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Original Article

Effect of MIPO combined with locking compression plate fixation on shoulder and elbow joint function and bone metabolic activity in adult patients with middle humeral shaft fracture

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Abstract: Objective: To analyze the effect of minimally invasive percutaneous osteosynthesis (MIPO) combined with locking compression plate fixation on middle humeral shaft fracture in adults. Methods: The clinical data of 88 adult patients with middle humeral shaft fracture treated in Xiang'an Hospital from August 2019 to August 2021 were retrospectively analyzed. According to different surgical methods, they were assigned into an anterograde group (treated with anterograde interlocking intramedullary nail fixation, N=42) and a joint group (treated with MIPO technique combined with locking compression plate fixation, N=46 cases). The perioperative indexes and complications were compared between the two groups. The changes of Constant-Murley shoulder joint function score, Mayo elbow joint function score, bone metabolic activity indexes [collagen hydroxyl terminal peptide (CTX), type I procollagen amino acid terminal peptide (PICP), osteoprotegerin (OPG), and osteocalcin (BGP)], and bone quality indexes [bone trabecular spacing (Tb.Sp), bone volume fraction (BV/TV), bone elastic stress (ES), bone trabecula number (Tb.N), and volume organic matter content (VOC)] were observed before and after the operation for 3 months. Results: The fracture healing time and postoperative hospitalization time in the joint group were shorter than those in the anterograde group. The intraoperative blood loss was less than that in the anterograde group (P<0.05). Three months after the operation, the scores of the Constant-Murley and Mayo, Tb.N, VOC, and ES in the joint group were higher than those in the anterograde group. The Tb.Sp and BV/TV were lower than those in the anterograde group (P<0.05). The serum CTX level in the joint group was lower than that in the anterograde group. The levels of PICP, OPG, and BGP were higher than those in the anterograde group (P<0.05). There was no significant difference in the total incidence of complications between the joint group and the anterograde group (P>0.05). Conclusion: MIPO technique combined with locking compression plate fixation can promote the healing of middle humeral shaft fracture in adults, improve the function of the shoulder joint and the elbow joint, regulate the activity of bone metabolism, and improve bone quality, without significant increase in complications.

Keywords: Adult middle humeral shaft fracture, minimally invasive percutaneous osteosynthesis, locking compression plate fixation

Introduction

Middle humeral shaft fracture is a common fracture type in orthopedics. It refers to the fractures occurring from 2 cm below the surgical neck of the humerus to 2 cm above the condyle of the humerus [1, 2]. Epidemiology showed that the proportion of humeral shaft fractures occurring in the upper, middle, and lower segments of the humerus was 30%, 60%, and 10%, respectively [3]. Surgery is the main treatment for middle humeral shaft fracture, including open reduction, plate internal fixation, locking compression plate, and external fixation bracket. There are significant differences in the advantages and disadvantages, and the fracture healing rate among different surgical methods. There is no consensus on an optimal surgical method for the clinical treatment of middle humeral shaft fracture in adults. Traditional open reduction and plate internal fixation is accurate in reduction. The periosteum needs to be stripped during the operation. The surrounding soft tissues are significantly damaged.

Postoperative complications such as loosening of internal fixation, soft tissue stripping injury, and iatrogenic radial nerve injury are at high risk. These are not conducive to functional recovery of the shoulder and elbow joint and the healing of the fracture site after the operation [4, 5]. The anterograde interlocking intramedullary nail fixation takes a short time, with a small incision, but the shoulder cuff needs to be cut. This delays the recovery of the shoulder joint function. Locking compression plate fixation is the main surgical method. It has the characteristics of a firm internal fixation and a high reduction success rate. There are complications such as poor blood supply at the broken end of the fracture, impaired vascular and nerve function, and delayed healing of the fracture after the operation [6]. It is critical to actively explore a highly effective and safe surgical approach for the treatment of middle humeral shaft fracture in adults.

Minimally invasive percutaneous osteosynthesis (MIPO) is a combination of biological internal fixation and minimally invasive concept. By establishing tunnels at the proximal and distal ends of the humeral shaft, it can reduce soft tissue injury and surgical trauma without affecting the blood supply at the fracture site, making up for the shortcomings of the above operations [7, 8]. Foreign studies have found that MIPO combined with locking compression plate internal fixation in the treatment of limb fractures can significantly restore the length, rotation, and force line of the fracture end of the femoral shaft. This sped up the reconstruction of joint function and fracture healing after the operation [9]. There are few reports about MIPO combined with locking compression plate internal fixation for middle humeral shaft fracture in China. The clinical data of 88 adult patients with middle humeral shaft fracture were retrospectively analyzed. The effects of MIPO technique combined with locking compression plate fixation and anterograde interlocking intramedullary nail fixation on the shoulder and elbow joint function, bone metabolic activity, bone quality, and complications were compared.

Materials and methods

Baseline data

From August 2019 to August 2021, the clinical data of 88 adult patients with middle humeral shaft fracture were retrospectively analyzed, including 50 males and 38 females. The age ranged from 25 to 72 years old, with an average of (45.08±4.29) years old. Before the operation, the swelling subsided in 2-6 days, with an average of (3.78±1.42) days. The causes of injury included car accident in 39 cases, machine crush in 25 cases, fall injury in 16 cases, and others in 8 cases. AO classification included 35 cases of type A, 45 cases of type B and 8 cases of type C. This research had been approved by the Medical Ethics Committee of Xiang'an Hospital of Xiamen University.

Inclusion and exclusion criteria

Inclusion criteria: Patients were diagnosed with middle humeral shaft fracture by CT or X-ray. There was a definite history of trauma. Patients were accompanied by pain and swelling of the forearm, movement disorder, and palpable bone fricative. Patients ranged in age from 18 to 80 years old. Patients had a closed fracture. The time from fracture to admission was less than 7 days. Patients met the surgical indications. The clinical data were complete.

Exclusion criteria: Patients with bilateral fracture, pathological fracture and open fracture, or pre-operative neurovascular injury; patients comorbid with other fractures; patients who did not undergo surgery within 1 week after admission; patients with an old fracture of humerus and incomplete development of humerus; patients with suspicious pathological fracture or bone tumour; patients with conservative treatment, systemic severe infection, or coagulation dysfunction; patients who were not interviewed after the operation; pregnant or lactating women.

Methods

Anterograde group: Anterograde interlocking intramedullary nail fixation: The patient was placed in the supine position and received brachial plexus nerve block anesthesia or general anesthesia. A 5 cm incision was made from the acromion to the tip of the greater tuberosity of the humerus. The subcutaneous tissue was cut layer by layer. The greater tuberosity of the humerus and the humeral head were exposed. The needle was inserted from the edge of the articular surface of the humeral head and the inner side of the greater tuberosity of the

humerus. The positive and lateral view was satisfactory under the fluoroscopy of the C-arm machine. The guide needle was inserted along the shaft of the medullary cavity with the help of mouth gag. The reaming drill was used to ream the marrow. The fracture site was closed and reduced. The appropriate intramedullary nail was placed into the medullary cavity in an anterograde manner. The position of intramedullary nail and fracture reduction were satisfactory under the fluoroscopy of the C-arm machine. With the aid of an aiming device, 2-3 locking nails were placed into the proximal and distal humerus respectively. The position of the screw was determined again under the fluoroscopy of the C-arm machine if there was no acromial impact during shoulder joint passive movement. After confirmation, the incision was washed repeatedly with normal saline, and placed for drainage. The incision was sutured layer by layer after hemostasis.

Joint group: MIPO technique combined with locking compression plate fixation: The patient was placed in the supine position and received brachial plexus nerve block anesthesia or general anesthesia. The patient's upper arm was abducted at 90° and the forearm supinated. An incision was made in the gap between the biceps brachii and the deltoid muscle, with a length of 3 cm. The biceps brachii and the deltoid muscle were pulled to the medial and lateral sides respectively to expose the proximal humerus. The compression plate was pre-bent and locked according to the anatomical shape of the anterior humerus. Bone stripping was used to make a tunnel under the muscle close to the front of humeral shaft, reaching the fracture. An incision (3 cm) was made at the lateral margin of the biceps brachii above the cubital crease. The biceps brachii was cut layer by layer and separated longitudinally. The 10-12-hole locking compression plate was placed in front of the humeral shaft through the fracture site. The manual reduction was performed under the longitudinal traction of the elbow flexion. Separating the radial nerve during the operation was not necessary. The lateral cutaneous nerve of the forearm should be protected during the whole process. The position of the plate was defined under X-ray. If the fracture is displaced, it should be reduced again. After the plate position and fracture reduction were confirmed to be satisfactory, 3-4 screws were screwed into the proximal and distal ends of the humerus. The shoulder and elbow joints were passively moved after fixation. The corresponding positions of the two broken ends of the fracture, the force line of the fracture site and the plate position were determined to be satisfactory under the fluoroscopy of the C-arm machine. The fracture site was firmly fixed. The incision was washed repeatedly with normal saline, and placed for drainage. The incision was sutured layer by layer after hemostasis. In the joint group, all patients were fixed with 4.5 mm locking compression plate.

Outcome measures

Main outcome measures: (1) Baseline data. (2) Perioperative indexes. (3) Shoulder and elbow joint function. The Constant-Murley scale [10] was used to evaluate the shoulder function of patients before the surgery and 3 months after the surgery. The Constant-Murley scale consisted of four dimensions, daily life (20 points), pain degree (15 points), muscle strength (25 points), and shoulder joint mobility (40 points), with a full score of 100. The shoulder joint function was directly proportional to the score. The Mayo scale was used to evaluate the elbow joint function of patients before the surgery and 3 months after the surgery. The Mayo scale consisted of four dimensions, motor function (20 points), pain (45 points), stability (10 points) and daily activities (25 points), with a full score of 100. The elbow joint function was proportional to the score. (4) Indexes of bone metabolic activity. The fasting venous blood (5 ml) was drawn in the morning before and after the surgery for 3 months. It was centrifuged at 3500 r/min with a radius of 6 cm for 5 min. The supernatant was obtained and stored in a refrigerator at -80°C for testing. Serum levels of collagen hydroxyl terminal peptide (CTX), type I procollagen amino acid terminal peptide (PICP), osteoprotegerin (OPG), osteocalcin (BGP) were measured by enzyme-linked immunosorbent assay (Shanghai Yuduo Biotechnology Co., Ltd.).

Secondary outcome measures: (1) Related indexes of bone quality. Before and after the operation for 3 months, the bone trabecular spacing (Tb.Sp), bone volume fraction (BV/TV), bone elastic stress (ES), bone trabecula number (Tb.N), and volume organic matter content

Table 1. Comparison of baseline data between the two groups (n, $\bar{X}\pm s$)

Data		Anterograde group (n=42)	Joint group (n=46)	t/χ^2	*P*
Gender	Male	24	26	0.003	0.953
	Female	18	20		
Age (year old)		45.16±3.34	44.91±4.74	0.283	0.778
Time from swelling regression to surgery (d)		3.96±1.57	3.62±1.34	1.096	0.276
Cause of injury	Traffic accident	18	21	0.841	0.840
	Crush injury caused by machine	12	13		
	Fall damage	7	9		
	Others	5	3		
AO classification	Type A	16	19	0.777	0.678
	Type B	21	24		
	Type C	5	3		

(VOC) were measured and calculated by using the plate model based on triangle algorithm in the software of Skyscan1176 Tomography System (Micro-CT) (manufacturer: SkyScan, Belgium). (2) Complications including bone nonunion, radial nerve injury, infection, and acromion injury were observed.

Statistical methods

GraphPad Prism 7 was used for figure rendering. SPSS23.0 was applied to process the data. $\bar{X}\pm S$ was applied to represent the measured data. Paired sample t test was used for intra-group comparison. Independent sample t test was used for inter-group comparison. The results of the enumeration data were presented as a percentage and tested by χ^2 test or Fisher's exact test. The difference was statistically significant with $P<0.05$.

Results

Baseline data

Compared with the anterograde group, there was no significant difference in gender, age, time form swelling regression to surgery, cause of injury and AO classification, and distribution in the joint group (all $P>0.05$) (**Table 1**).

Perioperative indexes

The fracture healing time and postoperative hospitalization time in the joint group were shorter than those in the anterograde group. The intraoperative blood loss was less than that in the anterograde group (all P<0.05). There was no significant difference in operation time between the two groups (P>0.05) (**Figure 1**).

Shoulder and elbow joint function

Three months after the operation, the scores of the Constant-Murley and the Mayo increased in both groups (all $P<0.05$). The scores of the Constant-Murley and the Mayo in the joint group were higher than those in the anterograde group (all $P<0.05$) (**Figure 2**).

Indexes of bone metabolic activity

Three months after the operation, the level of serum CTX decreased. The levels of PICP, OPG, and BGP increased in both groups (all $P<0.05$). The serum CTX level in the joint group was lower than that in the anterograde group. The levels of PICP, OPG, and BGP were higher than those in the anterograde group (all $P<0.05$) (**Figure 3**).

Related indexes of bone quality

Three months after the operation, Tb.Sp and BV/TV decreased, Tb.N, VOC and ES increased in both groups (all $P<0.05$), Tb.Sp and BV/TV in the joint group were lower than those in the anterograde group, and Tb.N, VOC, and ES were higher than those in the anterograde group (all $P<0.05$) (**Figure 4**).

Complications

There was no significant difference in the total incidence of complications between the joint group and the anterograde group ($P>0.05$) (**Table 2**).

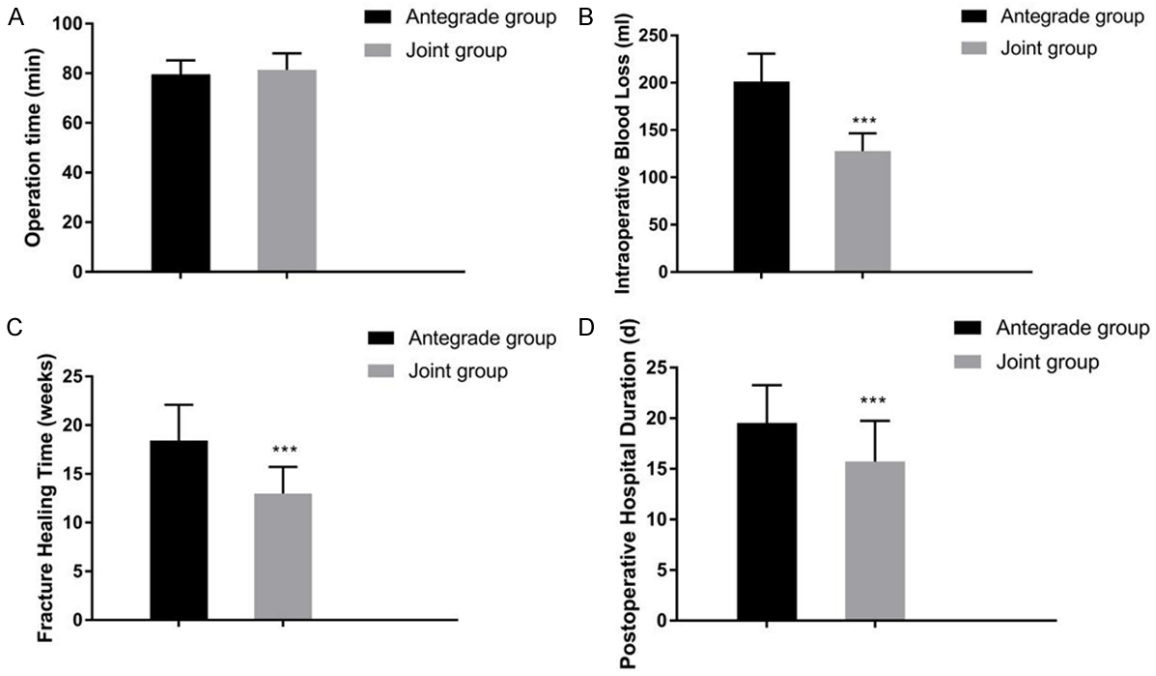

Figure 1. Comparison of perioperative indicators between the two groups. A: The time of operation; B: The blood loss during operation; C: The time of fracture healing; D: The postoperative hospital stay. Compared with the anterograde group, ***P<0.001.

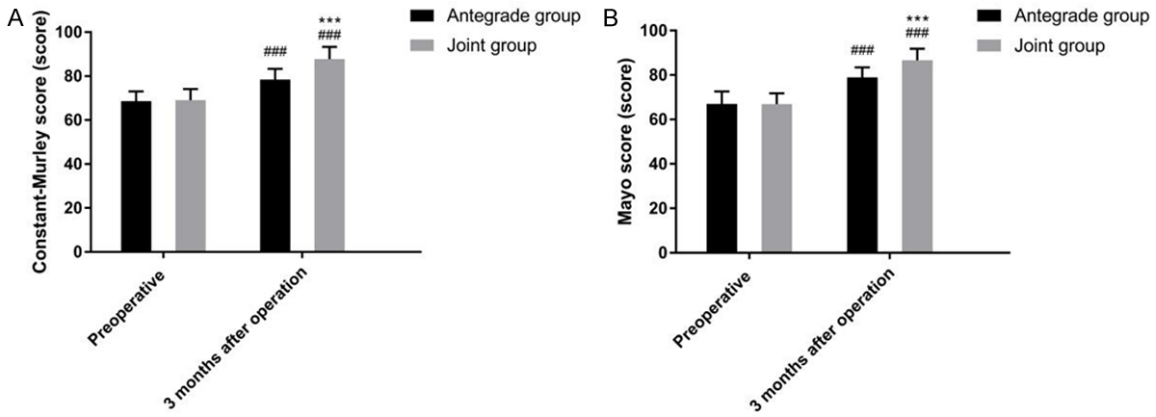

Figure 2. Comparison of Constant-Murley and Mayo scores between the two groups before and after operation. A: The Constant-Murley score; B: The Mayo score. Compared with the anterograde group, ***P<0.001; Compared with this group before operation, ###P<0.001.

Discussion

In recent years, studies have revealed that MIPO combined with locking compression plate fixation can effectively reset the force line, rotation, and length of the femoral shaft fracture in the treatment of limb fractures, which is helpful to rebuild joint function and speed up fracture healing [11-13]. There are few reports about the feasibility and safety of MIPO combined with locking compression plate fixation in the treatment of middle humeral shaft fracture at home and abroad. There is controversy about the impact of MIPO on radial nerve injury of patients through different approaches [14]. The results of this research revealed that compared with the anterograde group, the patients in the joint group had shorter fracture healing time, postoperative hospitalization time, less intraoperative blood loss, and higher Constant-

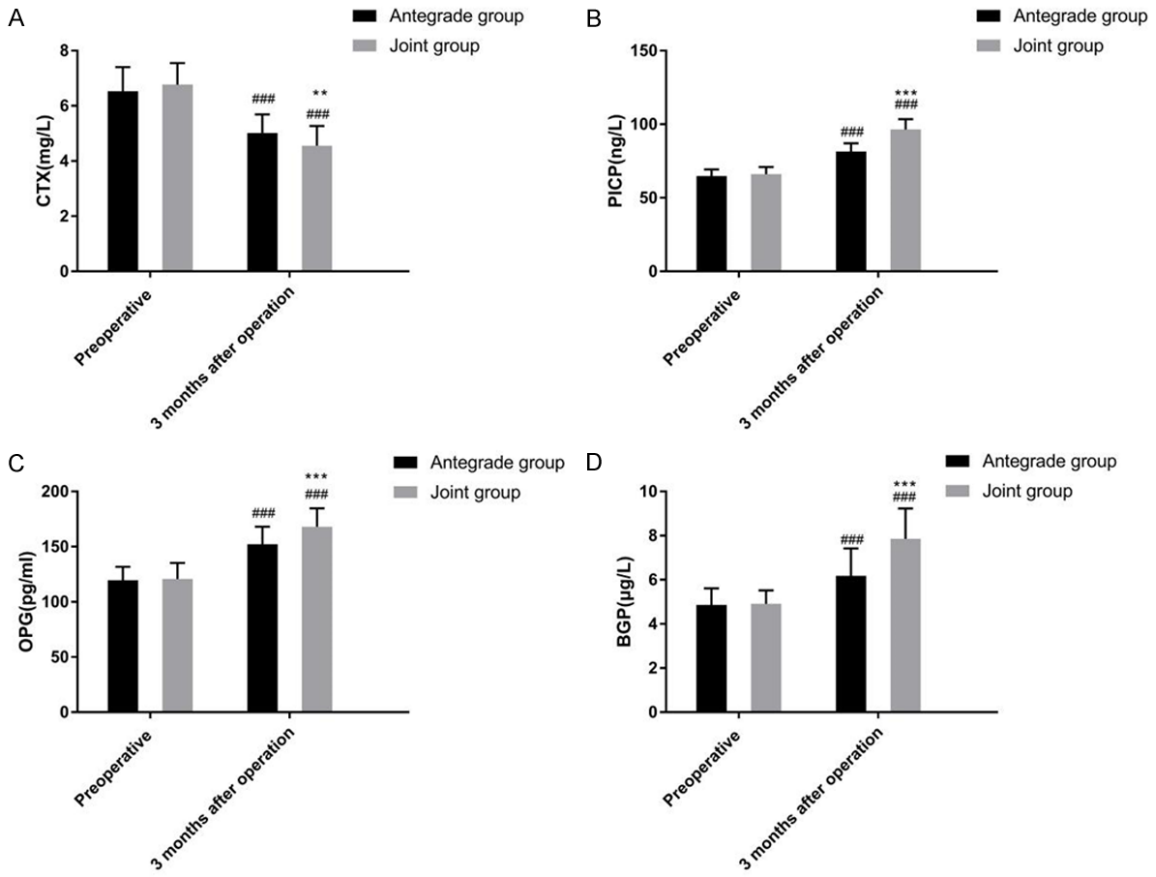

Figure 3. Comparison of bone metabolic activity indexes between the two groups before and after operation. A: Collagen hydroxyl terminal peptide (CTX); B: Type I procollagen amino acid terminal peptide (PICP); C: Osteoprotegerin (OPG); D: Osteocalcin (BGP). Compared with the anterograde group, $^{**}P<0.01$, $^{***}P<0.001$; Compared with this group before operation, $^{###}P<0.001$.

Murley and Mayo scores at 3 months after the operation. This was like the results of Yuan et al. [15]. It was confirmed that MIPO technique combined with locking compression plate fixation can accelerate the healing of the middle humeral shaft fracture in adults, and improve the shoulder and elbow joint function. This is because the lower end of humeral shaft is triangular, and the upper end is round, requiring high rotational stability. The intramedullary nail fixation may not match the size of the bone marrow cavity, leading to fracture displacement and instability of fracture site [16]. The nail tail fixed by intramedullary nail is too long and can cause acromion injury and aggravate shoulder pain after colliding with acromion. The deep rotator cuff of the deltoid muscle needs to be cut during the operation. This helps to lead to the destruction of the physiological structure of shoulder muscle group, reduce the function of shoulder joint, and cause complications such as inflammation of acromioclavicular joint and rotator cuff rupture. Locking compression fixation can avoid screw loosening, stabilize the angle between steel plate and screw, and reduce periosteal injury [17]. Locking compression fixation can select appropriate surgical incision according to different fracture sites. The incision in this research did not involve the shoulder joint. This ensured shoulder joint function, relieved shoulder joint pain, and sped up postoperative recovery of the shoulder and elbow joint. Based on the locking compression fixation, MIPO technology can reduce surgical trauma, promote biomechanical fixation to "physiological fixation", relieve the damage degree of biological reaction and mechanical environmental reaction, and reduce iatrogenic injury [18, 19].

There were 3 cases of radial nerve injury and 1 case of infection in the joint group, and 2 cases

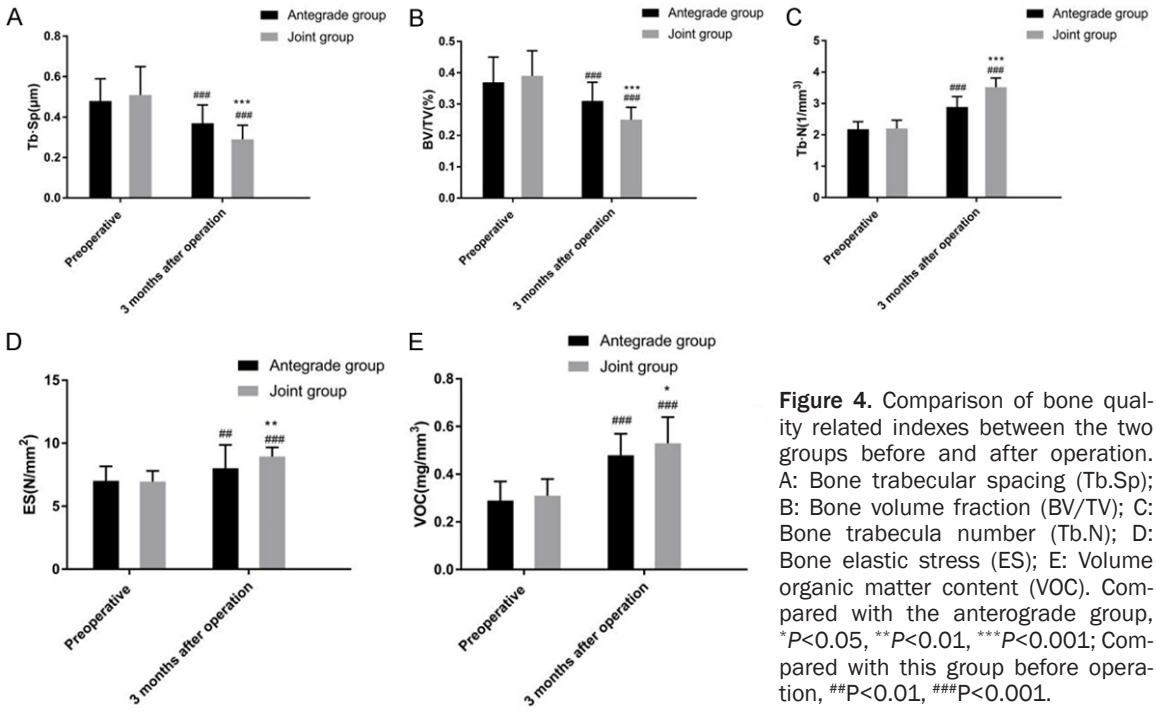

Figure 4. Comparison of bone quality related indexes between the two groups before and after operation. A: Bone trabecular spacing (Tb.Sp); B: Bone volume fraction (BV/TV); C: Bone trabecula number (Tb.N); D: Bone elastic stress (ES); E: Volume organic matter content (VOC). Compared with the anterograde group, $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$; Compared with this group before operation, $^{\#\#}P<0.01$, $^{\#\#\#}P<0.001$.

Table 2. Comparison of complications between the two groups n (%)

Groups	Cases	Nonunion	Radial nerve injury	Infection	Acromion injury	Total Incidence
Anterograde group	42	2 (4.76)	1 (2.38)	1 (2.38)	3 (7.43)	7 (16.67)
Joint group	46	0	3 (6.52)	1 (2.38)	0	4 (8.70)
χ^2		2.241	0.868	0.004	3.402	1.275
P		0.225^	0.618^	1.000^	0.105^	0.259

Note: ^indicates Fisher exact test results.

of nonunion, 1 case of radial nerve injury, 1 case of infection, and 3 cases of acromion injury in the anterograde group. The results revealed that MIPO technique combined with locking compression plate fixation did not significantly increase the risk of complications such as radial nerve injury, and had high safety. The radial nerve injury is caused by the radial nerve running along the humeral shaft and pulling during the operation. In this research, the anterior approach did not need to peel off the deltoid insertion and did not expose the radial nerve, reducing the radial nerve injury. There were no important blood vessels or nerves passing through the anterior margin of the humerus. It is relatively flat. The operation of inserting the steel plate through the anterior approach is simple. The radial nerve injury caused by the direct contact of the steel plate and radial nerve can be avoided under the protection of the lateral part of the brachialis [20].

The essence of fracture healing belongs to a process of bone reconstruction, which is related to the equilibrium state between osteoblasts and osteoclasts. The changes of their cell activity and function are the main links that cause the decrease of bone quality and the destruction of bone microstructure [21, 22]. When the activity and function of osteoclasts exceed that of osteoblasts, it can delay the process of bone regeneration and fracture healing. CTX is produced by partial degradation of mature type I collagen. This is closely related to osteoclast activity and bone resorption. PICP is a regulatory molecule during the synthesis of type I collagen, which can keep the integrity of bone microstructure [23]. OPG can block the differentiation and maturation of osteoclasts and inhibit the formation of osteoclasts. BGP is an essential substance for bone matrix mineralization, which can maintain the normal mineralization rate and inhibit the formation of abnor-

mal hydroxyapatite crystals [24]. In clinic, the bone fragility of fracture patients is often evaluated by two indexes: bone mass and bone quality. The mechanical properties of bone are often evaluated by some mechanical experiments. The mechanical strength of bone is related to mineral composition, organic matrix, bone microstructure, and injury repair. Elastic modulus of bone is a mechanical property index independent of bone structure and bone mass. It can be used as an objective index to evaluate bone fragility. Humeral shaft fractures are caused by rotational violence, indirect violence, or direct violence, and are often accompanied by changes in bone structure and bone loss. This study was designed to evaluate the bone quality and bone fragility at the fracture site by Micro-CT instrument. In this research, CTX, Tb.Sp, and BV/TV in the joint group were lower than those in the anterograde group. PICP, OPG, BGP, Tb.N, VOC, and ES were higher than those in the anterograde group at 3 months after the operation. This indicated that MIPO technique combined with locking compression plate fixation could promote osteoblasts, inhibit the proliferation and activation of osteoclasts, regulate the level of bone metabolism, improve bone quality and bone fragility, and accelerate the rapid healing of middle humeral shaft fracture in adults.

To improve the feasibility and safety of MIPO technique combined with locking compression plate fixation, the following points should be noted during the operation: (1) During the procedure, the patient's upper arm should be abducted at 90° with the forearm supination position and the palm toward the shoulder joint, and the radial nerve should be kept away from the humerus to minimize damage to the radial nerve. (2) Due to the special anatomical structure of the distal humerus and the high thickness of the locking compression plate, the locking compression plate should be pre-bent in advance according to the anatomical shape of the front humerus and kept close to the radian of the humeral shaft to avoid affecting the wound healing. (3) Screw fixation should be used at the nearest and distal end of the steel plate, and screw fixation should not be used at the middle part as far as possible to prevent damage to the posterior radial nerve. (4) After reduction, the elbow joint should be moved passively to correct the angulation, shortening, and rotation deformity of the broken end, and to avoid the soft tissue embedding of the broken end and the displacement of the fracture block, to ensure the fracture healing. (5) The distal and proximal humeral screws should be screwed under direct vision to avoid injury to the musculocutaneous nerve. We believe that with the improvement of anatomical knowledge and surgical skills of operators, MIPO technique combined with locking compression plate fixation will be popularized clinically.

There are some shortcomings in this study. For example, this was a retrospective study, leaving some deviations in data collection. The small sample size and single sample source may have led to the bias of the conclusion. The follow-up time was short. The short-term and long-term prognosis of patients were not analyzed. It is necessary to extend the follow-up time in future studies, and carry out a large-sample, multi-center, and prospective randomized controlled study.

To sum up, MIPO technique combined with locking compression plate fixation can promote the healing of middle humeral shaft fractures in adults, improve shoulder and elbow joint function, regulate bone metabolic activity, and improve bone quality, without a significant increase of complications.

Disclosure of conflict of interest

None.

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