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Original Article

Efficacy of proximal humeral internal locking system combined with allogeneic femoral head bone grafts for complex osteoporotic proximal humeral fractures

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Abstract: Objective: The aim of the current study was to investigate differences between the proximal humeral internal locking system (PHILOS) combined with allogeneic femoral head bone grafts and traditional PHILOS surgery for treatment of complex osteoporotic proximal humeral fractures. Methods: Eighty patients with complex osteoporotic proximal humeral fracture were selected and divided into the control group (n=38) and research group (n=42) using a random number table. The control group was treated with traditional PHILOS surgery, while the research group was treated with PHILOS combined with allogeneic femoral head bone grafts. Surgical duration, intraoperative blood loss, incision healing, postoperative complications, healing times, Neer shoulder joint function scores, hospital stays, pain visual analogue scale (VAS) scores, biochemical markers of bone turnover, and inflammatory cytokine levels were compared between the two groups. Results: Hospital stays and healing times in the research group were shorter than those in the control group (both $P<0.05$). Postoperative VAS scores in the research group were lower than those in the control group ($P<0.05$). There were no significant differences in surgical duration and intraoperative blood loss between the two groups (both $P>0.05$). There were no significant differences in primary incision healing rates between the research group (95.24%) and control group (92.11%) ($P>0.05$). Incidence of postoperative complications in the research group was lower than that in the control group ($P<0.05$). Excellent and good rates of Neer shoulder joint function scores in the research group were higher than those in the control group ($P<0.05$). VAS scores in the research group were lower than those in the control group ($P<0.05$). Levels of osteocalcin (OC), amino-terminal pro-peptide of type I procollagen (PINP), and bone alkaline phosphatase (BALP) in the research group were higher than those in the control group, while levels of pyridinoline (PYD), tartrate-resistant acid phosphatase (TRAP), cross-linked carboxy-terminal telopeptide of type I collagen (CTX), and deoxy pyridinoline (D-pyr) in the research group were lower than those in the control group (all $P<0.05$). There were no significant differences in levels of inflammatory cytokines interleukin (IL)-1β, IL-6, and IL-22 between the two groups (all $P>0.05$). Conclusion: PHILOS combined with allogeneic femoral head bone grafting has the advantages of fast fracture healing, shorter hospital stays, and less postoperative complications for treatment of complex osteoporotic proximal humeral fractures. Moreover, it alleviates postoperative pain, improves bone metabolism, avoids serious systemic inflammatory reactions, and is conducive to improving rehabilitation of shoulder joint function.

Keywords: Proximal humeral internal locking system, allogeneic femoral head structure, bone graft, complex osteoporotic proximal humeral fracture, bone metabolism

Introduction

Osteoporosis is common in elderly patients. Incidence rates have continually increased with the aging of the population in China. Incidence rates of osteoporotic proximal humeral fractures are also rising. Non-displaced stable proximal humeral fractures are mainly treated with conservative therapy, while surgical treatment is the main method when displacement occurs [1]. Traditional internal fixation surgery for osteoporotic proximal humeral fractures is prone to complications, such as screw loosening and avascular necrosis of the femoral head (ANFH) [2]. The proximal humeral internal locking system (PHILOS) has been recognized by many medical practitioners for clinical treatment of proximal humeral fractures due to less trauma, stable fixation, and divergent angles. Since complex osteoporotic proximal humeral frac-

tures are often accompanied by cancellous bone compression, resulting in reduction defects, it often causes postoperative complications and affects the rehabilitation of patients if not treated in a timely manner [3]. Bone grafts for restoration of the anatomical structure of the defect site can reduce postoperative complications in proximal humeral fractures [4]. Guo et al. used allogeneic bone grafts in open reduction and plate fixation to treat type A femoral shaft fractures. Results showed that healing times and complication rates in the bone graft group were significantly lower than those in the control group, suggesting that allogeneic bone implantation can effectively promote fracture healing, with fewer complications and satisfactory clinical efficacy in type A femoral shaft fracture surgeries [5]. Further exploring the efficacy of bone grafting in osteoporotic fractures, in the current study, PHILOS combined with allogeneic femoral head bone grafts was applied for osteoporotic proximal humeral fracture patients.

Materials and methods

General data

Eighty patients with complex osteoporotic proximal humeral fractures, admitted to Zhuji People's Hospital of Zhejiang Province, from June 2016 to June 2017, were selected and divided into two groups using a random number table, including the control group (n=38) and research group (n=42). Inclusion criteria: (1) Proximal humeral fractures confirmed by anteroposterior and lateral shoulder joint X-rays and shoulder joint CT scans and T values <-2.5 (osteoporosis) determined by dual-energy X-ray absorptiometry (DEXA); (2) Neer classification of fractures was III-IV; (3) Patients with closed fractures; (4) Within 3 days of fracturing; (5) No vascular or nerve injuries; (6) No contraindications to surgery; (7) Aged 60-79 years; and (8) Patients and their families provided informed consent. Exclusion criteria: (1) Patients with bone tuberculosis; (2) Complicated with serious endocrine system diseases; (3) Complicated with severe cardio-cerebral vascular diseases; (4) Complicated with severe liver, kidney, and lung dysfunction; (5) Fractures with severe suppuration and infections; (6) Complicated with autoimmune diseases; (7) Complicated with previous fracture operation histories in the same part; (8) Complicated with acute and chronic systemic infections; and (9) Complicated with coagulation dysfunction. The current study was approved by the Ethics Committee of Zhuji People's Hospital of Zhejiang Province.

Methods

Patients in the control group were treated with traditional PHILOS surgery. After brachial plexus block anesthesia, the deltoid and pectoralis major inter-spaces of the patients, set in a semi-supine position, were cut to fully expose the fracture end. Traction, reduction, and removal of hematoma and necrotic tissues were then performed. Femoral neck-stem angles and femoral collo-diaphyseal angles were restored and temporarily fixed with Kirschner wires. PHILOS (Shandong Wego-Orthopedic Materials Co., Ltd.) was inserted. Screw fixation was conducted, along with repair of the rotator cuff, joint capsule, and small fracture block. The incision was closed after fracture reduction and well fixation.

Patients in the research group were treated with PHILOS combined with allogeneic femoral head bone grafts. After brachial plexus block anesthesia, the patients were placed on a radiolucent operating table in a semi-supine position. A 4-6 cm transverse incision was made at 2 cm below the shoulder joint lateral acromion, exposing the deltoid muscles. Next, the deltoid muscles were separated bluntly and freed to protect axillary nerves. Soft tissues were removed to fully expose the fracture site. The anatomical relationship between the lesser and greater tuberosity of humeral head, humeral neck, and the humerus was restored. Fracture blocks were temporarily fixed with Kirschner wires. Allogeneic femurs (Hubei Osteolink Biomaterial Co., Ltd.) were pruned and implanted into the medullary cavity, according to the bone defect. Anatomical reduction was performed with the help of C-arm X-ray fluoroscopy and appropriate PHILOS was selected to be inserted tightly against the periosteum. The upper edge of the steel plate was 5-10 mm below the apex of the greater tuberosity of the humerus. The bone plate was 5 mm outside the bicipital groove, with the steel plate tightly attached to the surface of the humerus. The proximal humerus was drilled and 7-8 screws were placed for fixation. The length did not exceed the articular surface. Afterward, 2-3 screws were placed in humeral shaft for fixation. The rotator cuff, joint capsule, and small fracture block were repaired. Reduction and

Table 1. Comparison of general data between the two groups ($\bar{x}$ ± sd)

Groups	Research group	Control group	t/χ^2	P
n	42	38		
Gender			0.036	0.849
Male	19	18		
Female	23	20		
Age (year)	70.9±3.9	71.4±4.2	0.509	0.613
Time from fracture to surgery (d)	1.92±0.77	1.87±0.65	0.312	0.756
Neer classification of fracture			0.016	0.899
III type	26	23		
IV type	16	15		

Table 2. Comparison of intraoperative and postoperative conditions between the two groups ($\bar{x}$ ± sd)

Groups	Research group	Control group	t	P
n	42	38		
Surgical duration	122.29±13.85	120.73±15.77	0.471	0.638
Intraoperative blood loss	292.93±47.96	287.51±55.84	0.467	0.642
Fracture healing time	84.82±4.37	101.75±5.12	15.951	<0.001
Hospital stay	15.43±1.22	18.65±1.68	9.875	<0.001
VAS score	5.83±1.45	7.02±1.87	3.197	0.002

Note: VAS, visual analogue scale.

fixation were observed with C-arm X-ray fluoroscopies. Finally, incision hemostasis, flushing, and closure were performed.

Both groups were treated with anti-infection therapy for 3 days, as well as anti-osteoporosis therapy, including: 1) Calcitriol (Qingdao CP Haier Pharmaceutical Co., Ltd.) 0.5 μg/time, once a day orally; 2) Calcium carbonate (Zhuhai Tongyuan Pharmaceutical Co., Ltd.) 2 tablets/time and 2 times/d orally; and 3) Salmon calcitonin injections (Shanghai Pacific Pharmaceutical Co., Ltd.) at 200 IU/time and 1 time/2 d, intramuscularly injected, with continuous treatment for 1 year. Functional exercises were carried in combination with recovery.

Outcome measures

(1) Surgical duration, intraoperative blood loss, hospital stays, and fracture healing times in the two groups were recorded; (2) Determination of fracture healing: Shoulder joint X-rays showed callus formation and fuzzy fracture lines at fracture sites; (3) Neer shoulder joint function scores: One month after surgery, pain, function, mobility, and anatomical location were scored, with a total score of 100 points. Scores ≥90 are excellent, 80-89 are good, 70-79 are acceptable, and ≤69 are poor. Excellent rate = (excellent + good)/number of cases * 100%; (4) Pain degree scores: Visual analogue scale (VAS) scores were used one week after surgery. A blank scale was made in which 0-10 was marked, with 0 indicating painless and 10 severe pain. Patients were scored according to the pain degree, with higher scores indicating more severe pain; (5) Determination of biochemical markers of bone turnover: One month after surgery, 3 mL of venous blood of the patients was drawn. It was centrifuged at 3,000 r/min and stored in a refrigerator at -70°C for examination. Levels of osteocalcin (OC), amino-terminal pro-peptide of type I procollagen (PINP), bone alkaline phosphatase (BALP), pyridinoline (PYD), tartrate-resistant acid phosphatase (TRAP), cross-linked carboxy-terminal telopeptide of type I collagen (CTX), and deoxy pyridinoline (D-pyr) were determined using enzyme-linked immunosorbent assays (ELISA). All kits were manufactured by Shanghai J&L Biotechnology Co., Ltd; (6) Determination of inflammatory cytokine levels: One month after surgery, 3 mL of venous blood was drawn and centrifuged for testing. Interleukin-1β, 6, and 22 (IL-1β, IL-6, IL-22) were determined with ELISA. All kits were manufactured by R&D Company; and (7) Criteria for complication judging: 1) Humeral head necrosis: CT, MRIs, or X-rays showed humerus bone reduction and partial and complete absorption; 2) Screw cutting-out: X-rays showed screws penetrating the humeral head; 3) Humeral head varus: Humerus radiographs in the neutral position with rotation showing humerus head-shaft angles <120; and 4) Delayed fracture healing: After 3 months of treatment, the fracture site still had tenderness and percussion pain. X-rays showed that the fracture line existed and a small amount of callus grew at

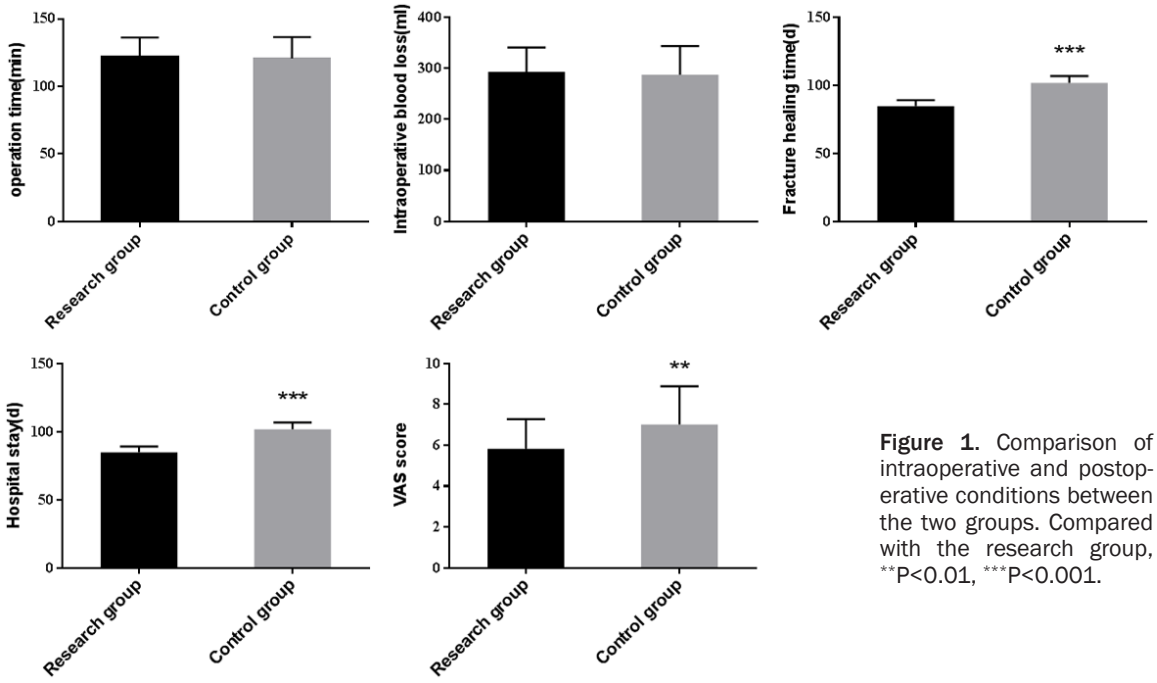

Figure 1. Comparison of intraoperative and postoperative conditions between the two groups. Compared with the research group, **P<0.01, ***P<0.001.

Table 3. Comparison of complications between the two groups (n, %)

Groups	Research group	Control group	χ^2	P
n	42	38		
Infection associated with internal fixation	2 (4.76)	3 (7.89)		
Humeral head necrosis	0	1 (2.63)		
Screw cutting out	0	2 (5.26)		
Humeral head varus	0	1 (2.63)		
Delayed fracture healing	3 (7.14)	6 (15.79)		
Incidence	5 (11.90)	13 (34.21)	5.692	0.017

the broken end, with no hardening phenomenon and an unobstructed bone marrow cavity.

Statistical analysis

SPSS19.0 statistical software was used to analyze data. Measurement data are expressed as ($\overline{x}$ ± sd) and were analyzed using t-tests. Count data are expressed as (%) and were analyzed using χ^2 tests. P<0.05 indicates statistically significant differences.

Results

Comparison of general data between the two groups

There were no significant differences in general data between the two groups (P>0.05), as shown in **Table 1**.

Comparison of intraoperative and postoperative conditions between the two groups

Hospital stays and fracture healing times in the research group were shorter than those in the control group. VAS scores in the research group were lower than those in the control group (P<0.05). There were no significant differences in surgical duration and intraoperative blood loss between the two groups (both P>0.05). See **Table 2** and **Figure 1**.

Comparison of wound healing between the two groups

There were 40 cases (95.24%) of primary wound healing in the research group and 35 cases (92.11%) in the control group. There were no significant differences between the two groups (P>0.05).

Comparison of complications between the two groups

Incidence of postoperative complications in the research group was lower than that in the control group (P<0.05). See **Table 3**.

Table 4. Comparison of shoulder joint function between the two groups (n, %)

Groups	Research group	Control group	χ^2	P
n	42	38		
Excellent	23 (54.76)	16 (42.11)		
Good	14 (33.33)	10 (26.32)		
Acceptable	4 (9.52)	9 (23.68)		
Poor	1 (2.38)	3 (7.89)		
Excellent and good rate	37 (88.10)	26 (68.42)	4.615	0.032

Table 5. Comparison of biochemical markers of bone turnover between the two groups ($\overline{x}$ ± sd)

Groups	Research group	Control group	t	P
n	42	38		
OC (μg/L)	7.17±0.92	5.34±0.55	10.656	<0.001
PINP (ng/mL)	92.71±8.23	79.46±7.60	7.456	<0.001
BALP (IU/L)	72.84±8.01	66.43±7.64	3.653	<0.001
PYD (U/L)	23.67±3.15	30.66±4.32	8.324	<0.001
TRAP (U/L)	3.58±0.47	4.45±0.69	6.645	<0.001
CTX (ng/mL)	4.92±0.68	7.75±0.93	15.638	<0.001
D-pyr (pg/mL)	1.32±0.16	3.05±0.28	34.336	<0.001

Note: OC, osteocalcin; PINP, amino-terminal pro-peptide of type I procollagen; BALP, bone alkaline phosphatase; PYD, pyridinoline; TRAP, tartrate-resistant acid phosphatase; CTX, cross-linked carboxy-terminal telopeptide of type I collagen; D-pyr, deoxy pyridinoline.

Comparison of shoulder joint function between the two groups

Excellent and good rates of the Neer shoulder joint function scores in the research group were higher than those in the control group (P<0.05). See **Table 4**.

Comparison of biochemical markers of bone turnover between the two groups

OC, PINP, and BALP levels in the research group were higher than those in the control group, while PYD, TRAP, CTX, and D-pyr levels were lower than those in the control group (P<0.05). See **Table 5** and **Figure 2**.

Comparison of inflammatory cytokines between the two groups

There were no significant differences in levels of inflammatory cytokines IL-1β, IL-6, and IL-22 between the two groups (P>0.05), as shown in **Table 6** and **Figure 3**.

Discussion

PHILOS is a new internal fixation system based on an improved proximal humerus locking plate. This plate matches well with the anatomical structure of the proximal humerus. Compared with common bone plates, PHILOS has the advantages of good angular stability, strong anti-loosening ability, and a direct effect on internal fixation [6, 7]. Conforming to the special anatomical characteristics of the proximal humerus, PHILOS does not need pre-bending and forced attachment [8]. PHILOS close to the periosteum can prevent it from stripping and damage. It can protect the blood supply, avoiding ischemic necrosis of humeral head and promoting fracture healing [9]. PHILOS has many locking holes, divergent angles, comprehensive coverage, stable fixation, and wide stress distribution. These factors are conducive to fracture stability. It is especially suitable for osteoporotic humerus fractures [10]. PHILOS has 10 suture holes at its proximal end. These can be used to suture and fix bone fragments. Osteoporotic proximal humeral fracture reduction defects can cause complications, such as postoperative humeral head necrosis, delayed union or nonunion of fracture, screw penetration, internal fixation loosening or pulling out, and even secondary surgery for patients [11, 12]. Therefore, fracture reduction and defects should be treated to prevent the above complications. The allogeneic femoral head belongs to structural bone grafts. An appropriate allogeneic femoral head is selected and trimmed according to the reduction defect of the patient to match the anatomical differences, better filling the bone defect. Trapezoidal support is the main support for most of the three- or four-part osteoporotic proximal humeral fractures [13]. Allogeneic bones have the advantages of low immunogenicity, convenient pruning, and good safety. They have been widely used in clinical bone graft treatment.

Results of the current study showed that PHILOS combined with allogeneic femoral head bone grafts could shorten hospital stays, re-

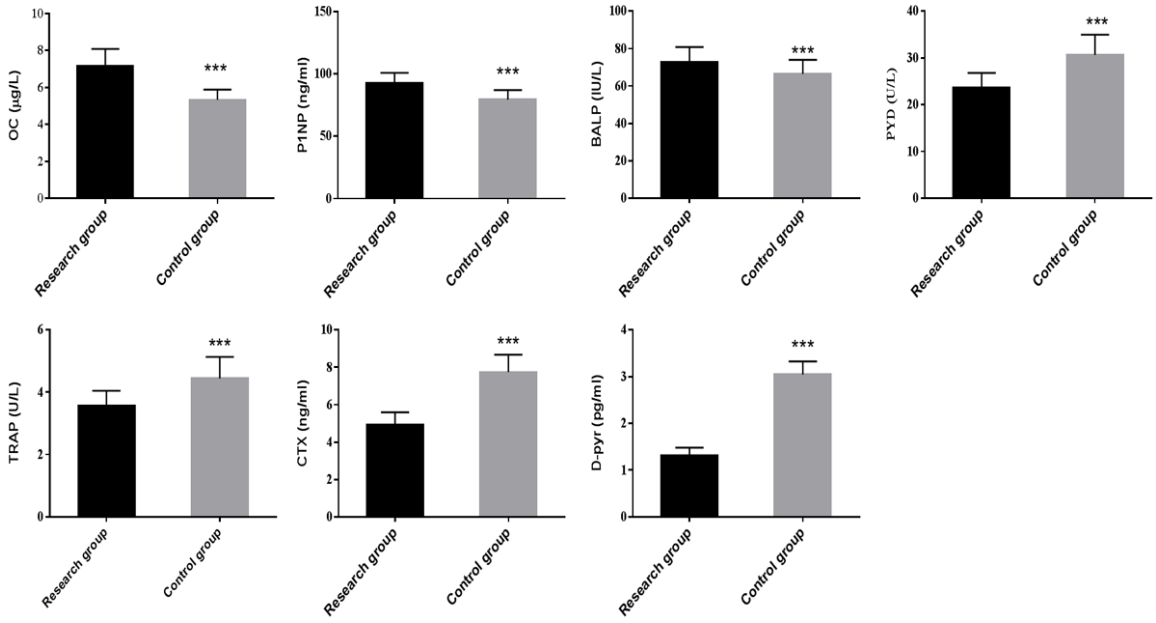

Figure 2. Comparison of biochemical markers of bone turnover between the two groups. OC, osteocalcin; PINP, amino-terminal pro-peptide of type I procollagen; BALP, bone alkaline phosphatase; PYD, pyridinoline; TRAP, tartrate-resistant acid phosphatase; CTX, cross-linked carboxy-terminal telopeptide of type I collagen; D-pyr, deoxy pyridinoline. Compared with the research group, ***P<0.001.

Table 6. Comparison of inflammatory cytokines between the two groups ($\bar{x}$ ± sd)

Groups	Research group	Control group	t	P
n	42	38		
IL-1β (pg/mL)	0.21±0.03	0.22±0.05	1.097	0.276
IL-6 (μg/mL)	24.72±1.63	24.06±1.98	1.634	0.106
IL-22 (μg/mL)	5.35±0.42	5.22±0.75	0.968	0.338

Note: IL-1β, interleukin 1β; IL-6, interleukin 6; IL-22, interleukin 22.

duce postoperative pain, accelerate fracture healing, reduce postoperative complications, and promote shoulder joint function recovery in treating complex osteoporotic proximal humeral fractures. Current results are in accord with previous research reports [14, 15]. One study showed that bone formation and resorption directly affected healing in fracture patients after surgery. Bone formation indexes include OC, PINP, and BALP. They directly reflect osteoblast activity and promote normal bone mineralization. Higher levels indicate more vigorous bone formation and better fracture healing [16]. Bone resorption indexes include PYD, TRAP, CTX, and D-pyr, which reflect the degree of osteoclast activity and overall bone formation of the fracture. Lower levels indicate lower osteoclast activity at the fracture site and better bone formation. In this study, OC, PINP, and BALP levels in the study group were higher than those in the control group, while PYD, TRAP, CTX, and D-pyr levels were lower than those in the control group. Results suggest that PHILOS combined with allogeneic femoral head bone grafts promote fractures to progress towards bone formation, with strong osteogenesis and better fracture healing. The reason may be that the internal fixation system used by PHILOS combined with allogeneic femoral head bone grafts does not need to be fully attached to the bone surface. This can reduce damage caused by friction, thus protecting the local blood supply and improving bone metabolism after surgery. Studies have proven that local or systemic inflammatory reactions are caused by blood scab absorption at fracture sites and foreign body stimulation formed by PHILOS and allogeneic femoral head bone grafts, while inflammatory cytokines damage tissues and affect fracture healing [17-19]. In this study, there were no significant differences in levels of inflammatory cytokines IL-1β, IL-6, and IL-22 between the study group and control group. This suggests that, although PHILOS

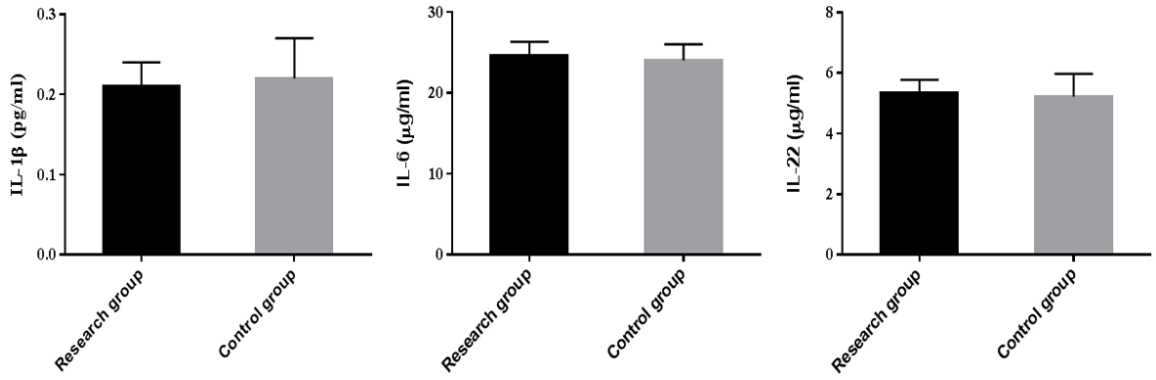

Figure 3. Comparison of inflammatory cytokines between the two groups. IL-1β, interleukin 1β; IL-6, interleukin 6; IL-22, interleukin 22.

combined with allogeneic femoral head bone grafts is a foreign body, it does not increase systemic inflammatory reactions, while promoting fracture healing after implantation [20, 21]. However, there were several limitations to the current study. For example, the sample size was too small. Study subjects included patients with three-and four-part fractures and the patients were all 60-79 years old. Therefore, whether PHILOS combined with allogeneic femoral head bone grafting is suitable for elderly patients over 80 years old and other patients with different types requires further exploration with expanded sample sizes.

In summary, PHILOS combined with allogeneic femoral head bone grafting has the advantages of fast fracture healing, shorter hospital stays, and less postoperative complications for treatment of complex osteoporotic proximal humerus fractures. Moreover, it alleviates postoperative pain, improves bone metabolism, avoids serious systemic inflammatory reactions, and is conducive to improving rehabilitation of shoulder joint function. Therefore, it is worthy of application.

Disclosure of conflict of interest

None.

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