Is the Bone-bonding Ability of a Cementless Total Hip Prosthesis Enhanced by Alkaline and Heat Treatments?

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Abstract

Background Cementless total hip arthroplasty (THA) implants using alkaline and heat treatments were developed to enhance bone bonding. Although bone-bonding ability of the alkali- and heat-treated titanium surface has been demonstrated in animal studies, it remains unknown whether it enhances or provides durable bone bonding in humans.

Questions/purposes We therefore (1) determined long-term survivorship, function, and radiographic signs of failure of fixation of alkali- and heat-treated THA implants; and (2) histologically examined their bone-bonding ability in two human retrievals.

Methods We retrospectively reviewed 58 patients who underwent 70 primary THAs, of whom 67 were available

for minimum followup of 8 years (average, 10 years; range, 8–12 years). Survival rate was calculated. Hip function was evaluated using the Japan Orthopaedic Association (JOA) hip scores, and radiographic signs of implant failure were determined from anteroposterior radiographs. Two retrieved implants were investigated histologically.

Results Using revision for any reason as the end point, the overall survival rate was 98% (95% confidence interval, 96%–100%) at 10 years. The patients' average JOA hip scores improved from 47 points preoperatively to 91 points at the time of the last followup. No implant had radiographic signs of loosening. Histologically we observed bone in the pores 2 weeks after implantation in one specimen and apparently direct bonding between bone and the titanium surface in its deep pores 8 years after implantation.

Conclusions Cementless THA implants with alkaline and heat treatments showed a high survival rate. Further study is required to determine whether the treatment enhances direct bone bonding.

Level of Evidence Level IV, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

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All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request. Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

This study was performed at Kyoto University, Kyoto, Japan, and Kanazawa Medical University, Ishikawa, Japan.

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Introduction

Cementless femoral and acetabular implants in THA are designed to provide sufficient initial mechanical stability [22] and to encourage osteointegration onto or into the implant for biological stability [37]. Surface microtextures, including porous coatings, serve as sources of initial stability and as long-term anchors as a result of the mechanical interlocking between bone and the porous coating [39]. The porous structure itself allows bone

ingrowth, and porous structures with a hydroxyapatite (HA) coating have demonstrated bioactive osteoconductivity, leading to a large degree of direct bone-to-implant contact [3, 13, 18, 21, 38]. Acceleration of osteointegration into the porous structure of the implant reportedly reduces the risk of subsidence and proximal stress shielding, enhances resistance to wear particle migration, and reduces the incidence of thigh pain [33]. However, concerns have been raised about the use of this coating on porous-surfaced implants, including the reduction of space available for bone ingrowth [25], weak bonding between the substrate and the HA coating layer [14, 26], and the relative rapid degradation of HA that may lead to the aseptic loosening of the implants or third-body wear caused by HA debris [2, 23]. Lazarinis et al. [20] reported that the use of HA coating on a cementless stem did not enhance implant survival by a Swedish register study.

Combining alkaline and heat treatments has been proposed as a surface modification of titanium and its alloys to provide them bioactivity [17]. Kokubo et al. [17] showed that after titanium metal had been subjected to this treatment involving soaking in a 5 M NaOH solution at 60 °C for 24 hours followed by a heat treatment at 600 °C for 1 hour, bone-like apatite formed on the surface of the titanium in simulated body fluid (which has an ion concentration similar to human blood plasma). Nishiguchi et al. [27] suggested that if a material forms a bone-like apatite layer on its surface in simulated body fluid, it could form a similar apatite layer in the living body and bond to living bone. This chemical treatment allows the homogeneous deposition of a thin bone-like apatite layer within a porous implant without any surface change. Because the implants are immersed in NaOH solution, the effects extend throughout the irregular structure of the implant. Furthermore, this treatment does not reduce the pore space available for bone ingrowth because it causes little change to the surface morphology of the implant, affecting only the top 1 µm [16]. Development of cementless metaphyseal fit-type THA implants made from a titanium alloy using alkaline and heat treatments was started in 1995 in Japan [17]. Subsequent animal studies using alkali- and heat-treated titanium [11, 27–29] have suggested treated titanium nonloadbearing implants enhanced bone-bonding ability mechanically and histologically between 4 and 24 weeks postoperatively compared with untreated titanium. In 2009 we reported 70 primary THAs using this method and found no instances of loosening or revision at a mean followup of 4.8 years [15]. However, it remains unknown whether alkaline and heat treatment enhances long-term survival or bonding of bone in humans.

We therefore (1) determined long-term survivorship, function, and radiographic signs of failure of fixation of alkali- and heat-treated THA implants; and (2) histologically

examined their bone-bonding ability in two human retrievals.

Patients and Methods

From September 2000 to February 2002, we performed 162 primary THAs that included 58 patients undergoing 70 primary THAs at two university hospitals as a clinical trial of cementless alkali- and heat-treated porous-coated titanium hip implants. A short-term followup study of these patients was reported previously [15]; this study was performed to assess longer-term survival. These implants were made available commercially in 2007. The indications for this implant system were: (1) secondary osteoarthritis caused by developmental dysplasia of the hip or osteonecrosis of the femoral head; and (2) calcar-to-canal ratio less than 0.75 [7]. The only contraindication was a high dislocated hip. Of the 58 patients, two (three hips) were lost to followup in less than 8 years. This left 56 patients (67 hips) for study. The diagnosis at the time of surgery was secondary osteoarthritis in 63 and osteonecrosis of the femoral head in four hips. There were three men and 53 women with a mean age of 52 years (range, 24–67 years), mean height of 150 cm (range, 140–180 cm), and mean weight of 53 kg (range, 35–90 kg) at the time of the operation. The minimum followup was 8 years (average, 10 years; range, 8–12 years). No patients were recalled specifically for this study; all data were obtained from medical records and radiographs.

The implants (AHFIX Q System; KYOCERA Medical Corporation, Osaka, Japan) were of the cementless metaphyseal fit type made from a titanium alloy (Ti6Al2Nb1Ta0.8Mo) (Fig. 1). All underwent alkaline and heat treatments on a 700-µm-thick circumferential porous surface made by pure titanium plasma-sprayed coating. The pore size of this coating was 350 to 450 µm. The acetabular shell was completely coated, but only the proximal third of the femoral stem was coated circumferentially. The acetabular component had a highly crosslinked polyethylene liner.

Operations were performed with the direct lateral approach with a partial trochanteric osteotomy in 33 hips or with the posterior approach in 34 hips. Autogenous bulk (15 hips) or chip bone (42 hips) obtained from a resected femoral head was grafted at the superolateral defect of the acetabular roof, and bone grafting was not performed in 10 hips. After the femur was prepared using reamers and broaches, the femoral component was implanted. Both the porous surface and the base portion of the screws used to fix the acetabular cup in position had been subjected to alkaline and heat treatments (Fig. 2). Thirty-five femoral heads had a diameter of 22.2 mm and 32 had a diameter of 26 mm. All femoral heads were made of zirconia ceramic.

Patients were allowed to walk with full weightbearing 2 days after surgery.

Patients were recorded clinically and radiographically at 3 and 6 months after surgery and annually thereafter. Hip function was rated by two authors (HA, TM; one of them was engaged in the surgeries) according to the scoring system proposed by the Japan Orthopaedic Association (JOA hip score) [19]. Two authors (KS, AK; one involved in the surgeries) examined all radiographs for location and extent of osteolytic lesions (endosteal, intracortical, or cancellous destruction of bone that was not linear, more than 2 mm in width, and was or had been progressive [24]),

reactive lines (radioopaque lines adjacent to the implants [10]), stress shielding (Grade 1: only the most proximal medial edge of the cut femoral neck was rounded off slightly, Grade 2: rounding off of the proximal medial femoral neck was combined with loss of medial cortical density at stem Zone 7, Grade 3: more extensive resorption of cortical bone involved the medial cortex at stem Zones 6 and 7, Grade 4: cortical resorption extended below Zones 6 and 7 into the diaphysis [8]), pedestal formation (a shelf of endosteal new bone either partially or completely bridging the intramedullary canal on the stem tip [10]), and cortical hypertrophy (an increase in outside diameter of the cortex [4]) from AP radiographs taken immediately after surgery and at the time of the last followup. To identify stem subsidence, the distance between the most proximal point of the greater trochanter and the proximal apex of the shoulder of the prosthesis along the axis of the femoral stem on AP digital images of the hip was measured. When stem subsidence was found on the last radiograph, all postoperative radiographs available were reviewed to identify when the subsidence stopped. Using the criteria described by Engh et al. [9], we categorized fixation of femoral components as bone ingrowth fixation, stable fibrous fixation, or unstable fixation. Radiographic loosening of the acetabular component was defined as a continuous radiolucent line at the bone–implant interface or any change in the position of the component over time. Gaps between the acetabular metal shell and the host bone were identified in the initial postoperative radiographs, and gap filling was defined when the gaps disappeared in the followup radiographs. Radiographic changes were described with the Gruen zones for the proximal femur and with the DeLee and Charnley zones for the acetabulum [5].

Fig. 1 A photograph of the AHFIX Q System implants is shown.

Fig. 2A–C Radiographs of a 49-year-old woman with secondary osteoarthritis are shown. (A) Her preoperative JOA score was 31 points. (B) Cementless THA using prostheses with alkali- and heat-treated porous coating was performed. (C) Her JOA hip score improved to 98 points and no signs of radiographic loosening of the components were found 11 years after surgery.

All clinical and radiographic data of the 56 patients (67 hips) necessary for analyses in this study were available in each hospital. Pairwise agreement in the assessment of osteolysis, reactive line, stress shielding, pedestal formation, cortical hypertrophy, stem subsidence, and stem fixation were 100%, 94%, 94%, 99%, 99%, 100%, and 100%, respectively.

We evaluated histologically two hip prostheses with alkaline and heat treatment retrieved during revision THAs from one patient with deep infection in this cohort and the other patient with periprosthetic femoral fracture. We sectioned the prostheses with a diamond knife stored in 10% phosphate-buffered formaldehyde for 3 days and dehydrated in serial concentrations of ethanol (5%, 70%, 80%, 90%, 99%, 100%, and 100% v/v) for 3 days in each solution. Specimens were then embedded in polyester resin. Thick sections (250 μ m) were cut with a band saw (BS-3000 N; EXACT Cutting System, Norderstedt, Germany) and ground to a thickness of 50 μ m using a grinding-sliding machine (Microgrinding MG-4000; EXACT Cutting System). Each section was then stained with Stevenel's blue and van Gieson's picrofuchsin. Cells and extracellular structures stain blue with Stevenel's blue and bone stains orange or purple with van Gieson's picrofuchsin. We examined the histological slides using transmitted light microscopy (Model Eclipse 80i; Nikon, Tokyo, Japan) in conjunction with a digital camera (Model DDS-5 M-L1; Nikon). In addition, to observe bone infiltration accurately, fluorescence microscopy (Model IX70; Olympus, Tokyo, Japan) was used in conjunction with a digital camera and the images superimposed on the transmitted light microscopy images. Thick sections (250 μ m) were polished using diamond paper and coated with a thin layer of carbon for observation using a backscattered scanning electron microscope (SEM) (S-3400 N; Hitachi, Tokyo, Japan) attached to an energy-dispersive x-ray (EDX) microanalyzer (Genesis; Ametek, Tokyo, Japan).

Kaplan-Meier survivorship analysis was used to determine implant survival with revision for any reason used as the end point. Statistical analyses were performed using Statcel2 software [40].

Results

The survival rate of the implant was 98% (95% confidence interval, 96%–100%) at 10 years when revision for any reason was set as the end point (Fig. 3). The JOA hip scores improved from 47 points (range, 25–74 points) preoperatively to 91 points (range, 76–100 points) at last followup; two hips (3%) were causing the patients mild thigh pain. Sixty-six hips remained unrevised at the last followup. Reactive lines were observed only on the femoral

Fig. 3 Kaplan-Meier survivorship analysis, with revision for any reason as the end point, is shown. CI = confidence interval.

side with none on the acetabular side. Reactive lines were seen adjacent to the nonporous surface of the stem with none on the porous surface (Fig. 4). Four hips (6%) had initial subsidence (3 mm in three hips, 5 mm in one hip) within 3 months after operation, but there was no progressive subsidence after this period. There was no change in the position of the acetabular component. Overall, there was no loosening of either the acetabular or the femoral component. In 46 hips (69%), a gap between the acetabular shell and the host bone was identified, and the other 21 hips had no gaps in radiographs taken immediately after operation. By 12 months, none of the gaps were visible radiographically (Table 1).

Intraoperative calcar fracture occurred in four hips (6%) requiring additional cerclage wiring. These hips did not undergo any further operation during the followup period. Postoperative dislocation occurred in one hip (1%) but required no further operation. Deep infection occurred in one hip 8 years after surgery and was cured by a two-stage revision.

Bone bonding to the alkali- and heat-treated porous surface was observed by histological examinations of the two retrieved implants (Figs. 4, 5). The first sample had been implanted in vivo for 2 weeks. Bone was attached to the surface of the alkali- and heat-treated plasma-sprayed coating of the stem, indicating bone bonding (Fig. 4A). Histological analysis using both optical microscopy and SEM showed small amounts of bone tissues on the surface and in the pores of the plasma-sprayed coating (Fig. 4B). SEM coupled with EDX was performed to identify the detailed chemical phases on the implant. These showed calcium (Ca) and phosphate (P) on the surface of the implant (Fig. 4C–E) with a Ca/P ratio of 1.9 w/w, indicating new bone formation had started through the porous network even by 2 weeks after implantation in vivo. The second sample had been implanted in vivo for 8 years. Bone was attached on the surface of the implant (Fig. 5A). Histology revealed mineralized mature bone tissues at the

Fig. 4A–E A 77-year-old woman underwent revision THA for a periprosthetic femoral fracture 2 weeks after primary THA. Gross appearance of a retrieved cup and histological analysis by Stevenel's blue and van Gieson's picrofuchsin staining are shown in (A and B, respectively). SEM analysis of the surface of a retrieved cup is shown

in C. SEM-EDX analysis of the surface of a retrieved cup in the square area in C (C = carbon; O = oxygen), and EDX mapping of the square area in C (Ti = titanium) are shown in D and E, respectively.

outer surface of the implant and in the deep pores (Fig. 5B). SEM and EDX analysis suggested direct bonding between the bone and the implant with bone ingrowth in the pores (Fig. 5C). The observed Ca/P ratio was 2.0 w/w (Fig. 5D–E).

Discussion

To provide sufficient initial mechanical stability and to encourage osteointegration onto or into the implant for biological stability in cementless THA, cementless THA implants made from a titanium alloy using alkaline and heat treatments were developed in Japan. Enhanced bone-bonding ability of the treated titanium was shown in animal studies in comparison with untreated titanium [11, 27–29]. We previously reported no instances of loosening and revision of alkali- and heat-treated implants at a mean followup period of 4.8 years [15]. However, it remains unknown whether alkaline and heat treatment enhances long-term survival or bonding of bone in humans. We

therefore (1) analyzed the 70 THAs again to determine long-term survivorship, function, and radiographic signs of failure of fixation of alkali- and heat-treated THA implants; and (2) obtained two samples harvested to examine their bone-bonding ability in humans histologically.

There are some limitations in our study. First, survival rates of recent THA implants are so high [6, 12, 31, 34, 35] that the number of hips and length of followup of this study are not sufficient to reveal the superiority of this implant. Although larger cohorts and longer followups would be necessary to confirm whether this implant enhances bone bonding and survival, it was associated with a high survival rate. Second, we have only a single-cohort retrospective study with no concurrent, randomized controls. Comparisons with other implants are discussed subsequently. Third, all operations were performed at one of two institutes in Japan, and these results may not be reproducible by other institutes, because the spectrum of diagnoses, ages, and weights/body mass indices are not those worldwide. Fourth, only two samples were available for histological examinations, and it was impossible to analyze the implant

Table 1. Radiographic findings in 67 hips at the average 10-year followup

Femur/acetabulum	Findings	Number
Femur	Reactive line	
	Zone 1	0
	Zone 2	1
	Zone 3	15
	Zone 4	42
	Zone 5	19
	Zone 6	8
	Zone 7	0
	Stress shielding	
	Grade 1	38
	Grade 2	29
	Grade 3	0
	Grade 4	0
	Cortical hypertrophy	8
	Pedestal formation	5
Acetabulum	Osteolysis	0
	Bone ingrowth fixation	67
	Stable fibrous fixation	0
	Osteolysis	0
	Reactive line	0
	Gap filling	46
	Zone 1	34
	Zone 1, 2	7
	Zone 2	5

surface and to measure bone apposition fraction in this study.

Alkali- and heat-treated implants showed a high survival rate at 10 years, which is comparative with other implants in previous reports (Table 2). In addition, we observed no obvious findings of loosening, osteolysis, or formation of a reactive line on the porous surface. The most important information of this study is that this implant with new surface treatment showed high survival rate with improvement in hip function score and no radiographic failures in the first decade after surgery. Radiographs taken just after operation showed a gap between the host bone and the socket; however, these gaps disappeared within 1 year. Although the disappearance might have been the result of osteoconductivity provided by this bioactive treatment, owing to the limited sensitivity of our radiographic measurements, we cannot eliminate the possible contribution of socket subsidence to their disappearance. Because there is no reactive line on the porous surface or any severe calcar resorption by stress shielding, osteointegration of the proximal porous coating and stress transfer seem to be achieved with this stem. However, the high incidence of

the reactive line in the distal zone may be caused by a relatively small porous surface area. In addition, pedestal formation is considered another potential radiographic sign of instability of the implant. In the present study, a pedestal was seen on the radiographs of five hips (7%), all fixed by bone ingrowth. Thus, these findings suggest a relatively small area of proximal porous surface may result in micromotion of the distal part of the stem. However, previous studies [1, 32] have noted reactive lines generally seen adjacent to the nonporous surface of the stem were not associated with other changes indicating stem loosening, suggesting these reactive lines do not correlate well with stem stability. In the case of proximally porous-coated femoral components, therefore, a complete radiolucent line is an indicator of loosening, whereas partial radiolucencies, not adjacent to the ingrowth surface and pedestal formation, are not indicators of loosening.

The two specimens histologically showed direct bonding between bone and alkali- and heat-treated titanium. Although many previous studies using animals reported good bone-bonding ability [11, 27–29], this was the first report in humans. Moreover, bonding with bone within 2 weeks after surgery indicates high bioactivity of alkali- and heat-treated titanium. Direct bone bonding to the titanium metal observed at 8 years revealed that bioactivity was maintained long term in vivo.

The surface of the titanium subjected to the alkaline and heat treatments is considered to be covered with crystalline apatite in body fluid. This apatite layer is integrated tightly into the treated layer. Apatite formed on titanium metal probably promotes bone formation by osteoblasts. Indeed, the production of alkaline phosphatase, osteocalcin, and type I collagen by osteoblasts on the alkali- and heat-treated titanium surface was more pronounced than for the untreated titanium metal [30]. Therefore, alkali- and heat-treated titanium metal is converted into a bioactive material and provides favorable conditions for bone marrow cell differentiation and osteoblast maturation. The cost of this treatment is approximately USD 10 for each component, but because the Japanese government determines the price of all implants, the charges for the prosthesis are the same in Japan as other cementless implants.

Titanium metal fashioned to generate an interconnected macroporous structure permits bone ingrowth. Coating a porous surface with a bioactive material is potentially an attractive way to enhance bonding between an implant and bone. The effect of our alkaline and heat treatment extends over the entire irregular surface of the implant because the implants are immersed into the NaOH solution [17]. This homogeneous bioactive surface of the pore walls within the porous implant promotes penetration of the newly formed bone into the most deeply seated pores. In addition, direct chemical bonding between the bone and the treated

Fig. 5A–E A 67-year-old man underwent revision THA for infection of the femoral component 8 years after primary THA. Gross appearance of a retrieved cup and histology using Stevenel's blue and van Gieson's picrofuchsin staining are shown in **A** and **B**, respectively. The arrows denote bone tissues. SEM analysis of the

surface of a retrieved cup is shown in **C**. SEM-EDX analysis of the square area in **C** (C = carbon; O = oxygen; P = phosphate), and EDX mapping of the square area in **C** (Ti = titanium) are shown in **D** and **E**, respectively.

Table 2. Previous articles on cementless THA

Author	Number of total hips/lost hips	Average followup period (years; range)	Characteristic of the porous surface	Survival rate (%)	Number of loosened acetabular/femoral component
Garcia-Cimbrelo et al. (2003) [12]	124/11	11.3 (10–13)	Grit-blasted	94.1*	7 / 0
Shetty et al. (2005) [35]	134/6	14.2 (13–15)	HA-coated	99*	0 / 0
de Witte et al. (2011) [6]	102/3	11.8 (10–17)	HA-coated	92.2*	9 / 2
Sariali et al. (2012) [34]	131/11	10 (8–11)	HA-coated	96.8*	1 / 0
Nourissat et al. (2012) [31]	90/7	9.2 (8–10.2)	HA-coated	94.2 [†]	0 / 0
Current study	67/3	10 (8–12)	Plasma spray, alkali- and heat-treated	98*	0 / 0

* End point was set as revision for any reason; [†] end point was set as reoperation for any reason; HA = hydroxyapatite.

titanium surface gives high bonding strength [27]. Therefore, these alkali- and heat-treated porous titanium implants can be stabilized in bone by both chemical bonding and mechanical interlocking. Another potential benefit of the direct bonding between bone and our implant material is that it can prevent the invasion of particles and subsequent osteolysis [36]. Thus, this bioactive porous titanium is likely to represent an attractive alternative for

advanced orthopaedic implants under load-bearing conditions.

In conclusion, alkali- and heat-treated implants have high long-term survival rate, comparable with other cementless implants, with improvement in hip function score and no radiographic failure. In addition, data from two specimens suggest direct bone-bonding ability in humans at the initial stage and long-term period after surgery.

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