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A retrospective study of antibacterial iodine-coated implants for postoperative infection

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Abstract

Postoperative infection is one of the most serious complications in orthopedic surgery. We have developed and use iodine-coated implants to prevent and treat postoperative infection in compromised hosts. This study evaluated outcomes using iodine-coated implants for postoperative infections.

We treated 72 postoperative infected patients using iodine-coated implants. Of these, 38 were males and 34 were females, with a mean age of 59.3 years. The mean follow-up period was 5.6 years. The patients included 23 with an infection following total knee arthroplasty, 20 following total hip arthroplasty, 11 following osteosynthesis, 11 following spine surgery, 6 following tumor excision, and 1 following osteotomy. Of these, 37 underwent single-stage surgery and 35 underwent staged revision surgery. We performed staged surgery in any case with active infection. The survival of iodine-coated implants was determined using Kaplan-Meier analysis. White blood cell (WBC) and C-reactive protein (CRP) levels were measured pre- and postoperatively. To evaluate the systemic effects of iodine, serum thyroid hormone levels were examined.

Five patients underwent re-revision surgery. In 3 patients, periprosthetic infection recurred at an average of 18 months after surgery. The reinfection rate was 4.2%. These patients recovered following reimplantation of iodine-coated prostheses. No patients required amputation. The survival rate of iodine-coated implants was 91%. There were no signs of infection at the latest follow-up. The median WBC level was nearly in the normal range, and CRP levels returned to normal within 4 weeks after surgery. No abnormalities of thyroid gland function were detected.

Iodine-coated titanium implants can be very effective in the treatment of postoperative infections. An iodine coating can be safely applied to infected regions.

Abbreviations: CRP = C-reactive protein, FT3 = free triiodothyronine, FT4 = free thyroxine, MRSA = methicillin-resistant Staphylococcus aureus, MRSE = methicillin-resistant Staphylococcus epidermidis, MSSA = methicillin-susceptible Staphylococcus aureus, MSSE = methicillin-susceptible Staphylococcus epidermidis, PJI = periprosthetic joint infections, SSI = surgical site infection, THA = total hip arthroplasty, TKA = total knee arthroplasty, TSH = thyroid stimulating hormone, WBC = white blood cell.

Keywords: infection rate, iodine-coated implant, postoperative infection, revision surgery, treatment

1. Introduction

With medical progress and societal aging, the popularity of and demand for implant surgery are continually increasing. In parallel, postoperative complications are also increasing. Postoperative infections associated with implants are among the most serious complications in orthopedic surgery. The reported rates of surgical site infection (SSI) ranged from 0.57% to 2.23% for total hip arthroplasty (THA),[1] 0.4% to 2% for total knee arthroplasty (TKA),[2] 2.1% to 8.5% for spine surgery with instrumentation,[3] and 4% to 36% for megaprostheses.[4] Revision surgery is performed if SSI occurs. Recently, the efficacy of debridement-irrigation, antibiotic therapy, and implant retention was reported for periprosthetic joint infections (PJI) and instrumented spine infections.[5,6] Standard treatment for implant-associated infections has been removal of the implant. Reported reinfection rates after revision for SSI were very high in surgery using implants, accounting for 18.2% of THA cases,[7] 28% of TKA cases,[8] and 40% of tumor prosthesis cases.[9] In spine surgery, the incidence of wound infection without instrumentation is relatively low. However, using spinal instrumentation clearly increases the risk of postoperative soft tissue infections, and recent estimates from retrospective reviews range from 2.1% to 8.5%.[3] Removal of spine instruments after postoperative infection is difficult, causing instability and deformity of the spine. Therefore, irrigation and debridement only tend to be performed for postoperative instrumented spine infection. However, the reported reinfection rate with irrigation

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and debridement was 47%.[10] It is very important to prevent postoperative infections.

Many biomaterial surface treatments have been proposed to decrease SSIs.[4,11–14] Among these, various silver coatings have been studied.[12,13] Silver coatings are already used in prostheses, and good results have been reported.[12] However, some reports have raised concerns about the toxicity of silver.[13] We have developed an iodine coating for titanium implants. The anodic oxide film was produced electrically, and use of a povidone-iodine electrolyte resulted in the formation of an adhesive porous anodic oxide with the antiseptic properties of iodine. The thickness of the anodic oxide film containing iodine was between 5 and 10 μm, with more than 100,000 pores/mm^2 and capacity to support 10 to 12 μg/cm^2 iodine. We have conducted basic research on iodine coatings since 2005 and have reported their usefulness.[15,16] A clinical trial using iodine-coated titanium implants for compromised hosts, which was approved by the ethics committee of our institution, commenced in 2008. Iodine-coated implants have been investigated for the prevention of postoperative infections.[17–20] However, we have not evaluated the outcomes using iodine-coated implants for postoperative infections in detail. It was recently reported that silver-coated hip and knee megaprostheses have been used for postoperative infections. That report found no significant reduction in the reinfection rate.[4] The present study evaluated the outcomes of iodine-coated implants for postoperative infections.

2. Patients and methods

We investigated 72 cases in which iodine-coated implants were used to treat postoperative infections between 2008 and 2015. This study was approved by the ethics committee of the institution (approval no. c-1211) in which it was performed and all subjects gave informed consent. The mean age of the patients was 59.3 years (15 to 83 years). Of these, 38 were males and 34 were females. The mean follow-up period was 5.6 years (2 to 9 years). The primary disease included degeneration of the hip, knee, and spine in 44 cases, tumor in 16, fracture in 11, and bone necrosis in 1. The patients included 23 with an infection following TKA, 20 following THA, 11 following osteosynthesis, 11 following spine surgery, 6 following tumor excision, and 1 following osteotomy. The implants included hip prostheses in 20, tumor prostheses in 19, 11 each of plates with screws and spine instruments, knee prostheses in 8, and nail with screw instrumentation in 3. The causative organisms were unknown in 50 cases, methicillin-resistant *Staphylococcus aureus* (MRSA) in 9, methicillin-susceptible *S epidermidis* (MSSE) in 3, methicillin-susceptible *S aureus* (MSSA) in 3, methicillin-resistant *S epidermidis* (MRSE) in 2, and 1 each with *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter*, *Corynebacterium*, and *Serratia*. Single-stage surgery was performed in 37 patients, with staged revision surgery in 35. Staged surgeries were performed in any cases with active infection (positive culture or elevated C-reactive protein [CRP] level, purulent exudate, etc.). A first-generation intravenous cephalosporin was usually administered for 1 week after revision surgery, followed by oral antibiotics for another 3 weeks. When the causative bacteria were MRSA, MRSE, or *P aeruginosa*, intravenous antibiotics were administered for 2 weeks after surgery instead of 1 week. Vancomycin was administrated intravenously for 2 weeks at a twice-daily dose of 1 g to the patients with MRSA and MRSE. Then, for oral administration, rifampin 450 mg and trimethoprim/sulfamethoxazole 160 mg/800 mg daily were used for 3 months. On the other hand, meropenem was administered intravenously at a dose of 0.5 g three times a day for 2 weeks to the patients with *P aeruginosa*.

The reinfection rate after revision surgery using iodine-coated implants was evaluated, along with the survival of iodine-coated implants using Kaplan-Meier analysis. WBC and CRP levels were measured pre- and postoperatively. Serum thyroid hormone levels were used to evaluate the systemic effects of the iodine implants.

3. Results

Only 5 patients (all were tumor cases: 1 in stage 4, 1 in stage one) underwent re-revision surgery. The causative organisms were unknown in all 5 cases. Among the 5 patients, 1 underwent 2 revisions due to implant failure with non-union of recycled bone, and 1 had mechanical loosening of the stem of the endoprosthesis at 24 months. Both recovered with re-implantation using iodine-coated implants. In the 3 patients with tumor prostheses (2 had infected megaprostheses and 1 had an infected TKA), periprosthetic infection recurred at an average of 18.7 months (12–26 months) after surgery. The reinfection rate was 4.2% (3/72 patients). These recovered with re-implantation of iodine-coated megaprostheses. The case shown in Figure 5A–C had reinfection after revision using an iodine-coated tumor prosthesis. Amputation was not required for any patients. The survival rate of the iodine-coated implants was 91% (Fig. 1). In all but 1 case that died of disease, there were no signs of infection at the latest follow-up. The median WBC level was nearly in the normal range, and CRP levels returned to normal within 4 weeks after surgery (Figs. 2 and 3). Table 1 shows the values of CRP and WBC over time. Abnormalities of thyroid gland function were not detected in any patients (Fig. 4A–C).

4. Discussion

The iodine-coated implants effectively decreased the reinfection rate to 4.2% in revision surgery for implant-related postoperative infections. Moreover, even in reinfected cases, the iodine-coated implants were curative without need for amputation. It is usually very difficult to cure deep infections after implant surgery. The reported rates of SSI ranged from 0.57% to 2.23% for THA,[1] 0.4% to 2% for TKA,[2] 2.1% to 8.5% for spine surgery with instrumentation,[3] and 4% to 36% for megaprostheses.[4] It is very important to prevent postoperative infections. Reported reinfection rates after staged revision surgery for THA and TKA were 18.2%[7] and 28%,[8] respectively. Castellani et al reported that the reinfection rate was 13% for hip and knee revision surgery.[21] In cases with spine instrumentation infections, irrigation and debridement or removal of instruments is performed. The risk of removal is the loss of deformity correction. Even with apparent solid fusion at exploration, removal of spinal implants is sometimes associated with deformity progression.[22] A review by Kasliwal et al[23] found that instrumentation was usually preserved in patients with early infections (e.g., <6 weeks), but instrumentation removal should be considered for infections presenting in a delayed fashion (e.g., >6 weeks to even years). Ho et al reported that the reinfection rate with irrigation and debridement for spine instrument

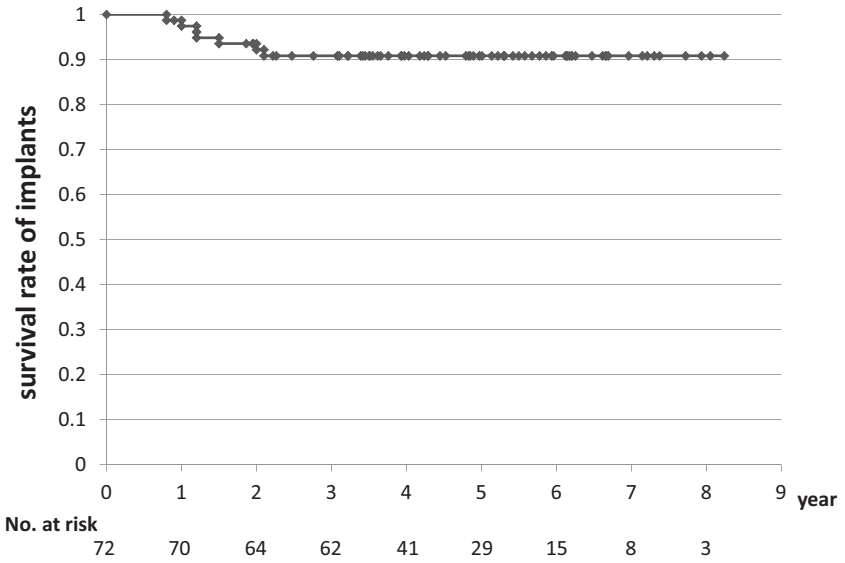

Figure 1. Survival of iodine-coated implants for postoperative infection.

Table 1

The values of CRP and WBC over time.

Operation	Pre	1w	2w	3w	4w	6w	8w	12w	6m	1y
Median WBC ($\times 10^3/\mu l$)	5.58	5.46	5.73	4.97	4.99	4.97	4.91	5.26	5.27	5.12
Median CRP (mg/dl)	0.4	2.05	0.7	0.45	0.3	0.3	0.2	0.2	0.2	0.1

CRP = C-reactive protein, WBC = white blood cell.

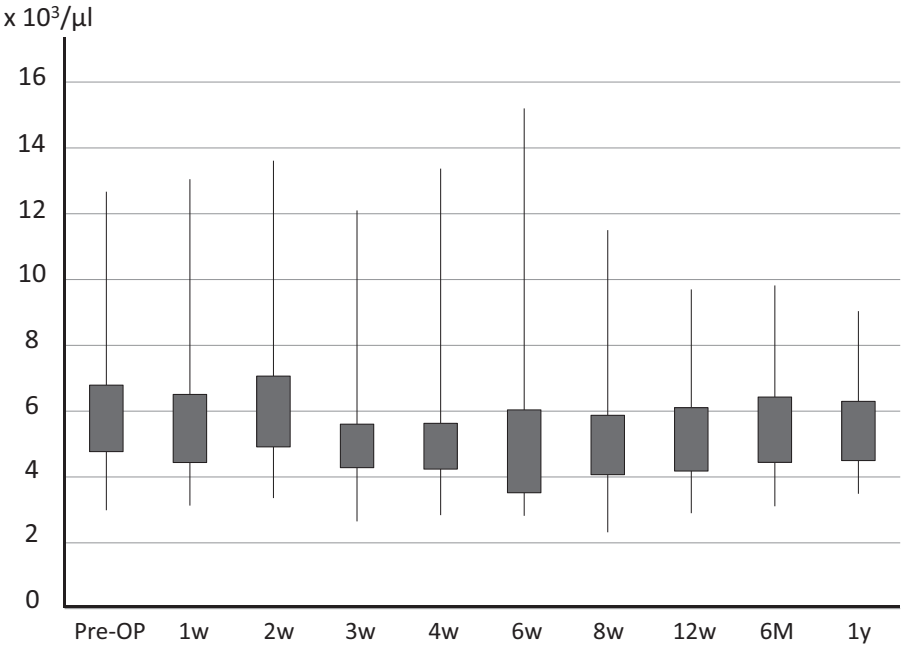

Figure 2. Change in WBC over time: WBC levels throughout this study. The median WBC levels remain below the normal range (< 8000/μl) throughout the study. WBC counts are shown as a total number of cells/μl of blood.

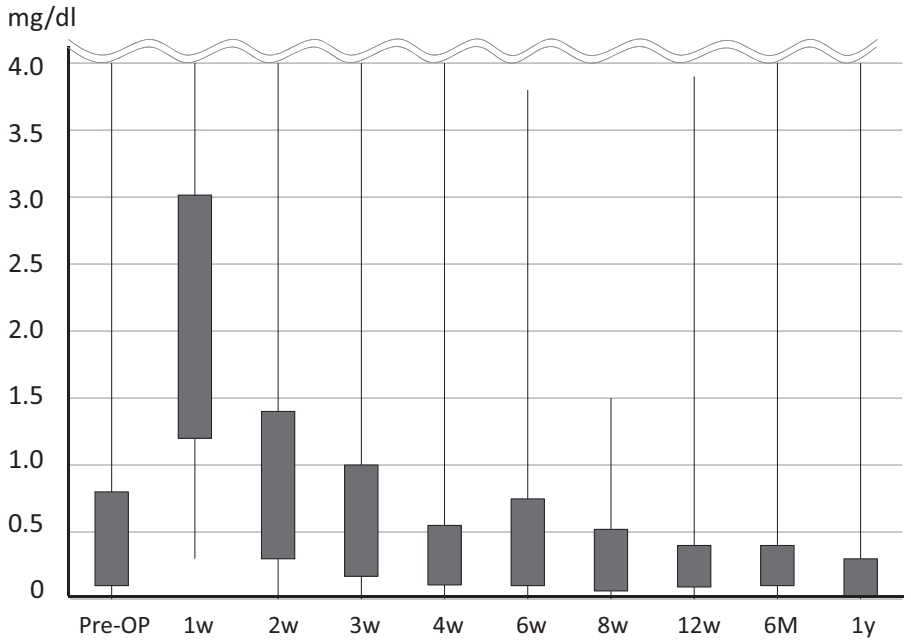

Figure 3. Change in CRP over time: CRP levels throughout this study. The median CRP levels return to <0.3 within 4 weeks after surgery. The units for the CRP levels are mg/dl.

infections was 47%.[10] Rohmiller et al reported that the reinfection rate with closed suction irrigation for SSIs in posterior spinal fusion was 25%.[24] However, there has been no report of primary revision surgery for spinal instrumentation infection. In this study, no patient had reinfection despite being compromised, although 11 cases of single-stage revision with spine instrumentation were treated. We believe that this is a consequence of iodine coating. For revision surgery in tumor cases, the reinfection rate is very high due to large defects in normal tissue, longer duration of surgery, and multiple morbidities. Zajonz et al reported that the reinfection rate in revision surgery using megaprostheses was still around 40%.[9] In the present study, 2 of the 3 reinfected cases were tumor patients. However, these recovered with reimplantation of iodine-coated megaprostheses. The reinfection rate in tumor cases was 12.5% (2/16), and was lower than the rate in previous reports. The reinfection rate in the present study was also very low at 4.2%, likely resulting from the antibacterial effect of the iodine coating.

Various reports have examined implant survival in revision surgery for SSIs. Pelt et al reported that implant survival in 2-stage revision TKA for periprosthetic infection was 78%.[25] Berend et al reported that implant survival in revision THA for PJI was 78%.[26] Implant survival after revision surgery in megaprostheses has been evaluated by Wafa et al.[27] In their report, implant survival rates using silver-coated and non-coated endoprostheses were 70% and 31.6%, respectively. In the current study, iodine-coated implant survival in revision surgery for postoperative infection was 91%; this survival rate was very high compared to that in previous reports.

Reinfection is an increasing problem in revision surgery for patients with infections associated with primary endoprosthetic replacement.[4] These patients may need multiple revision surgeries and, in some cases, even amputation.[9] The reported amputation rate was 18% for infected endoprostheses used in tumor surgery.[28] Myers et al reported that the amputation rate was 42% in postoperative infections after tumor resection.[29] However, no patients required amputation in the present study because reinfections were decreased with use of iodine-coated implants.

Use of an antibacterial implant can be toxic to normal cells. Indeed, there are reports of local argyria with use of silver-coated implants.[30] We found no toxicity due to the iodine coating in basic and clinical research studies.[15,19,20] In the present study, the effects of iodine-coated implants in the postinfection environment were investigated. When an iodine coating was used for prevention, the CRP required 4 weeks on average to normalize.[23] In the present study as well, the median CRP normalized at an average of 4 weeks postoperatively. Moreover, as in past reports,[20] there were no obvious abnormalities in thyroid function tests. High safety was even shown with use of iodine-coated implants in infected foci. The results with use of iodine and silver coatings are compared in Table 2.

This study had limitations. The reinfection rate was compared to that in a historical control. Moreover, the original disease and patient background were not unified. Further studies with larger numbers of unified patients, longer follow-up periods, and randomization with a control group are warranted to confirm these results.

5. Conclusions

Iodine-coated titanium implants can be very effective in the treatment of postoperative infections. An iodine coating can be safely applied, since no cytotoxicity and no adverse effects were detected.

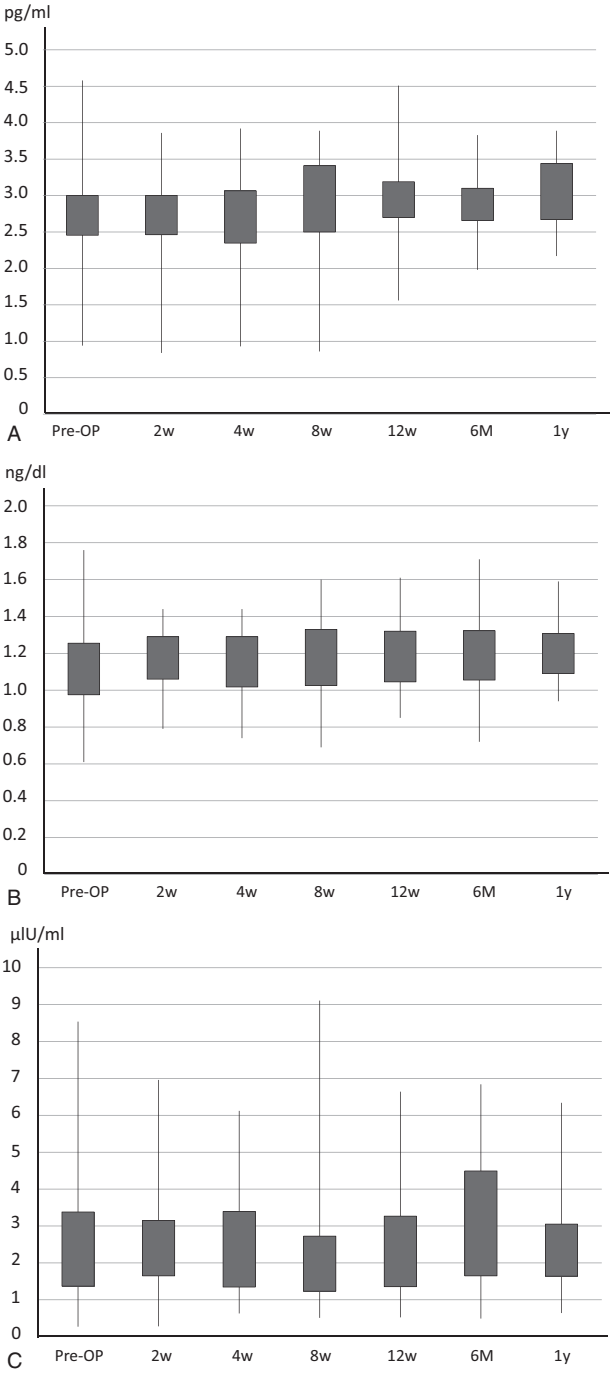

Figure 4. Thyroid gland function: Thyroid hormone levels are in the normal range during the study period. (A) Free triiodothyronine (FT3) levels (pg/ml), (B) Free thyroxine (FT4) levels (ng/dl), (C) Thyroid stimulating hormone (TSH) levels (μIU/ml).

Table 2

Comparison between iodine coating and silver coating.

	Iodine coating	Silver coating	*P* value*
Reinfection rate	4.2% (3/72)	40%[4] (8/20)	<.01
Toxicity	none	algyria[30]	

* Fisher exact test.

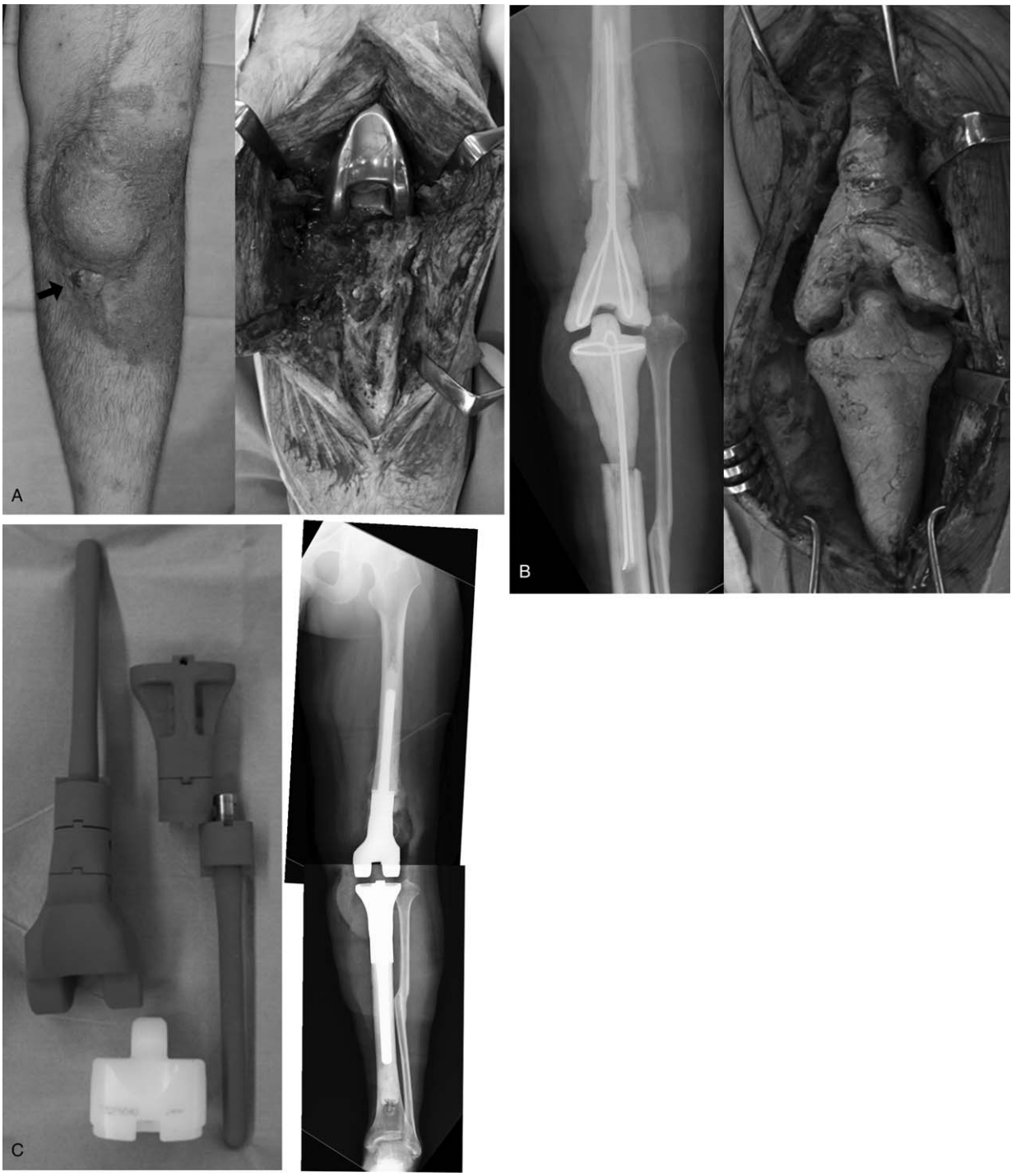

Figure 5. A 24-year-old man. (A) A fistula (arrow) is present, and the skin is in poor condition due to reinfection. (B) Irrigation, debridement, removal of implants, and cement spacer insertion have been performed. (C) Following re-implantation of an iodine-coated megaprosthesis, reinfection is completely cured.

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