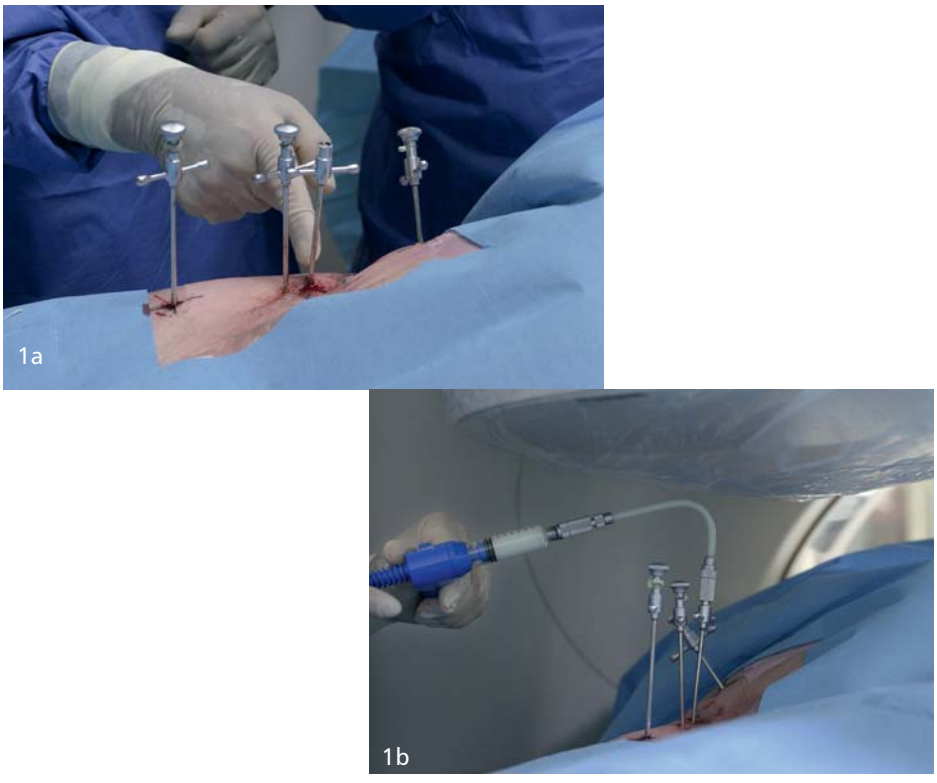


Figure 2. CT-guided verification of correct needle tip position. Needle tip is facing the prosthesis

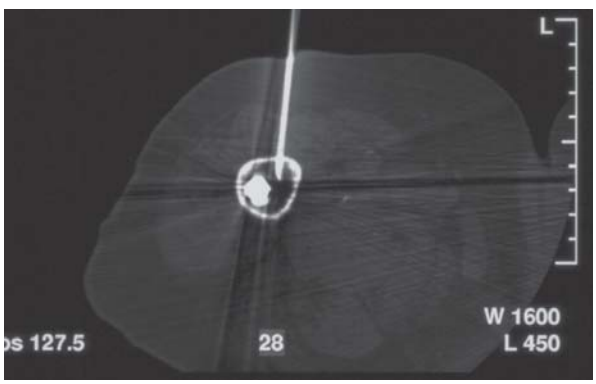


Figure 3. Positioning of the fluoroscopy C-arm over the patient (a) and position of the fluoroscopy C-arm over the patient (b).

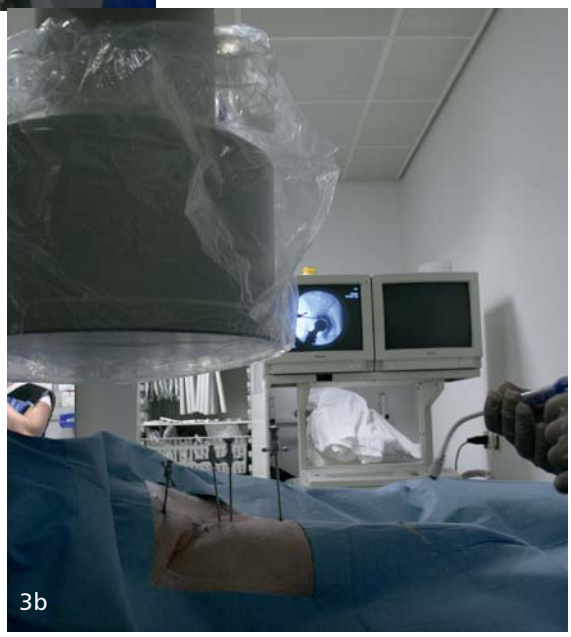
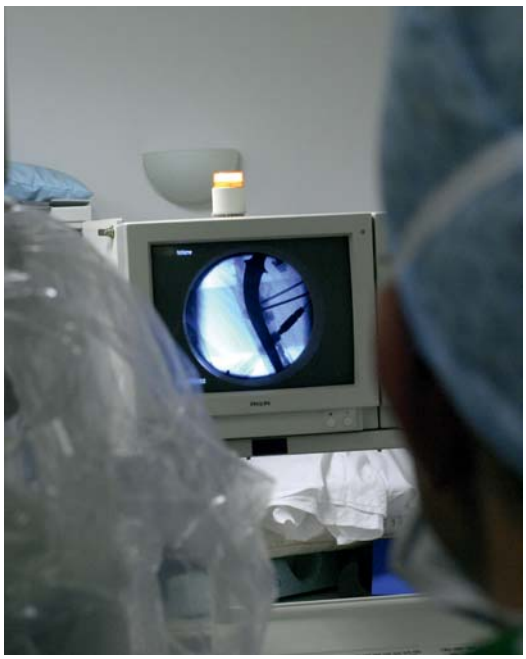


Figure 4. Fluoroscopy-guided injection of bone cement



threatened to leak into the joint space or when there was leakage of cement into the soft tissues (i.e., extraosseous) (Figure 4). Before removal, the needles were turned in a clockwise or counterclockwise manner several times to ensure easy removal.

Follow-up

Standard anteroposterior (AP) and lateral radiographs of the hip were performed in all patients pre- and post-operatively (before discharge) and whenever patients came to visit the outpatient's clinic. On the radiographic images the periprosthetic space was divided into 14 zones according to Gruen, McNeice, and Amstutz.[50] The maximal cement layer thickness was measured with Ortho-CMS software (Medis, Leiden, The Netherlands). These measurements were performed for X-rays made pre-operatively and the first post-procedural X-ray. The differences between these measurements were analysed.

The objective was to measure functional outcome in this small, diverse patient group the patients were asked about the differences in pain before and after the procedure, changes in walking distance and changes in walking aids. No statistical analyses were performed.

Table 1. Patient characteristics

Patient	Sex	Age (years)	ASA-category	Side	Age of prosthesis (years)	Volume of cement injected
1	F	88	2	R	14	Stem: 18 mL
2	F	84	3	R	20	Stem: 25 mL; cup: 12 mL
3	M	91	2	R	16	Stem: 23 mL; cup: 2 mL
4	F	83	2	R	7	Not registered
5	M	81	3	R	11	Cup: 4.5 mL
6	F	87	3	R	25	Stem: 10 mL; cup: 7 mL
7	F	76	2	R + L	17 and 16	L: stem: 10 mL; cup: 3 mL R: stem: 8 mL; cup: 4.5 mL
Mean		85	2.4		16	Stem: 16 mL; cup: 5.5 mL

Results

5 Female and 2 male patients, with a mean age of 85 years (range 76-91 years) were treated. One patient had cement injections around both hips. Table 1 shows patient characteristics and the volumes of cement that could be injected. One patient could be discharged to her home on the same day of treatment; 3 patients could be discharged the next day. The patient with injections in both hips was admitted for 3 days, and the other 2 patients were admitted for 5 and 11 days. In the patient with bilateral cement injections a periprosthetic fissure was initiated in the right femur. This patient had to mobilise with partial weight bearing for 3 months. X-rays after this period showed good consolidation of the fracture and full weight bearing was allowed. No other adverse events occurred.

Figure 5 shows an example of radiographic examination before and after cement injection in patient 2. The figure shows that the injected cement can easily spread through the periprosthetic space to provide more strength and stability. To objectively measure the changes on anteroposterior and lateral X-rays taken before and after cement injection, in each Gruen zone (except for zones IV and XI) the maximal cement thickness was digitally measured for each patient. In one patient accidentally no post-procedural X-ray was made, and consequently this patient was excluded from X-ray analysis. Figure 6 shows the mean (with standard deviation and range) increase in cement mantle thickness per Gruen zone after cement injection compared to the cement mantle before the procedure. The largest increase in cement thickness were in Gruen zones I (mean 3.8 mm, range -0.5 – 7.9 mm), zone VIII (mean 6.5 mm, range 2.1 – 13.8 mm) and zone XIII (mean 4.0, range 1.2 – 8.6 mm).

Figure 5. X-rays of right hip in anteroposterior and lateral view before percutaneous cement injection (a) and after percutaneous cement injection (b).

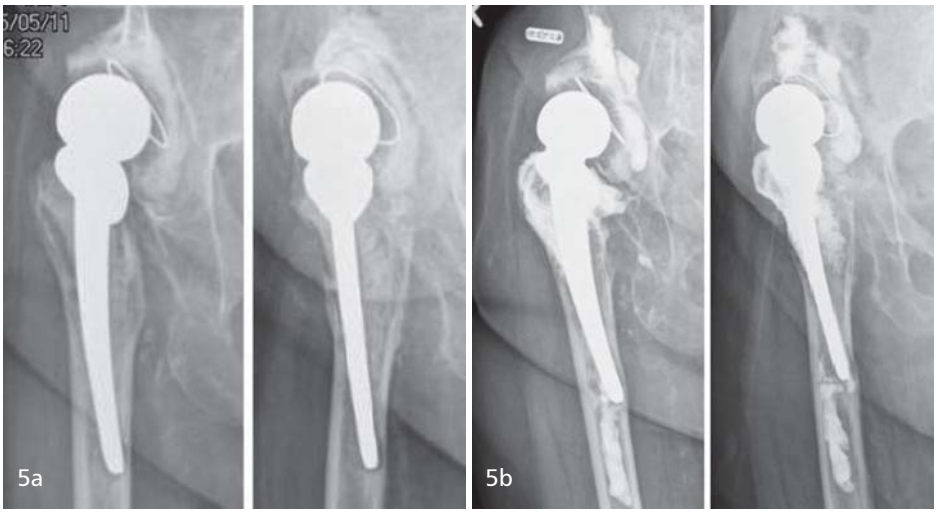
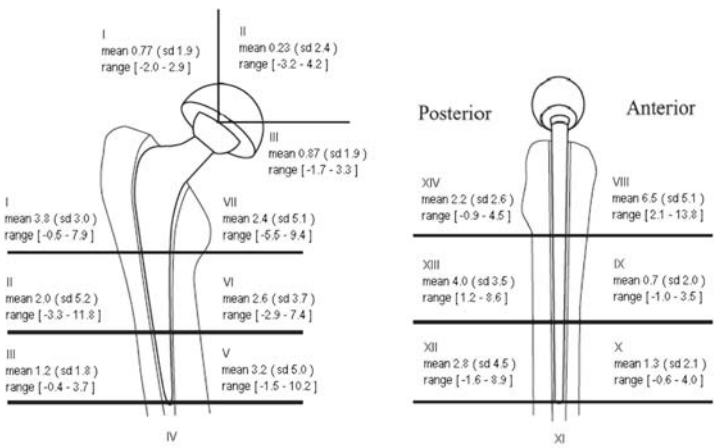


Figure 6. Increase in cement mantle thickness after percutaneous periprosthetic cement injection.



Number show mean increase in millimetres, with standard deviations in brackets and the range in square brackets.

Before the cement injection, patients were asked about the walking aids they needed and the maximal distance they could walk. After cement injection patients were asked again about the walking aids and distance, and differences in pain and performance.

Patient 1 could walk less than 500 meters using a walker and had pain in the hip before the cement injection. Acetaminophen had no effect on the pain. 14 Months after the procedure she could walk for 800 meters with a walker, she reported only mild pain in the groin, and better movement of the hip. Putting on her shoes was easier than before the cement injection.

Patient 2 could walk 50 meters with a cane in-house and used a scoot-mobile for mobilisation outside the house before the procedure. She had pain in her right hip. 10 Months after percutanous cement injection she reported no pain and she did not need home care anymore. Walking had improved.

Patient 3 had complaints of the right hip with nocturnal pain and problems with raising the right leg. His left hip was revised three times, even more both his knees showed severe osteoarthritis. He walked with 2 canes before the procedure. In order to distinguish between right joint pain and pain in the other lower extremity joints marcainisation of the right hip was performed. This completely resolved the pain in his right leg and improved his walking capability despite the instability complaints of his left leg. 12 Months after cement injection the patient reported only mild pain in the groin, he still walked with 2 canes (due to complaints of the knees and left leg), but could now do his own grocery shopping.

Patient 4 had pain in her right leg and groin for which she used Indometacin 3 times a day, Acetaminophen, and morphine. She could only walk for 40 meters with a walker in-house. 2 Years after cement injection she had no pain and did not use any painkillers. She still used a walker, but could now walk for 300 meters, and she could do her own grocery shopping.

Patient 5 had pain in his right hip and could walk 100-200 meters without any walking aids. 9 months after cement injection the patient could walk for 1 kilometre without any walking aids, and he had no pain.

Patient 6 had debilitating pain in the right hip and could only walk in-house with a walker. She used Acetaminophen as a painkiller. 7 weeks after cement injection she reported no pain and an improvement in walking.

Patient 7 had pain in both hips with nocturnal pain and pain during walking. Her walking distance was 100 meters maximum. She used Acetaminophen and tramadol as painkillers. During the procedure a fissure occurred in the right femur. Directly after the procedure she was told to minimise weight bearing of the right leg. After 6 weeks weight bearing of the right leg could be increased to 50%, and six weeks later full weight bearing was allowed. Consecutive X-rays showed increasing consolidation of

the fissure. At 10 months follow-up she still used Acetaminophen as a painkiller for pain in the left hip. She could walk 1 kilometre using 2 crutches. Pain recurred after 12 months, due to the severe bone loss and the varus position of the hips.

Discussion

This small case series shows that it is possible to inject cement around a loose total hip prosthesis percutaneously without previously removing the interface layer. However, the effect of this extra cement was different among patients. In the 7 patients a mean volume of 16 ml could be injected around the stem and 5.5 ml around the cup. All patients reported an increase in walking distance and a decrease in pain. Although peri-prosthetic cement injection is possible without removing the interface layer it seems logical that a better fixation of the prosthesis is achieved when the interface is removed. In a previous study we performed percutaneous periprosthetic cement injection in elderly patients with aseptic loosening of the hip after gene directed enzyme prodrug therapy to remove interface tissue. In this study patients also reported increase in walking distance and decrease in pain.[28] However, the gene therapy itself required at least one week hospital admittance and some of the patients suffered from systemic adverse events by the prodrug.[29] Due to the low numbers of patients in both studies no conclusions can be drawn on the best method to refix the prosthesis. Furthermore, no predictions can be made for follow-up results.

Although the percutaneous cement injection is a relatively small procedure with probably low risks for the patient, the procedure should only be performed in patients with very high risks for peri-operative morbidity and mortality during normal revision surgery. This is because normal revision surgery in low risk patients has proven to be effective and has better functional results at long time follow-up compared to the percutaneous cement injection technique. On the other hand, after percutaneous cement injection, regular revision surgery can always be considered as a last resort option. Furthermore, if a high risk patient of 80+ years has less or no nocturnal pain and can walk better for more ADL indepency with a small procedure, quality of life will be improved. Percutaneous cement injection can only be performed when fixation in the present prosthesis position will relieve the complaints, i.e., not in patients with complaints due to polyethylene wear or recurrent dislocations.

In conclusion, this small series shows that percutaneous cement injection around an aseptically loosened prosthesis without previously removing the interface tissue is a feasible approach, but based on the current data no conclusions can be made on the preference to remove the interface tissue before injecting cement. However, it seems

logical that removal of the interface tissue will give an improved stabilisation compared to a situation where this soft tissue is left in place. The patient with the best clinical results had a radiolucency of <1mm, indicating presence of little soft interface tissue.