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Appendix Table 1. Co-therapies between the two groups.

	Postoperative follow-ups	FA group (n=39) N (%)	LP group (n=41) N (%)
Vitamin D supplement	1 day	27 (69)	24 (58)
	1 month	17 (44)	14 (34)
	3 months	8 (20)	3 (7)
	6 months	5 (13)	1 (2)
	12 months	3 (8)	1 (2)
	24 months	2 (5)	0
Calcium supplement	1 day	27 (69)	27 (66)
	1 month	9 (23)	9 (22)
	3 months	6 (15)	4 (10)
	6 months	3 (8)	2 (5)
	12 months	2 (5)	0
	24 months	2 (5)	0
Analgesics#	1 day	15 (38)	20 (50)
	1 month	14 (36)	14 (34)
	3 months	6 (15)	3 (7)
	6 months	5 (13)	3 (7)
	12 months	2 (5)	2 (5)
	24 months	0	2 (5)
Transfer to physical therapist	1 day	0	0
	1 month	5 (13)	4 (10)
	3 months	2 (5)	1 (2)
	6 months	1 (3)	0

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12 months	0	0
24 months	0	0

Results were based on the recorded prescription information in healthcare information system of our hospital. FA, fibular allograft; LP, locking plate.
Most of the analgesics were (topical or oral) NSAIDs. Three patients were prescribed with tramadol.

Appendix: Study protocol of a randomized clinical trial:

Locking plate augmented with a fibular allograft versus locking plate alone in treating medial column comminuted proximal humeral fracture

Primary objective

The primary objective of this trial is to assess whether looking plate augmented with a fibular allograft presents superior clinical outcome in patients with medial comminuted proximal humeral fracture, compared to looking plate alone. The primary clinical outcome is measured with the Disabilities of the Arm, Shoulder and Hand (DASH) score at 1-year follow-up after surgery.

Secondary objectives

This trial will also evaluate shoulder function (measured with the Constant-Murley score and range of motion), pain level (measured with the visual analog score (VAS)), stability of fixation (measured with the changes of neck-shaft angle and humeral head height), patient satisfactory, complication and side effect. The difference between the two groups will be assessed from short (1 month) to long term (2 years) to test the superiority hypothesis.

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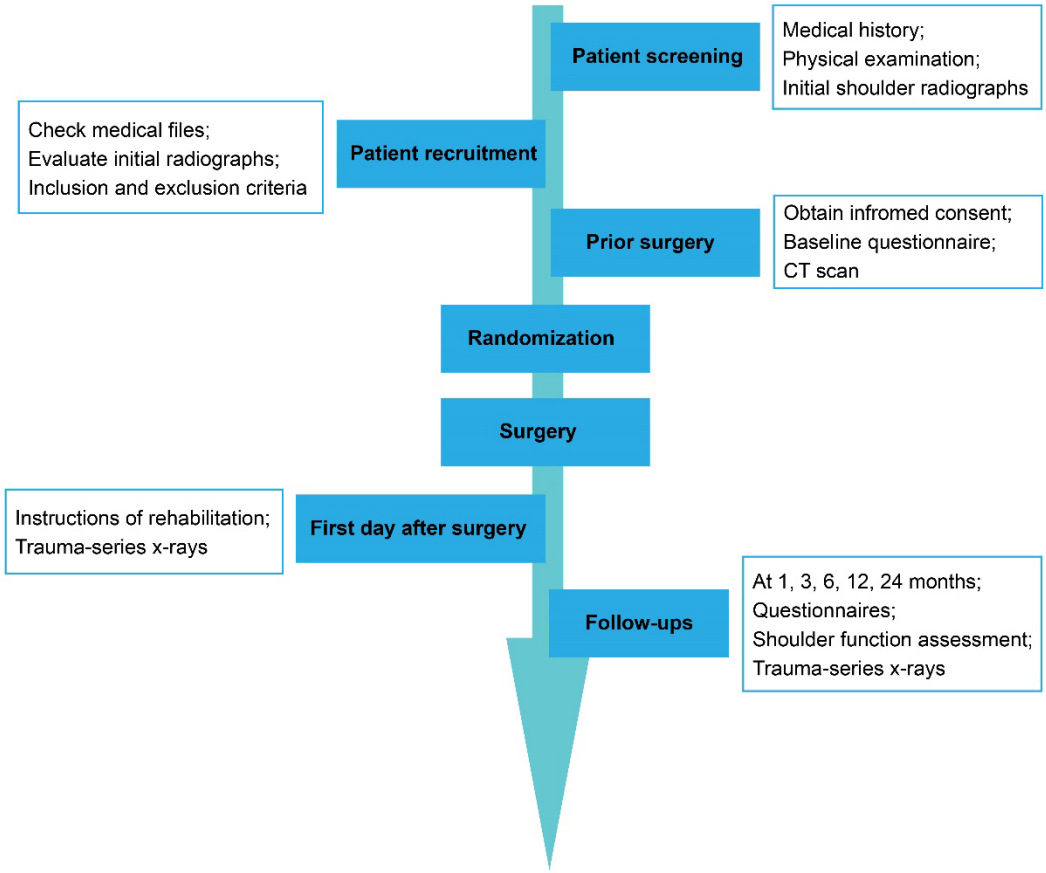
Design

This is a single-center, open-label, randomized controlled superiority trial with two parallel groups with a follow-up of 2 years. This trial is prospectively registered in the Chinese Clinical Trial Registry (ChiCTR-IOR-16008817). The Medical Ethics Committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital approved this protocol (2016-67- (1)). All patients will give written informed consent prior to interventions. The procedures of this trial are illustrated in **Figure 1**.

Appendix Figure 1. Flow chart of this trial.



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Patient selection

Patients with proximal humeral fracture, either administered into our hospital's emergency rooms or outpatient clinics, will be screened. During this phase, the first-line doctors diagnose 'proximal humeral fracture' by reviewing patients' medical history, physical examinations and initial radiographs. Initial radiographic examination is performed with plain standard posterior-anterior (PA) and lateral X-ray projections on the injured shoulder.

Once the diagnosis is determined, they will contact one of the two researchers (QW and NS) to check the eligibility. Researchers will review patient’s digital files of medical history, physical examinations and radiographic films within 24 hours. If potentially eligible, the patient will be contacted face-to-face or by telephone for further evaluation and detailly informed about this trial. Once receive a positive response from a patient, a researcher will further explain the study and provide written information (digitally or papery). Patients agree to participate will be asked to give written informed consent.

Patients meet the following inclusion criteria and not the exclusion criteria are eligible to participate in this trial (Table 2).

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Appendix Table 2. Eligibility criteria.

Inclusion criteria:
1. Aged 18 years and over
2. Unilateral proximal humeral fracture with medial column comminution#
3. Acute fracture (within 3 weeks)
4. ORIF* surgery is indicated and patient is able to tolerate the operations¶
5. Agree and give written informed consent
Exclusion criteria:
1. Have fractures in any other regions
2. Fracture extends to humeral shaft
3. Previous operative treatment of the ipsilateral upper extremity fractures or have chronic arthritis
4. Open fracture†
5. Pathological fracture (caused by malignant tumor, osteomalacia, osteomyelitis or cysts)§

*ORIF, open reduction and internal fixation.

#Medial column will be assessed by the two researchers based on the initial radiographs, comminution is determined if fractured with ≥ three fragments.

¶According to the health guideline, surgical treatment (ORIF) can be considered for an unstable proximal humeral fracture with displaced fragments (>45°angulation or >1cm displacement) in our hospital. The two researchers (QW and NS) will decide whether there is an indication of ORIF. The option of shoulder replacement surgery will also be suggested for elderly patients (age ≥ 65) and

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patients will be excluded when choosing shoulder replacement surgery. The ability of tolerating surgery will be assessed by anesthetists. In general, patients with American Society of Anesthetists (ASA) grade III or less will be considered eligible for orthopaedic surgery.

†Fracture with a break in skin, Gustilo Grade≥I.

§Pathological fracture will be assessed based on patient's medical history and the initial radiographs, and re-assessments will be done after inclusion (via CT scan and direct inspection during surgery).

Procedures prior surgery

Once included in this trial, patients will be informed to administer into the orthopedic ward within 48 hours. One of the researchers (co-authors) will ask the patient to finish baseline assessments, including questionnaires (papery) and a shoulder CT scan (Table 3).

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Appendix Table 3. Baseline questionnaire items and CT scan.

Age	Years
Sex	Male/Female
Body mass index (BMI)	Kg/m^2
Comorbidity	Diabetes, hypertension, cardiovascular disease, fracture history, osteoporosis.
Smoking (currently)	Yes/NO
Alcohol (currently)	Yes/NO
Side of injury (fracture)	Right/Left
Dominant arm	Right/Left
Date of injury	DD/MM/YY
Cause of injury	Traffic incident/fall on the ground/others (free text)
CT scan	uCT780; Manufacturer: UIH, united image healthcare, Shanghai; Images of horizontal, coronal and axial plains, as well as 3-demention reconstruction will be collected.

Two independent researchers (NS, JTH) will classify the fractures according to Neer[1] and OA/OTA[2] classification systems based on initial radiograph and CT scan images. The two researchers are blinded for patient demographics, medical history and results of randomization while doing the classification.

Intra-class correlation (ICC) and (prevalence adjusted) kappa index will be quantified.

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Then a consensus meeting will be held between the two researchers for drawing agreements on discrepant cases.

Randomization

An independent researcher (TM), who is not involved in the medical procedures, has prepared a computer-generated randomization group index using 1:1 allocation with random sizes of block on an encrypted website. Nobody except this researcher has access to the randomization list. After a patient gives written consent and finishes baseline assessments, a unique trial number will be issued for the patient. The researcher who helps patients complete baseline assessments will inform TM of inclusion. Then, TM will inform the surgical operators and patients of the randomization results at least 24 hours before the surgery.

Blinding

Since this is a pragmatic trial and fibular allograft can be easily identified on the radiographic film, it is impossible to blind the surgical operators and patients for the treatment allocations (all patients will receive their after-operation radiographic films on the day of checking out). Similarly, the two independent researchers (NS, JTH) cannot be blinded when assessing the radiographic films. At follow-ups, the researcher (BR) assessing shoulder function (range of motion and arm strength) will be blinded; patients are instructed not to tell the study allocations. After completion of this trial, researchers involved in statistical analysis will be blinded, and data analysis will be conducted strictly following the statistical analysis plan stated below.

Surgical interventions

After the completion of baseline assessment, the patient will be scheduled for shoulder surgery within 3 working days. Two experienced (20-year experience of performing shoulder surgery) surgeons (LW and YC) will perform all the operations for this trial. The two surgeons are required to write down the operation process in the patient's

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medical records within 24 hours. The exact procedure could be varied from one patient to another, while the surgeons agreed on the general instructions:

Intervention group using fibular allograft: The primary goal of this operation is to achieve anatomic fracture reduction and fixation. Patient is placed in a beach-chair position under general anesthesia. The deltopectoral approach is used. Fracture fragments are reduced with the help of K-wires as “joy-sticks” and a fibular allograft as medial support. The fibular allograft is inserted into the distal intramedullary canal, and medialized maximally toward the medial calcar to indirectly reduce the medial column as well as support humeral head fragment. The length of the fibular allograft will be decided by the surgeon during the operation. Tuberosity fragments (if exist) will be re-connected to the rotator cuff using nonabsorbable sutures to promote reduction, and the sutures will be attached on the looking plate afterwards. Rotator cuff tears (if exist) will be sutured at the same time. After fracture reduction, K-wires are used for temporary fixation, and a C-arm X-ray machine is used to ensure reduction. A locking plate (Philos, Synthes®, Switzerland) will be placed on the lateral to the bicipital groove when the reduction is satisfactory. The superior part of the locking plate is placed no higher than 5 mm below the top of the greater tuberosity. Calcar screws are carefully used and inserted into the inferomedial quarter of the humeral head. Medial buttress plate is not allowed to be used as this is thought to provide the same benefits as the fibular allograft. Cancellous bone grafting from the ipsilateral iliac crest or a bone substitute can be used with judgment during the surgical procedure and will be recorded. After fracture fixation, the wound will be irrigated and closed in layers.

Control group without using fibular allograft: All the surgical procedures are the same as the intervention group, except that fibular allograft is not allowed to be used either as a reduction tool or for enhancing stability (Figure 2).

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Rehabilitation

All the patients follow the same protocol of rehabilitation, and they will receive the instructions on the first day after surgery. Patients are encouraged to perform active exercises of wrists and elbows immediately and are suggested to use a sling for the injured arm for 4 weeks. Passive exercises and pendulum exercises are allowed from the second week. Active shoulder exercises, including forward elevation, abduction, and internal and external rotation, are allowed from week 6.

Besides, to enhance the adherence to the protocol, the researcher (BR) will teach the patient the way of home exercise at each follow-up after assessing shoulder function. Patients are allowed to contact physical therapists for help, and the consultations will be recorded.

Follow-up measurements

See Table 4 for an overview of follow-up measurements. On the first day after surgery, patients are required to have an x-ray examination (trauma-series projections, including AP, Y and axillary views). Two independent researchers (NS, JTH) will assess the quality of reduction based on the images. The quality of reduction, as previously described[3], is defined as well-reduced (fulfill the following three criteria: a neck-shaft angle between 110° and 150°; head-shaft displacement less than 5 mm; and greater tuberosity displacement less than 5 mm) or mal-reduced (failing to meet at least one of these criteria). Discrepancies will be solved via a consensus meeting between the two researchers.

Besides, the two researchers will measure neck-shaft angle (°) and humeral head height (mm) independently, and the final results will be using the mean of the two measurements. See the method for measuring neck-shaft angle and humeral head height in Figure 2.

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Patients will be invited via telephone to return to our hospital at 1, 3, 6, 12 and 24 months after surgery. Patients will come to the outpatient clinics to meet an orthopedic surgeon for medical consultations and x-ray prescriptions, and another researcher (BR) for shoulder function assessments and questionnaires.

Paper questionnaires, including DASH score[4] (primary outcome; 0-100; 0=no disability), visual analogue scale (VAS) pain score[5] (0-10; 0=no pain) and Constant-Murley score[6] (0-100; 0=worst situation; two objective parts will be measured by the shoulder function assessor: range of motion (ROM) and strength) will be completed by patients from 3 months after surgery. An independent and blinded researcher will assess shoulder function. The assessment items are adopted from the Constant-Murley score, including ROM and strength. Radiographic measurements include neck-shaft angle and humeral head height and will be measured at all time points by the same two researchers using the same method described above. Complications and sides effects will be monitored throughout the study. At the final follow-up, the patient will also score satisfactory (0-100; 100=extremely satisfied).

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Appendix Table 4. Follow-up measurements.

	1 d	1 m	3 m	6 m	12 m	24 m
Primary outcome measure						
DASH score			x	x	x	x
Secondary outcomes						
Constant-Murley score			x	x	x	x
Visual analogy score			x	x	x	x
Range of motion			x	x	x	x
Humeral head height	x	x	x	x	x	x
Neck-shaft angle	x	x	x	x	x	x
Complications	x	x	x	x	x	x
Patient satisfactory						x

d, day; m, month(s).

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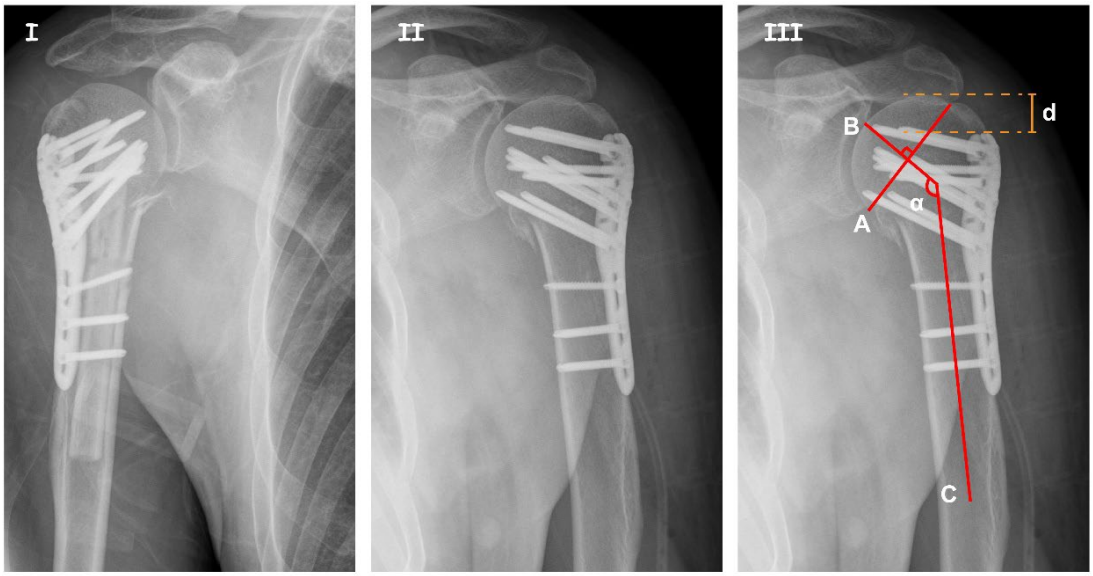
Appendix Figure 2. Images on the first day after surgery and the method of measuring neck–shaft angle and humeral head height



Picture I: looking plate combined with fibular allograft (intervention group);

Picture II: looking plate alone (control group);

Picture III: the method of measuring neck–shaft angle and humeral head height. Line A is drawn along the border of the articular surface and line B is drawn perpendicular to line A through the centre of the humeral head. Line C is parallel to the humeral shaft, and the neck–shaft angle is determined as the angle α. Two lines (indicated by the orange horizontal dashed lines) are drawn across the superior borders of the humeral head and the plate. The distance (d) between the two lines is measured as humeral head height.

Sample size

This trial is powered to detect the superiority of looking plate treatment combined with fibular allograft, compared to looking plate alone. According to the results of the study of Gummesson *et al.*[7], a standard deviation (SD) of 15 is used for the DASH score with a minimal clinically important difference of 10 points between the two groups.

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Significance level is set at 0.05 and power at 90%; 50 patients for each group are needed. However, after a year of patient recruitment, we found it challenging to reach enough cases since many fractures did not fulfill the medial column communition. Thus, we downregulated the power to 80%, for which 37 patients for each group are needed. Since the primary time point is set at 1-year follow-up and most patients will come at 1-year follow-up to consult for removing implants, we assume a low rate of loss to follow-up (<10%) at this time point. Taken together, this trial needs to include 80 patients.

Statistical analysis plan

1. Analysis principle: the primary analysis will be done based on an intention-to-treat (as randomized) principle. All the patients who have been randomized will be included in analysis and be grouped by the results of randomization. Significance level is set at 0.05. The data analyst (QW) is blinded for treatment allocations.

2. Baseline characteristics: following characteristics of the two groups will be presented as mean (standard deviation) or number (percentage), where appropriate. No statistical analysis will be performed for comparing these characteristics.

Demographics: age, sex, BMI, comorbidity, smoking, alcohol, dominant arm.

Fracture features: cause of injury, side of injury, Neer classification, AO/OTA classification.

Surgical factors: days from injury to surgery, quality of reduction (assessed on the first day after surgery).

3. Primary outcome: DASH score (primary time point: 1 year follow-up).

Linear mixed models with repeated measures will be used to calculate group differences over time for DASH scores. A structure will be chosen with lowest Akaike's information criteria. Fixed effects will be time and time by group. Factors related to

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outcomes and are imbalanced at baseline (clinically relevant differences between groups of over 10%) will be added into model as co-variates. Mean between group differences and their 95% confidence intervals will be calculated at all time points.

4. Secondary outcomes: Constant-Murley score, visual analogy score, range of motion, change in humeral head height, change in neck-shaft angle, complications, side effects and patient satisfactory.

Changes in humeral head height and neck-shaft angle are defined by subtracting the results on the first day after surgery from the follow-up results. The cumulative incidence rate of complications and side effects are expected to be low; thus, they will be described without statistical tests. Analysis conducted on other outcomes uses the identical method for the primary outcome.

5. Missing values: missing values can be caused by incompletely filled questionnaires or loss to follow-up. Although linear mixed models will take missing values into account, the results can be invalid in the dataset with a considerable number of missing values (>5%, rule of thumb)[8]. Additionally, the assumption of missing at random can be violated[9]. Therefore, to test the robustness of our results, a sensitivity analysis combined with multiple imputation will be performed.

Subsequent amendments after registry

1. As stated above, we re-set the sample size to 37 patients for each group to reach a power of 80%.

2. Oxford Shoulder Score was also registered as a primary outcome. However, we found unable to obtain a license for the questionnaire after launching the trial. Besides, previous literature suggested that Oxford Shoulder Score is highly correlated with Constant score in proximal humeral fractures[10]. Therefore, we removed the Oxford

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Shoulder Score from the outcome list.

3. For statistical analysis, an ‘unstructured’ covariance structure was chosen as it resulted in the lowest Akaike’s information criterium. Baseline status of smoking, alcohol drinking and diabetes were found with clinically relevant difference betw between the 2 groups, thus they were adjusted in the linear mixed model.

4. A chi-square test was used for testing the cumulative incidence rate of complication.

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