CLINICAL ARTICLE

Early Rehabilitation and Periprosthetic Bone Environment after Primary Total Hip Arthroplasty: A Randomized Controlled Trial

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Objective: To investigate whether the periprosthetic bone environment could be affected by activity during the early rehabilitation period after primary total hip arthroplasty (THA) and to evaluate the safety and efficacy of activity during the early rehabilitation period.

Methods: This random clinical trial was conducted from January 2017 to July 2017. A total of 22 selected patients with advanced osteonecrosis of the femoral head (ONFH) who underwent primary unilateral THA were randomized (1:1) to a high activity level group (HA group) or a low activity level group (LA group). The HA group included nine men and two women, aged 53.18 ± 13.29 years. The LA group included five men and six women, aged 55.73 ± 11.73 years. The intervention was different postoperative daily walking distances guided by researchers: 1727.27 ± 564.08 m 0–2 months and 4272.73 ± 904.53 m 3–6 months postoperation for the HA group and 909.09 ± 583.87 m 0–2 months and 2409.09 ± 1068.13 m 3–6 months postoperation for LA group. The primary outcomes were radiographic evaluation (prosthetic stability and stress shielding based on the Engh scale) and bone mineral density (BMD) with a femoral prosthesis (individual and intergroup comparison using seven Gruen zones) at 6 months postoperatively. Secondary outcomes were set to confirm the safety and efficacy of activity during early rehabilitation, including day 1 erythrocyte sedimentation rate (ESR), day 1 hypersensitive C-reactive protein (CRP), length of hospital stay (LOS), and the Harris hip score (HHS) at discharge, 2 months postoperatively, and 6 months postoperatively.

Results: Patients were followed up for 6 months after surgery. Regarding primary outcomes, all prostheses were assessed as stable, with bone in-growth. There were no adverse events in any cases. The HA group had a higher incidence of stress shielding than the LA group, but there was no statistical significance (63.64% *vs* 18.18%; $P > 0.05$). The degree of stress shielding had a different distribution for the two groups ($P < 0.05$). In the HA group and the LA group, the median percentage difference of the BMD on the operated side was −25% and was −13% in Zone 1, −8% and − 1% in Zone 2, +1% and 3% in Zone 3, +6% and + 6% in Zone 4, −2% and +2% in Zone 5, −3% and −1% in Zone 6, and −24% and −12% in Zone 7 compared with the unoperated side. The BMD was significantly reduced in the medial proximal femur (Zone 1) and the lateral proximal femur (Zone 7) in both groups ($P < 0.05$). Furthermore, it was increased in the distal femur (Zone 4) in the HA group ($P < 0.05$). No difference was found in the BMD when comparing between groups. Regarding secondary outcomes, there was no statistical difference in day 1 ESR and day 1 CPR. The average LOS was similar in the HA and LA groups (7.00 days *vs* 7.18 days, $P > 0.05$). The HHS on day of discharge was higher in the HA group than in the LA group (60.73 ± 5.37 points *vs* 51.18 ± 8.05 points, $P < 0.05$); however, no statistically significant difference was found in postoperative the HHS at 2 months (81.73 ± 6.92 points *vs* 78.36 ± 9.18 points, $P > 0.05$) and 6 months (90.45 ± 5.24 points *vs* 91.55 ± 4.03 points, $P > 0.05$).

Conclusion: High activity levels during early rehabilitation after primary THA accelerate the process of bone remodeling and aggravate stress shielding, with no significant benefits for functional recovery.

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Introduction

Osteonecrosis of the femoral head (ONFH) is defined as death of bone cells around the femoral head due to decreased blood flow, especially in lateral epiphyseal arteries branching from medial circumflex arteries[1]. It can be caused by traumatic or non-traumatic events. Direct and indirect risk factors include femoral head fractures, hip dislocation, alcoholism, use of glucocorticoids, and radiation. However, the etiology and pathogenesis of ONFH remain unknown because this local bone ischemia derives from a complex combination of genetic factors, metabolic changes, and vascular impairment[2]. In China, at least 8.12 million people over the age of 15 years suffer from ONFH[3]. Individuals between 40 and 50 years of age are typically affected by ONFH[4]. Incorporating X-rays, CT, MRI, and histological examinations, the Association Research Circulation Osseous (ARCO) staging system for ONFH is widely used to guide therapy. The system comprises five stages (stages 0 to 4), with subclassification based on the location and size of the lesion[5]. Conservative treatment and hip-preserving surgery can be used in the early stages (ARCO stage 0 to 1) and the middle stages (ARCO stage 2 to 3b); however, the progressive course of ONFH is rarely reversed. Persistent groin pain and decreased range of motion in the hip joint ultimately arise in the late stages (ARCO stage 3c to 4), which severely impacts quality of life[6]. When the femoral head has collapsed, total hip arthroplasty (THA) is the only treatment that can relieve pain and restore function.

In the 1990s, application of THA for ONFH was not considered the optimum choice because of the short longevity of prostheses and the high postoperative complications compared to its use in other diseases[7,8]. However, thanks to innovations in prosthetic materials, improvements in surgical technology, and developments in research over the past decade, the clinical benefits for ONFH patients have now been established as substantial[9,10]. Today, there are more than 1 million THA are performed worldwide each year[11], and the estimated proportion of THA based on ONFH is nearly 10%[12].

Fast track surgery (FTS), namely enhanced recovery after surgery (ERAS), initiated with abdominal surgery by Dr Henrik Kehlet, is an evidence-based multidisciplinary perioperative protocol followed for surgical patients to restore postoperative function rapidly without additional' morbidity and mortality[13]. Orthopaedic surgeons pioneered this concept in joint replacement surgery in Denmark in 2003[14]. Since then, THA has continued to demonstrate positive results in terms of shortened length of hospital stay (LOS), reduced medical expenses, and high patient satisfaction with no increased complications[15,16]. Early rehabilitation, as an important component of FTS, benefits patients, especially in terms of restoration of function[17]. However, there is little data available on how much activity is appropriate postoperatively taking into consideration the periprosthetic bone environment. One reason for this lack of information is that rather than specific patient factors, the process of bone remodeling has been supposed to be affected more by surgical factors, such as preoperative osteoporosis, the surgeon's technique, and the characteristic of prostheses[18,19].

To evaluate the variation of the periprosthetic bone environment, bone resorption and bone dissolution (osteolysis) are measured, generally using X-rays. They are two independent processes that persisting after arthroplasty. Bone resorption is an adapted change to stress variation and osteolysis is a result of complicated immunologic responses initiated by prosthesis wear particles. In THA, the dynamic balance between osteoblasts and osteoclasts is broken unavoidably because of the load transfer from the prosthesis and the bone resorption (i.e. stress shielding) commonly at the proximal femur[20]. The reported incidence of stress shielding varies considerably, from 13.5% to 84%[18,21]. This variation is mainly due to subjectivity and judgments based on X-rays. To ensure accuracy, dual-energy X-ray absorptiometry (DEXA) has been introduced as a standard procedure for evaluating postoperative bone conditions[22]. The earliest evidence of stress shielding could be found on X-ray in some patients at 3 weeks postoperatively[18], and reduction of bone mineral density (BMD) was seen in patients at 3 months through DEXA[23].

In summary, ONFH is a public health concern worldwide, and the sole effective end-stage therapy is THA. Nevertheless, in ONFH patients, patients that undergo THA have relatively poor clinical outcomes compared to patients who undergo THA for other diseases. ONFH patients have high activity levels due to the younger age of onset of the disease. So far, no research has focused on the potential relationship between activity and periprosthetic bone pathophysiological changes. In this context, we designed this primary clinical trial using X-rays combined with DEXA to investigate whether early rehabilitation was related to the periprosthetic bone environment in ONFH patients undergoing THA. The hypothesis was that patients with high activity levels would have an enhanced periprosthetic bone remodeling process compared with those with low activity levels because, theoretically, their total load transfer over the same period should be larger. Our research had three main goals: (i) to test the hypothesis that high activity levels after THA lead to an accelerated bone remodeling process; (ii) to determine whether high activity levels are beneficial for postoperative functional recovery; and (iii) to confirm the safety of early rehabilitation in a fast-track THA.

REHABILITATION EFFECTS ON TOTAL HIP ARTHROPLASTY

Materials and Methods

Our randomized controlled trial complies with the Declaration of Helsinki and was registered in the Chinese Clinical Trail Registry (Reg. no. ChiCTR-INR-17010451). The trial was approved by the ethics committee at Jilin University, First Clinical Hospital (no. 2017-250) and carried out at the same institute. Written informed consent was obtained from all patients.

Inclusion and Exclusion Criteria

Inclusion criteria were based on the PICOS principle: (i) patients diagnosed with unilateral advanced ONFH (ARCO stage IIIC-IV); (ii) patients treated with unilateral THA with a posterolateral approach and prescribed different postoperative daily walking distances (2000 m at 0–2 months and 4000 m at 3–6 months *vs* 1000 m at 0–2 months and 2000 m at 3–6 months); (iii) stress shielding based on X-rays and BMD based on dual-energy X-ray absorptiometer (DEXA) at 6 months after surgery were used to evaluate the periprosthetic bone environment and the postoperative erythrocyte sedimentation rate (ESR), hypersensitive C-reactive protein (CRP), LOS, and Harris hip score (HHS) to assess clinical outcomes; (iv) patients with longer postoperative daily walking distances were more likely to show stress shielding at 6 months postoperatively and had better HHS on day of discharge, and there were no significant differences between the two groups in terms of postoperative BMD, ESR, CRP, and LOS; and (v) this study was a randomized controlled trial.

The exclusion criteria were: (i) patients aged under 18 years or above 75 years; (ii) patients with extreme body mass index (BMI) (<18 or >30); (iii) preoperative complications with uncontrollable comorbidity; (iv) previous surgery on the affected hip; (v) history of smoking and alcoholism; (vi) patients lacking essential economic and social support; (vii) American Society of Anesthesiologists (ASA) physical status >III; and (viii) undesirable bone condition as determined by preoperative X-ray. The full experimental approach can be found at www.chictr.org.cn.

General Information

This trial was a single-center, prospective, randomized, double-blind, controlled clinical study that complied with the Consolidated Standards of Reporting Trials (CONSORT) guidelines[24]. From January to July 2017, 22 patients with ONFH underwent a single total hip arthroplasty participated in the experiment.

All surgeries were performed by the same experienced chief physician using a posterolateral approach and cementless prostheses (Exceed ABT Biomet Delta Ceramic Acetabular Liner; Exceed ABT Ceramic Acetabular Cup; Biomet Delta Ceramic Femoral Head; Echo Bi-Metric Titanium Alloy Femoral Stem), the stem was Echo Bi-Metric RPP stem (Reduced Proximal Profile; Fig. 1). The stem was a collarless 3° bi-planer tapered stem, which was made of titanium alloy. The neck angle of the stem was 135°. The proximal part was

Fig. 1 The stem used in this study: An Echo Bi-Metric RPP stem, which was a collarless 3° bi-planer tapered stem made of titanium alloy. The neck angle of the stem was 135°. The proximal part was porous-coated with a plasma-sprayed high activity (HA) layer, and the distal part was polished and bullet-shaped.

porous-coated with a plasma-sprayed HA layer, and the distal part was polished and bullet-shaped. Patients were monitored in a post-anesthesia care unit after surgery for 2–4 h until their vital signs were stable.

Randomization

An assigned person not involved in the study used a random number table to determine whether patients should be allocated to the HA group or the LA group and then saved the randomization sequence into numbered, opaque sealed envelopes.

Blinding

Only the person who set the sequence (not involved in the study) knew the allocation. They would notify the chief researcher after surgery immediately so that a different rehabilitation schedule could be provided to patients in each group. All subjects and personnel in this study were blinded to the treatment group until the trial had been completed.

Once the patients left hospital, the staff who collected follow-up data were blinded regarding the treatment group, as were the evaluators who were responsible for checking and grading the outcomes.

Surgical Procedure

Anesthesia and Position
All patients received general anesthesia. The patient was placed in the lateral decubitus position with supports. The involved leg was disinfected preoperatively and kept free to move during surgery.

Approach and Exposure
A posterolateral approach to the hip was used to expose the posterior hip capsule. The 12-cm curved incision rounded the greater trochanter from the posterior to the lateral side with its proximal 6 cm pointed to the posterior superior iliac spine and distal 6 cm along the femoral axis. In line with the skin incision, a sharp dissection of the fascia lata and gluteal muscle was made across the greater trochanter. The tendinous insertions of the short external rotators were bluntly dissected, and nonabsorbable sutures were placed in the piriformis. Obturator and gemellus tendons were prepared for final repair. After reflection of the short rotator muscles, a full thick, broad-based flap of the posterior hip capsule was necessary to expose the hip joint. Surgical dislocation was performed by flexion, adduction, and slight internal rotation of the hip joint for the subsequent THA.

Pathological Changes and Resection
To confirm ARCO stages 3a and 4 in ONFH patients, femoral head collapse and acetabular arthritis were verified in each operation after surgical dislocation. Because preoperative measurement for the prosthesis had been done, the femoral head was directly cut using a swing saw accordingly and the round ligament of the femur was removed. The surgical field of the acetabulum was then clear, and the chief surgeon used the acetabular file to grind the acetabulum to the preoperatively planned size.

Placement of Prosthesis
The models were used before prosthesis implantation. The appropriate acetabular component was placed after management of the acetabulum. The femoral medullary canal was reamed using cylindrical reamers and rasps so that the maximal stem could be inserted and the initial stability was ensured. After placement of a suitable femoral component and reset, the stability of the test molds was verified, and the size of femoral head, the range of motion and the soft tissue balance were assessed. Subsequently, the corresponding prosthesis substituted the molds, and the same test was performed again.

Reconstruction
In the final stage of the surgery, the posterior hip capsule and the piriformis were repaired to provide enhanced postoperative muscle strength and to lower the dislocation rate. Tranexamic acid was infiltrated around the soft tissue to reduce postoperative blood loss. Whether a drainage tube was used depended on the local blood loss before closure.

Perioperative Management
The perioperative management of the two groups was based on the theory of FTS[14]. In the preoperative period, patients in each group received the same education. Nerve blocks and local infiltration anesthesia were not used. Blood, pain, and sleep management were unremarkable in all patients postoperatively. The patients were mobilized on the day after the operation under supervision of a physiotherapist, and protected weight-bearing on the operated leg was initiated for 4 weeks. Anteroposterior and lateral radiographs were taken on the day of discharge to ensure initial stability.

Intervention and Follow Up
One researcher was in charge of maintaining the connection with all subjects after discharge by phone. Different targets for postoperative rehabilitation were given in each group by the chief researcher: 2000 meters 0–2 months postoperation and 4000 m 3–6 months postoperation in the HA group and 1000 m 0–2 months postoperation and 2000 m 3–6 months postoperation in the LA group. Daily walking distance was recorded using a pedometer and patients were followed up by phone interview. At 6 months after surgery, patients came back to our outpatient service to complete their clinical and radiological evaluation.

Outcomes
The basic preoperative characteristics were classified into demographic and clinical factors. Demographic variables included gender, age, BMI, and ASA physical status. The clinical factors were ESR, hypersensitive CRP, duration of surgery, intraoperative bleeding, and HHS.

Primary Outcomes

Radiographic Evaluation
Stress shielding and prosthetic stability were evaluated using anteroposterior and lateral radiographs at 6 months postoperatively, focusing on the femoral prosthesis. The incidence and degree of these indicators were collected. According to the Engh scale, stress shielding could be divided into five levels, from 0 (none) to 4 (4th degree), based on X-ray, with a higher degree of stress shielding representing more severe bone resorption[25]. Prosthetic stability was judged using the criteria of Engh *et al.*; that is, no subsidence and radio-opaque lines could be found along the implant in consecutive examinations[26].

Bone Mineral Density

Bone mineral density examination was conducted at 6 months postoperatively. A DEXA (DPX-L; Lunar, Madison, WI, USA) using specific software for measuring BMD was applied in the coronal plane. The femoral side that was operated on was scanned, and BMD values were analyzed in seven Gruen zones. Then the unoperated side was superimposed with a prosthesis mask, which was stimulated from the opposite by the software at the same level. The values were expressed as real BMD (g/cm^2). The ratio between the operated side and the unoperated side was calculated in each zone.

Gruen Zone

The Gruen classification is a system for evaluating periprosthetic bone changes around the femoral stem[27]. There are seven areas in this classification system: Zone 1, greater trochanter; Zone 2, proximal lateral; Zone 3, distal lateral; Zone 4, tip; Zone 5, distal medial; Zone 6, proximal medial; and Zone 7, calcar region. With the help of specialized software, DEXA can be used to analyze BMD changes in these zones automatically.

Secondary Outcomes

Secondary outcomes were day 1 ESR, day 1 CRP, LOS, and the HHS. ESR and CRP were collected at the first postoperative day. HHS was evaluated by a chief doctor on the day of discharge and at 2 months and 6 months postoperatively.

Harris Hip Score

The HHS is an instrument for evaluating the functional ability in THA. The HHS contains four items: pain, function, degree of deformity, and range of motion of the hip joint[28]. Final scores range from 0 to 100. A score <70 is considered poor, while 70–80 is fair, 80–90 is good, and 90–100 is excellent.
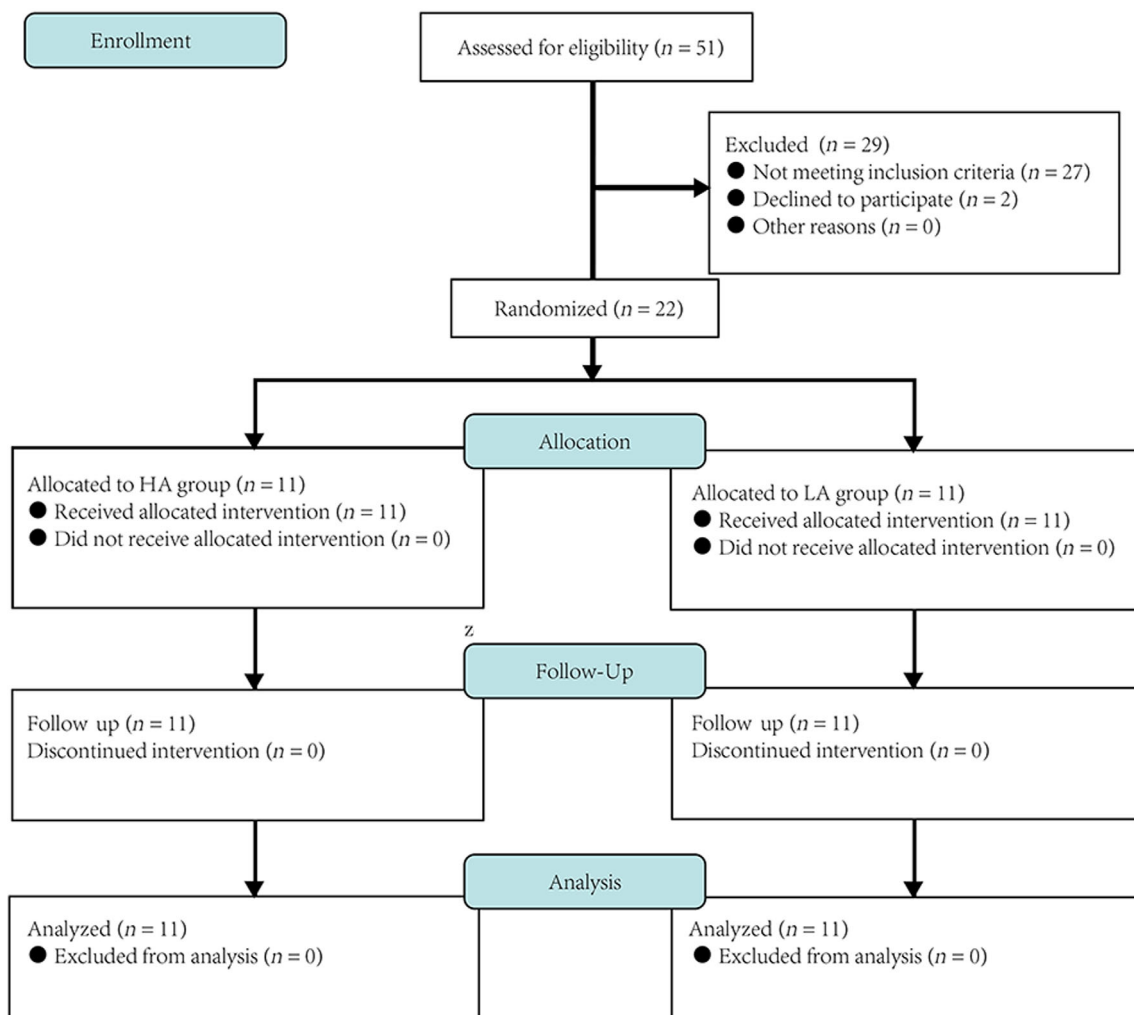

Fig. 2 Flow diagram according to CONSORT. HA, high activity group, LA group, low activity group.

TABLE 1 Demographics and clinical factors: Age, BMI, duration of surgery, intra-operative bleeding, preoperative ESR, preoperative CRP, and preoperative Harris hip score as mean ± standard deviation

	HA group	LA group
Gender (male/female)	9/2	5/6
Age (years)	53.18 ± 13.29	55.73 ± 11.73
BMI (kg/m^2)	22.99 ± 2.39	22.01 ± 1.68
ASA physical status		
I	0	1
II	10	7
III	1	3
Duration of surgery (min)	146.38 ± 54.31	128.57 ± 42.34
Intraoperative bleeding (mL)	300.00 ± 291.55	270.00 ± 347.28
Preoperative ESR (mm/1 h)	18.36 ± 22.50	18.18 ± 9.50
Preoperative CRP (mg/L)	7.84 ± 8.57	4.33 ± 2.22
Preoperative Harris hip score	47.23 ± 12.50	47.43 ± 16.38

Gender and American Society of Anesthesiologists (ASA) status presented as numbers. No significant differences were found between the groups. BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Statistical Analysis

Referring to previous research[8,22, 29] and data from our hospital, we presumed that stress shielding in the ER group would be more severe than in the LR group. Thus, we set a primary end point (incidence rate of stress shielding) of 75% in the ER group and 15% in the LR group for an exploratory study. A total of 20 cases (10 cases per group) were thought to be essential to reveal a difference, with a type I error rate of 5% and a statistical power of 80%. We decided to enroll 22 subjects, anticipating a 10% dropout rate. Analysis in this study followed the intention-to-treat (ITT) principle.

All tests were two-sided, with a significance level of 5% (α value). Numerical data were described as mean ± standard deviation, including ESR, CRP, HSS, and LOS. Degree of stress shielding was compared between the two groups using the rank-sum test. Fisher's exact test was used for the rate comparison for stress shielding. The percentage changes in BMD were expressed by the median values (25th–75th percentiles). The Wilcoxon signed-rank test (paired observations) was used to compare differences in sides, while the Mann–Whitney U-test (unpaired observations) was used for intergroup comparison. We used SPSS software version 22.0 (IBM SPSS, Armonk, New York, USA) to analyze the collected data. Statistical significance was confirmed if P-values < 0.05.

Results

Study Flow and Patient Characteristics

A total of 51 patients met the criteria; 27 patients were excluded based on the inclusion criteria and two patients refused to participate. Ultimately, a total of 22 subjects were enrolled in this study. All subjects were followed up and data collection was complete. The follow-up period was 6 months after surgery. A flow diagram is presented in Fig. 2. There were nine men and two women in the HA group, with an average age of 53.18 years (range, 26–70 years). There were five men and six women in the LA group, with an average

TABLE 2 Completion of daily walking distance (m) in each group: Walking distance was recorded daily using a pedometer and followed up by phone interview

	High activity group	Low activity group	t	P-value
2 months postoperation	1727.27 ± 564.08	909.09 ± 583.87	3.343	0.003*
6 months postoperation	4272.73 ± 904.53	2409.09 ± 1068.13	4.416	0.000*

* Statistically significant.

TABLE 3 Primary outcomes: Incidence and degree of stress shielding at 6 months postoperatively

Stress shielding level	High activity group	Low activity group	Z	P-value
0	4	9		0.023*
1	4	2		
2	3	0	−2.279	
3	0	0		
4	0	0		
Incidence rate	63.64%	18.18%	NA	0.080

* Statistically significant.

age of 55.73 years (range, 40–73 years). The mean preoperative HHS was 47.23 ± 12.50 (range, 26–63) and 47.43 ± 16.38 (range, 21–78) for HA and LA groups, respectively. Patients in the HA group had a mean ESR of 18.36 ± 22.50 mm/1 h (range, 2–79 mm/1 h) and a mean CRP of 7.84 ± 8.57 mg/L (range, 3.02–29.60 mg/L) preoperatively. They had a mean duration of surgery of 146.38 ± 54.31 min

(range, 80–240 min) and intraoperative bleeding of 300.00 ± 291.55 mL (range, 50–800 mL). In the LA group, the mean preoperative ESR and CRP were 18.18 ± 9.50 mm/1 h (range, 3–36 mm/1 h) and 4.33 ± 2.22 mg/L (range, 3.02–9.03 mg/L), respectively. The mean duration of surgery and intraoperative bleeding were 128.57 ± 42.34 min (range, 80–210 min) and 270.00 ± 347.28 mL (range, 50–1200 mL),
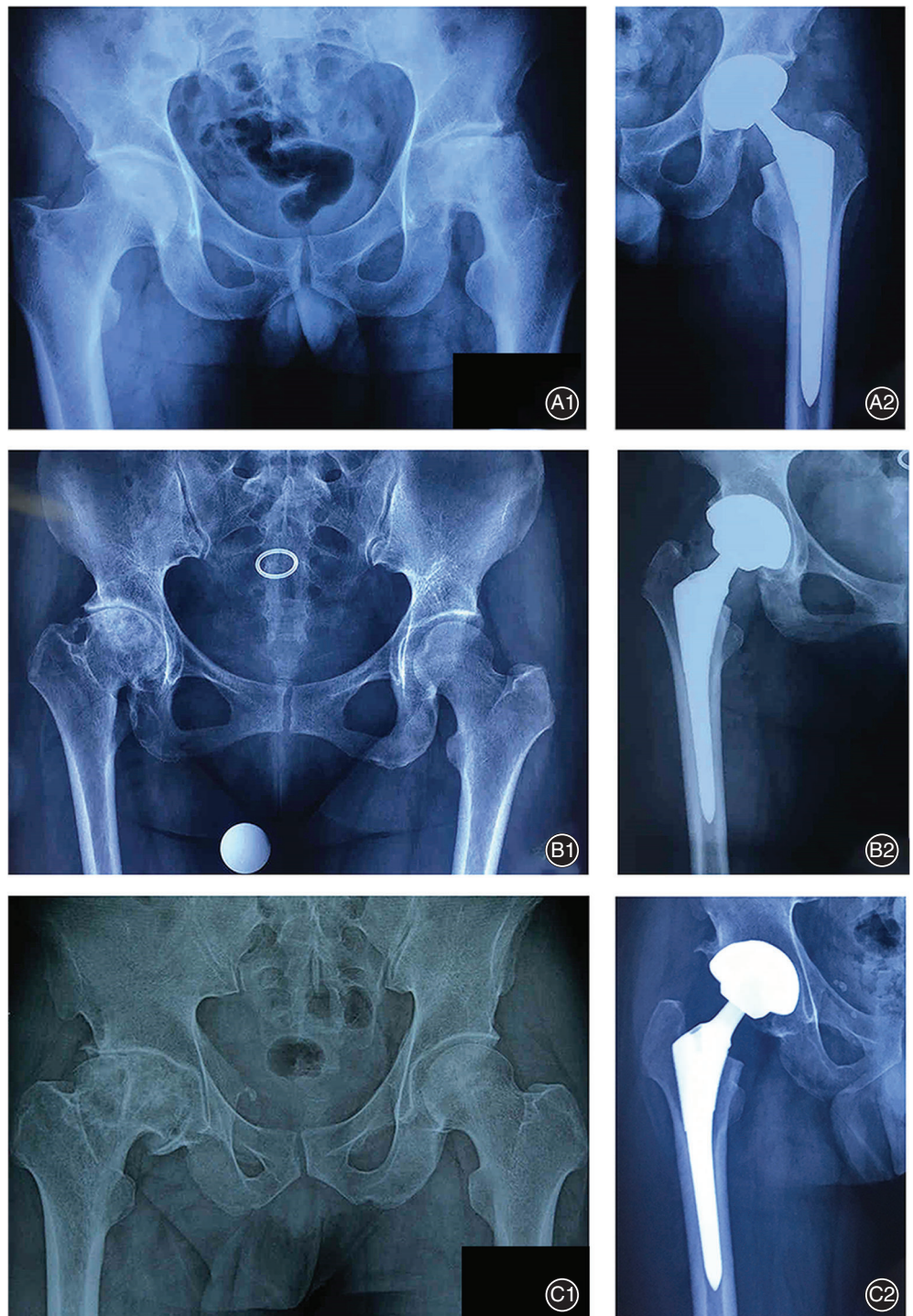

Fig. 3 X-ray of three patients with osteonecrosis of the femoral head (ONFH). Femoral collapse and acetabular arthritis could be found on preoperative X-ray (A1, B1, and C1). Stress shielding levels of 0, 1, and 2 were apparent on X-ray 6 months postoperatively (A2, B2, and C2).

REHABILITATION EFFECTS ON TOTAL HIP ARTHROPLASTY

TABLE 4 High activity group: Percentage side difference in bone mineral density (BMD) in 1–7 Gruen's zones 6 months postoperatively in self-comparison (operated side vs unoperated side)

	High activity group	Z	P-value
Zone 1	−25% (−12% to −30%)	−2.934	0.003*
Zone 2	−8% (−6% to 15%)	−0.889	0.374
Zone 3	+1% (+10% to −5%)	0.267	0.790
Zone 4	+6% (+32% to 0%)	2.134	0.033
Zone 5	−2% (+2% to −9%)	−0.533	0.594
Zone 6	−3% (+10% to −5%)	0.178	0.859
Zone 7	−24% (−10% to −30%)	−2.934	0.003*

Median values (25th–75th percentiles) are given; * Statistically significant.

TABLE 5 Low activity group: Percentage side difference in bone mineral density (BMD) in 1–7 Gruen's zones 6 months postoperatively in self-comparison (operated side vs unoperated side)

	LA group	Z	P-value
Zone 1	−13% (−10% to −18%)	−2.934	0.003*
Zone 2	−1% (+8% to −10%)	−0.267	0.790
Zone 3	+3% (+5% to −7%)	−0.178	0.859
Zone 4	+6% (+20% to −2%)	1.379	0.168
Zone 5	+2% (+17% to −4%)	1.245	0.213
Zone 6	−1% (+12% to −2%)	0.533	0.594
Zone 7	−12% (−6% to −21%)	−2.934	0.003*

Median values (25th–75th percentiles) are given.; * Statistically significant.

respectively. The above demographic and clinical factors at baseline are shown in Table 1. The baseline balance was assured because of complete randomization in this randomized controlled trial. The target daily walking distance (interventions) was accomplished in each group (Table 2). For HA and LA groups, the mean daily walking distance was 1727.27 ± 564.08 m and 909.09 ± 583.87 m 0–2 months postoperatively and 4272.73 ± 904.53 m and 2409.09 ± 1068.13 m 3–6 months postoperatively, respectively ($P < 0.05$).

Primary Outcomes

Radiographic Evaluation

At the endpoint, all prostheses were assessed as stable with bone ingrowth (with spot welds, absence of subsidence, and radiolucent lines). The distribution of the stress shielding scale was different between groups: four with no stress shielding, four with first-degree stress shielding, and three with second-degree stress shielding in the HA group, while nine with no stress shielding and two with first-degree stress shielding in the LA group ($P < 0.05$; Table 3). Although the HA group had a higher incidence of stress shielding, no statistical significanve was found compared with the LA group (63.64% vs 18.18%, $P > 0.05$; Table 3). The relative risk (RR) was 3.5 (confidence inteval 0.9–13.2). Typical cases are displayed in Fig. 3.

Bone Mineral Density

Compared with the contralateral side, a significant reduction of BMD was found at Zone 1 and Zone 7 in both groups. In comparing the operated side and the unoperated side, the BMD change was −25% for Zone 1 and −24% for Zone 7 in the HA group, while it was −13% for Zone 1 and −12% for Zone 7 in the LA group ($P < 0.05$; Tables 4 and 5). Furthermore, the BMD was significantly increased at Zone 4 in the HA group (+6%, $P < 0.05$; Table 4). However, when comparing the BMD change of the operated side between HA and LA groups, no significant difference was found at all zones (Table 6).

Secondary Outcomes

Comparing the HA and LA groups, day 1 ESR was 24.00 ± 23.56 mm/1 h and 24.55 ± 21.33 mm/1 h, day 1 CRP was 49.10 ± 33.66 mg/L and 69.36 ± 46.71 mg/L, and LOS was 7.00 ± 2.53 days and 7.18 ± 2.71 days, respectively. No statistical significance was found for these data ($P > 0.05$). The HHS was higher in the HA group than the LA group on the day of discharge (60.73 ± 5.37 vs 51.18 ± 8.05, $P < 0.05$); it was not different at follow up at 2 months and 6 months postoperatively (Table 7).

TABLE 6 Median percentage difference in bone mineral density (BMD) at Gruen zones 1–7 in intergroup comparison (Mann–Whitney U-test)

	High activity group	Low activity group	Z	P-value
Zone 1	−25%	−13%	1.511	0.133
Zone 2	−8%	−1%	1.215	0.243
Zone 3	+1%	+3%	−0.197	0.847
Zone 4	+6%	+6%	−1.108	0.332
Zone 5	−2%	+2%	1.280	0.217
Zone 6	−3%	−1%	0.920	0.365
Zone 7	−24%	−12%	1.871	0.065

TABLE 7 Secondary outcomes: Day 1 means the first postoperative day

	High activity group	Low activity group	t	P-value
Day 1 ESR (mm/1 h)	24.00 ± 23.56	24.55 ± 21.33	−0.057	0.955
Day 1 CRP (mg/L)	49.10 ± 33.66	69.36 ± 46.71	−1.167	0.257
Harris hip score				
Discharge day	60.73 ± 5.37	51.18 ± 8.05	3.273	0.004*
2 months postoperative	81.73 ± 6.92	78.36 ± 9.18	0.971	0.343
6 months postoperative	90.45 ± 5.24	91.55 ± 4.03	−0.547	0.590
LOS (days)	7.00 ± 2.53	7.18 ± 2.71	−1.665	0.111

* Statistically significant. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Adverse Events

Patients were observed for signs of fracture, dislocation, severe pain, and lack of mobility. No adverse events occurred during the study.

Discussion

Summary of Results

To our knowledge, the present study was the first to investigate the relationship between early rehabilitation and the periprosthetic bone environment after primary THA, and the primary finding was that patients with high activity levels had a different distribution on the stress shielding scale (more severe), and the risk of appearance of stress shielding was 3.5 times higher in patients with high activity levels compared with those with low activity levels. Furthermore, an enhanced process of periprosthetic bone remodeling could be confirmed by considering BMD changes together. Based on secondary outcomes, the functional recovery of the HA group was better that that of the LA group on the day of discharge, which was revealed by HHS; however, at follow up, the results for the two groups no longer differed.

Radiographic Evaluation: Stress Shielding

Although few studies have focused on the relationship between rehabilitation and the periprosthetic environment, there are some previous related published studies that are useful for reference. First several demographic and surgical factors, including gender, age, BMI, cortical index, and surgeon's technique, have been suggested to affect stress shielding[30–32]. Second, based on finite element analysis (FEA), optimal load transfer (good stress shielding) was thought to be achieved in short stems. However, Rietbergen et al. showed that reducing the stem length provided no benefit in reducing stress shielding[33]. In addition, a trade-off between stress shielding and initial stability was found with a reduction in stem length in an in vitro biomechanical study[34]. Results can be contrary in theory and in practice. Lerch et al. showed that reduction of femoral bone dissolution was minimal in a patient 3 years after THA, while it was calculated to be high based on FEA[35]. In clinical trials, bone loss areas were observed to be different in various uncemented stems and femoral canal shapes[36, 37]. One explanation was that loading conditions were changed by each matching situation and this effect was magnified over time. In the same way, after controlling the above factors, we believed that activity, as an important part of rehabilitation, will influence the periprosthetic bone environment by creating substantial daily pressure, which could lead to an earlier and higher degree of stress shielding by enhancing load transfer. In the present study, the HA group had a higher incidence (although not statistically different) and a more severe degree of stress shielding than the LA group, which could be confirmed by comparison of BMD. These results demonstrated that the speed of bone remodeling was faster in the HA group, which was supported by the changes in BMD.

Bone Mineral Density

For BMD, the results showing the bone remodeling procedure, reflected by self-comparision, were in accordance with those of Bodén et al., who showed lateral proximal and medial proximal bone loss (Zone 1 and Zone 7) and distal cortical hypertrophy (Zone 4) in hydroxyapatite coated Bi-Metric modular femoral stems[38]. Although the variation of BMD was more substantial in the HA group than in the LA group in all zones, particularly Zone 1 (−25% vs −13%) and Zone 7 (−24% vs −12%), there were no statistical differences between the groups in this study. However, comparing the absence of statistical differences between operated and unoperated sides in the LA group in Zone 4 (+ 6%[+32% to 0%]; P < 0.05), the opposite result in the HA group (+ 6% [+20% to −2%]; P > 0.05) indicated an enhanced process of bone remodeling. Therefore, we assumed that the acceleration of bone remodeling with intense activity may be found in a larger sample size and/or with a greater stimulus factor (amount of activity). Future studies in which the design is focused on BMD are needed to understand this effect. Considering the high degree of stress shielding in the HA group, the significant distal BMD change (Zone 4) in HA group and unremarkable medial BMD change (Zone 1 and Zone 7) in both groups, we concluded that the difference in HA group was a consequence of the earlier achievement of bone remodeling.

Clinical Outcomes

The aim of monitoring secondary outcomes was to observe potential influences on prosthesis and patients' motivation to participate in activity. ESR and CRP were used to reflect postoperative physiological status, while LOS and HHS were used to indicate patients' motivation to participate in activity. The non-significance of day 1 ESR and CRP indicated that patients in both groups experienced a similar pathophysiology process after surgery. Early rehabilitation has been proven to have a positive impact on functional recovery, but the duration of this effect may only last for 6–8 weeks[39,40]. In the present study, only HSS on discharge day was different between HA and LA groups (60.73 ± 5.37 *vs* 51.18 ± 8.05); this was no longer significant at 2 months and 6 months, postoperatively, which was consistent with other studies. Consequently, high activity levels after THA had a limited impact on functional recovery. Considering that there were no differences in LOS, functional outcomes contributed little in terms of patients' willingness to stay. There was no occurrence of adverse events. Therefore, any change in the bone environment after surgery should be attributed to rehabilitation.

Clinical Significance

Despite activity being encouraged for patients, there is no standard criteria for the recommended quantity of activity (walking distance) per day after THA. A range of 500–3500 steps after THA was recorded during hospitalization (first week approximately) and gender difference was found[41]. The activity level in THA or TKA patients could be increased to 4000–7000 steps per day at 6 weeks after surgery[42]. In the present study, activity level was set as high and low postoperatively in two groups, with a range of set walking distances as the sole variable, with changes analyzed based on X-rays and BMD. Consequently, as the RR showed for the primary outcomes, although the integral mechanism of bone remodeling around the prosthesis was unclear, according to the present study, activity did play a role in changing the progress of bone remodeling. Therefore, intense rehabilitation (high activity level) after primary THA should be considered as a stimulus factor enhancing the process of periprosthetic bone remodeling.

Limitations

As an initial exploratory trial to investigate the connection between rehabilitation and the periprosthetic environment, some limitations were inevitable. First, defining whether a daily walking distance was high or low was difficult. A contrary conclusion is possible in future studies if the variable is changed between groups. Thus, plenty of work is needed to find a critical value for producing earlier stress shielding to provide a guideline for postoperative home rehabilitation after primary THA. Furthermore, even if the conclusion was subsequently confirmed, whether an enhanced bone remodeling procedure would lead to related complications, such as periprosthetic fractures, remains unknown. Ultimately, overestimation of the influence of activity on the periprosthetic environment was possible prior to this trial, which could have led to an insufficient sample size. Therefore, a multicentric, consecutive, long-term follow-up study on this topic would be worthwhile.

Conclusion

High activity levels during early rehabilitation after primary THA accelerate the process of bone remodeling and aggravate stress shielding, with no significant benefits for functional recovery.

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