GUIDELINE

Chinese Clinical Practice Guidelines in Treating Knee Osteoarthritis by Periarticular Knee Osteotomy

Xin-long Ma, MD[1], Yong-cheng Hu, MD[1], Kun-zheng Wang, MD[2], The Chinese Hospital Association Clinical Medical Technology Application Committee, The Joint Surgery Branch of the Chinese Orthopaedic Association, The Subspecialty Group of Osteoarthritis, Chinese Association of Orthopaedic Surgeons

[1]*Department of Orthopaedics, Tianjin Hospital, Tianjin and* [2]*Department of Orthopaedic Surgery, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an Shaanxi, China*

Unicompartmental knee osteoarthritis (UKOA) is the early stage of knee joint degeneration, which is characterized by unicompartmental degeneration and mostly occurs in medial compartment. Pain and limited motion are main symptoms, which affect patients' life quality. Periarticular knee osteotomy (PKO) for lower extremity alignment correction is an effective treatment for UKOA with abnormal alignment, which could relieve pain and improve joint function by adjusting lower extremity alignment. At present, no clinical guidelines are available for the treatment of UKOA by PKO for lower extremity alignment correction. Experts from the Clinical New Technology Application Committee of the Chinese Hospital Association, Joint Surgery Study Group of the Chinese Orthopaedic Association of the Chinese Medical Association, and Osteoarthritis Study Group of the Chinese Association of Orthopaedic Surgeons of the Chinese Medical Doctor Association formulated these guidelines. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) grading system and the Reporting Items for Practice Guidelines in Healthcare (RIGHT) were adopted to select 25 most concerning questions. Finally, 25 recommendations were formulated through evidence retrieval, evidence quality evaluation, and the determination of directions and strength of recommendations. Recommendation items 1–5 are indications and contraindications for PKO for lower extremity alignment correction, items 6–21 are surgical methods and principles, item 22 describes 3D printing corrective osteotomy technique, and items 23–25 address the perioperative period, follow-up management, and other content. These guidelines are designed to improve the normalization and standardization of KOA treatment by PKO for lower extremity alignment correction.

Key words: Evidence-based medicine; Guidelines; Osteoarthritis; Knee; Osteotomy

Formulation Background

Osteoarthritis (OA) is a degenerative joint disease characterized by pain and limited joint mobility. With the aging of the population and the exposure to risk factors (e.g. obesity, osteoporosis) leading to OA, the incidence of OA has been increasing gradually. To date, more than 300 million people worldwide have OA[1]. Among the joints affected by OA, the prevalence is the highest in the knee joint at 9.5%–38.4%[2], followed by the hip joint (4.2%–10.0%)[3–5] and ankle joint (1%)[6]. According to a research report from China in 2020, the number of patients with knee OA in China increased from 26.1 million in 1990 to 61.2 million in 2017[7]. The pathological features of knee OA mainly include articular cartilage degeneration, subchondral sclerosis or cystic degeneration, articular hyperosteogeny and synovitis, joint capsule contracture, ligament relaxation or contracture, and muscle atrophy[8]. Health economics research on knee OA also confirmed that the diagnosis and treatment of knee OA, as well as related costs, increased year on year, resulting in a serious economic burden on patients and society[7].

The diagnosis and treatment of knee OA are one of the hotspots in clinical research and practical work in the field of orthopaedics. According to preliminary statistics, 21 sets of influential guidelines for the diagnosis and

Address for correspondence Xin-long Ma, MD, Department of Orthopaedics, Tianjin Hospital, No. 406 Jiefangnan Road, Hexi District, Tianjin, China 300211 Tel: 0086-22-23197009; Fax: 0086-22-23197009; Email: maxinlong8686@sina.com

Disclosure: The authors have no conflicts of interest to declare.
Received 17 February 2022; accepted 21 March 2022

treatment of knee OA are currently available, including 16 in English and five in Chinese. Among them, three sets of guidelines are widely used. The 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee is a set of evidence-based guidelines for the comprehensive treatment of OA that summarizes the advantages and disadvantages of education, behavior, society, psychology, physics, mind and body, as well as drug therapy[9]. The 2019 Osteoarthritis Research Society International Guidelines for the Non-surgical Management of Knee, Hip, and Polyarticular Osteoarthritis elaborates in detail on the application principles and treatment outcomes of drugs with different mechanisms of action (non-steroidal anti-inflammatory drugs, corticosteroids, hyaluronic acid, chondroitin, diacerein, glucosamine, duloxetine, opioids, etc.) for the treatment of knee OA[10]. The 2013 American Academy of Orthopaedic Surgeons Evidence-Based Guideline on the Treatment of Osteoarthritis of the Knee 2nd Edition[11] evaluates body mass index, diabetes, chronic pain, depression and/or anxiety, and liver cirrhosis and/or hepatitis C as risk factors and makes suggestions regarding preoperative physical therapy, periarticular local infiltration anesthesia, peripheral nerve block, central nervous system block, tourniquet, tranexamic acid, antibiotic bone cement, polyethylene components, etc. Thus, it is a set of clinical guidelines focusing on the surgical treatment of knee OA.

Osteotomy is an effective method for treating unicompartmental knee OA. Unicompartmental knee OA usually manifests as significant degeneration of a unicompartmental knee joint, while other compartments have relatively mild degeneration. For patients with unicompartmental knee OA accompanied by abnormal lower extremity alignment, choosing a scientific and targeted treatment method is worthy of attention. Periarticular knee osteotomy for lower extremity alignment correction can relieve knee joint pain and improve knee joint function by adjusting lower extremity alignment and thus transferring pressure from the affected compartment to the normal compartments or resulting in a normal alignment position. In 1965, Coventry[12] first reported the use of high tibial osteotomy (HTO) to treat varus knee OA. Subsequently, distal femoral osteotomy (DFO) and proximal fibular osteotomy (PFO) were successively applied in clinical practice. With the continuous advancement in surgical techniques and internal fixation devices, as well as the deepening of the concepts of digital medicine and enhanced recovery after surgery (ERAS), periarticular knee osteotomy for lower extremity alignment correction has become the mainstream surgical method for treating unicompartmental knee OA. However, at present, some controversies remain regarding the treatment of knee OA by periarticular knee osteotomy.

Currently, there are no clinical guidelines for the treatment of unicompartmental knee OA by periarticular knee osteotomy for lower extremity alignment correction. To further standardize the clinical diagnosis and treatment of unicompartmental knee OA by periarticular knee osteotomy, the Clinical New Technology Application Committee of the Chinese Hospital Association, Joint Surgery Study Group of the Chinese Orthopaedic Association of the Chinese Medical Association, and Osteoarthritis Study Group of the Chinese Association of Orthopaedic Surgeons of the Chinese Medical Doctor Association successively organized several seminars on guidelines in Nanjing, Tianjin, and elsewhere since November 2020. A total of 25 questions that orthopaedic surgeons are most concerned about were selected. Finally, 25 recommendations were formulated through evidence retrieval, evidence quality evaluation, as well as the determination of the directions and strength of the recommendations. Recommendation items 1–5 are indications and contraindications for periarticular knee osteotomy for lower extremity alignment correction, items 6–21 are surgical methods and principles of intraoperative treatment, item 22 describes a 3D printing corrective osteotomy technique, and items 23–25 address the perioperative period, follow-up management, and other content. These guidelines are designed to improve the normalization and standardization of knee OA treatment using periarticular knee osteotomy for lower extremity alignment correction.

Definitions

Periarticular Knee Osteotomy for Lower Extremity Alignment Correction

Lower extremity alignment is corrected through osteotomy of the distal femur, proximal tibia, and/or proximal fibula, and the pressure is transferred from the affected compartment to the normal compartments, or a normal alignment position is achieved to relieve knee joint pain and improve joint function. Periarticular knee osteotomy includes HTO, DFO, and PFO.

HTO

Based on preoperative imaging measurement, wedge osteotomy of the proximal tibial tubercle is used to correct lower extremity alignment and redistribute the pressure on the knee joint to delay the degeneration of the knee joint. HTO, including closed wedge osteotomy and open wedge osteotomy, is a common surgical method for treating unicompartmental knee OA.

DFO

Based on preoperative imaging measurement, medial or lateral supracondylar wedge osteotomy of the femur is used to correct lower extremity alignment so that the pressure on the knee joint is transferred from the affected compartment to the normal compartments or to achieve a normal alignment position, thus relieving pain and improving the function of knee joint. DFO includes closed wedge osteotomy and open wedge osteotomy.

PFO

Through PFO, the fibula's support to the lateral tibial plateau is reduced, the lower extremity alignment is transferred from the medial to the lateral compartment of the knee joint, and the pressure on the medial knee joint is reduced, thus delaying the degeneration of the medial compartment of the knee joint.

3D-Printed Corrective Osteotomy Guide

Based on Digital Imaging and Communications in Medicine (DICOM) data of preoperative computed tomography (CT) scans of the affected limb, the position and degree of alignment restoration during surgery are determined by computer-simulated osteotomy, and the guider with osteotomy and orthopaedic guiding functions are performed by 3D printing to achieve accurate correction of lower extremity alignment.

Clinical Questions

Clinical Question 1: What Is the Applicable Age Range for Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 1: Patients undergoing periarticular knee osteotomy for lower extremity alignment correction should be <65 years for men and <60 years for women (evidence level and recommendation strength: 1C).

Age is an important factor affecting the clinical outcome and failure period of surgery. Older patients often have multicompartmental OA, which may increase the intraarticular pressure in the contralateral compartment and the risk of osteotomy failure; thus, osteotomy is not recommended in these patients.

Evidence from the literature: To analyze the influence of age on the postoperative outcomes of HTO, Trieb *et al.*[13] enrolled 94 patients who underwent HTO and divided them into two groups according to age (<65 and ≥65 years). The results showed that patients older than 65 years had a higher proportion of knee replacement surgery after HTO, and the replacement surgery was performed earlier than in patients younger than 65 years. Bonasia *et al.*[14] retrospectively analyzed 123 patients who underwent medial open HTO. Through a univariate logistic regression model, it was found that age >56 years was significantly correlated with a poor prognosis after HTO (knee joint replacement), and the risk of a poor prognosis in patients older than 56 years was five times higher than that in patients younger than 56 years. Similarly, Flecher *et al.*[15] followed up 313 patients (average age, 42 years) who had undergone HTO for an average of 18 years and defined revision after HTO as surgical failure. A Cox regression model analysis showed that age >50 years was a risk factor for HTO failure.

However, some scholars believe that HTO is equally effective for older people. Goshima *et al.*[16] divided 57 patients who underwent HTO into two groups according to age (<65 or ≥65 years). The results of the last follow-up showed that the Oxford Knee Score or postoperative femorotibial angle was not significantly different between the two groups, and it was considered that age would not affect the function and imaging indexes after HTO. Therefore, old age should not be an absolute contraindication of HTO; however, considering the potential risk of surgical failure in older patients, it is recommended that the age of patients undergoing periarticular knee osteotomy for lower extremity alignment correction should be <65 years for men and <60 years for women.

Clinical Question 2: What Are the Limitations of Body Mass Index (BMI) for Patients Undergoing Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 2: The BMI of patients undergoing periarticular knee osteotomy for lower extremity alignment correction should be <27.5 kg/m^2 (evidence level and recommendation strength: 1D).

The higher the BMI, the greater the pressure on the knee joint, and the higher the risk of meniscus injury and cartilage wear. Therefore, patients with a high BMI have a low tolerance for pressure transfer to the contralateral compartment, and the risk of surgical failure is high.

Evidence from the literature: Akizuki *et al.*[17] enrolled 132 patients with an average BMI of 25.8 kg/m^2 (range: 19.4–37.9 kg/m^2) who underwent HTO. Postoperative failure of HTO was defined as total knee arthroplasty (TKA) or a Hospital for Special Surgery (HSS) score <70. The results showed that a BMI >27.5 kg/m^2 was related to the postoperative failure of HTO; thus, it was suggested that the BMI of patients undergoing HTO should not exceed 27.5 kg/m^2. In a 9-year follow-up study by Giagounidis and Sell[18] of 112 patients undergoing HTO, the average BMI of women was 27.1 kg/m^2 (range: 20.1–40.0 kg/m^2) and that of men was 26.8 kg/m^2 (range: 18.2–37.6 kg/m^2). The results showed that patients with a lower BMI could achieve a longer joint pain-free period. Yokoyama *et al.*[19] divided 47 patients undergoing open wedge HTO into two groups, namely the early-cure group (complete recovery within 9 months) and late-cure group (complete recovery requiring 12 months). The results showed that the average BMI of the early-cure group was significantly lower than that of the late-cure group, and patients with a higher BMI had a longer postoperative recovery time. Therefore, these guidelines recommend that the BMI of patients undergoing periarticular knee osteotomy for lower extremity alignment correction should be <27.5 kg/m^2. Thus far, there has been no research on the correlation between BMI and the prognosis of HTO in Chinese people.

Clinical Question 3: What Are the Requirements for the Classification of Knee OA for Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 3: The Kellgren–Lawrence (K-L) classification of the affected knee joint compartment of patients undergoing periarticular knee osteotomy for lower extremity

alignment correction should be below Grade III, and the joint space of the contralateral compartment should be relatively normal (evidence level and recommendation strength: 1D).

The principle of periarticular knee osteotomy for lower extremity alignment correction is to correct lower extremity alignment and transfer the pressure from the affected compartment to the normal compartments or achieve a normal alignment position to relieve knee joint pain and improve knee joint function.[52] After osteotomy, the high pressure in the affected compartment is relieved. If the cartilage of the contralateral compartment is severely worn, the pressure in the contralateral compartment will increase further with the adjustment of the alignment after surgery, which will reduce the survival rate of the osteotomy. Therefore, preoperative assessment of the degrees of cartilage degeneration in the medial and lateral compartments is essential for the prognosis of patients.[53]

Evidence from the literature: The K-L grading system is an X-ray grading method to evaluate the severity of knee OA that is divided into Grade 0 (normal knee joint), Grade I, Grade II, Grade III, and Grade IV, ranging from mild to severe. To explore the correlation between knee OA with different K-L grades and postoperative failure of HTO (TKA), Efe *et al.*[20] retrospectively analyzed 199 patients (98 cases of Grade I, 96 cases of Grade II, and five cases of Grade III); among them, 36 patients had undergone TKA at the last follow-up. The Kaplan–Meier method was used to analyze the postoperative survival rate of HTO, with failure of HTO as the outcome indicator. It was found that patients with K-L Grade III had the lowest postoperative survival rate. Sohn *et al.*[21] included 140 patients who underwent HTO, including 114 patients with K-L Grade I-III and 26 patients with Grade IV. The Knee Society Score (KSS) was used to evaluate the patients' satisfaction (a score <20 was considered to indicate dissatisfaction with the postoperative effect of HTO). Multivariate logistic regression analysis confirmed that preoperative K-L Grade IV was a risk factor for patients' dissatisfaction with HTO. Kuwashima *et al.*[22] retrospectively included 144 patients (16 cases of K-L Grade II, 81 cases of K-L Grade III, and 47 cases of K-L Grade IV) undergoing HTO surgery and pointed out that the severity of preoperative OA was closely related to the clinical treatment outcomes and failure period of HTO surgery.

Clinical Question 4: For What Degree of Joint Deformity Is Periarticular Knee Osteotomy for Lower Extremity Alignment Correction Suitable?

Recommendation 4: Periarticular knee osteotomy for lower extremity alignment correction is indicated for patients with varus deformity >5° or valgus deformity >10° (evidence level and recommendation strength: 1D).

Periarticular knee osteotomy for lower extremity alignment correction can not only relieve the pain caused by unicompartmental knee joint wear but also correct the extraarticular deformity. The bone deformity in most patients with genu varus originates from the proximal tibia, for which HTO is suitable, whereas DFO is appropriate for genu varus originating from the femur. However, the degree of deformity for which osteotomy is indicated remains controversial.

Evidence from the literature: Rudan and Simurda[23] included patients with varus knee OA with a varus deformity <15° to analyze the relationship between the degree of preoperative knee deformity and the prognosis of HTO. Poor prognosis after HTO was defined as (i) undergoing TKA; (ii) revision surgery of HTO; and (iii) an HSS score <64 points. The statistical analysis results showed that a tibia vara <5° was associated with a high risk of postoperative failure; thus, it was considered that a varus deformity >5° is a surgical indication of HTO. However, some scholars hold different views. Na *et al.*[24] retrospectively included patients with varus knee OA and divided them into the mild varus group (31 cases) and severe varus group (40 cases) according to whether the varus exceeded 4°. After surgery, the American Knee Society (AKS) scores in both groups were significantly improved; thus, HTO was also considered to result in satisfactory results in patients with mild varus deformity (<4°). Based on the above research findings, these guidelines recommend that a varus deformity >5° is an indication of HTO; DFO can be selected when the valgus deformity is >10°.

Clinical Question 5: What Are the Requirements Regarding Knee Joint Range of Motion before Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 5: For patients undergoing periarticular knee osteotomy for lower extremity alignment correction, the preoperative knee joint range of motion should be >100°, and flexion contracture should be <15° (level of evidence and recommendation strength: 1D).

The knee joint range of motion is an important index for preoperative evaluation of osteotomy. Osteotomy is aimed at correcting lower extremity alignment; however, its treatment outcomes for joint motion limitations caused by soft tissue contracture or severe joint degeneration are limited. If the patient's knee joint range of motion is severely limited, it is difficult to achieve satisfactory recovery of the joint range of motion even after alignment correction.

Evidence from the literature: To analyze the factors influencing the long-term treatment outcomes after HTO, Akizuki *et al.*[17] prospectively followed up 132 patients for an average of 16.4 years after HTO; the Kaplan–Meier survival analysis model confirmed that preoperative knee joint range of motion <100° and flexion contracture >15° were risk factors for early surgical failure. Naudie *et al.*[25] followed up 85 patients for more than 10 years after HTO and analyzed the correlation between preoperative joint range of motion and HTO prognosis. Cox regression showed that a preoperative range of motion <120° and flexion contracture >5° were correlated with early failure of HTO. Combining currently available evidence from the literature with China's national

conditions and social factors, knee joint range of motion >100°, and flexion contracture <15° are recommended as relative indications for periarticular knee osteotomy for lower extremity alignment correction.

Clinical Question 6: What Is the Principle of Choosing Lateral Closed Wedge or Medial Open Wedge HTO for Varus Knee OA?

Recommendation 6: Lateral closed wedge HTO and medial open wedge HTO have similar imaging corrections, postoperative joint functions, and risks of complications in the treatment of varus knee OA. Medial open wedge osteotomy may reduce the patella height and increase the tibial plateau declination, whereas lateral closed wedge HTO takes a long time to heal and reduces the posterior inclination of the tibial plateau. Therefore, the osteotomy method should be selected according to the actual needs and comprehensively judged according to the lengths of both lower extremities (evidence level and recommendation strength: 1D).

HTO can achieve the goal of corrective osteotomy regardless of the medial or lateral approach. Imaging correction, postoperative joint function, and risk of complications are similar between the medial and lateral approaches. However, medial open wedge HTO osteotomy takes a long time to heal, and bone grafting may be needed during surgery; lateral closed HTO requires fibular osteotomy; thus, there is a potential risk of common peroneal nerve injury.

Evidence from the literature: Smith *et al.*[26] systematically reviewed 324 patients undergoing medial open wedge HTO and 318 patients undergoing lateral closed wedge HTO to compare the safety of the two surgical procedures. The results showed that there was no significant difference in postoperative infection rate, revision rate, deep vein thrombosis, peroneal nerve paralysis, or risk of nonunion between the two groups. Therefore, the two surgical procedures were considered to be safe and effective intervention measures for the treatment of varus knee OA. Sun *et al.*[27] included eight randomized controlled trials and 15 observational studies for meta-analysis. The results showed that there was no significant difference in postoperative imaging indexes (posterior tibial slope and alignment correction), Lysholm knee joint function score, knee joint range of motion, or visual analog scale (VAS) between the two surgical procedures; however, lateral closed wedge HTO took a longer time to heal. Based on results in the literature, it can be concluded that both lateral closed wedge osteotomy and medial open wedge osteotomy can achieve satisfactory clinical outcomes in the treatment of varus knee OA. Medial open osteotomy may reduce the height of the patella; thus, it should be avoided for patients with a low patella before surgery. Alternatively, in coronal osteotomy, the osteotomy direction should be inclined anteroinferiorly, and the tibial tubercle should be kept at the proximal osteotomy block to avoid further aggravating the low patella position and affecting joint mobility after the surgery. Closed lateral wedge osteotomy may reduce the posterior inclination of the tibial plateau, whereas open medial wedge osteotomy may increase the posterior declination. Therefore, the osteotomy approach should be personalized according to actual needs, and the lengths of both limbs should be comprehensively assessed.

Clinical Question 7: What Is the Principle of Choosing Medial Closed Wedge or Lateral Open Wedge DFO for Valgus Knee OA?

Recommendation 7: Medial closed wedge and lateral open wedge DFO have similar effects in the treatment of valgus knee OA. The healing time of the stump of medial closed wedge DFO is shorter than that of lateral open wedge DFO (evidence level and recommendation strength: 2D).

Regardless of the medial or lateral approach, DFO can achieve the goal of corrective osteotomy; thus, it can alleviate knee joint pain and improve joint function after surgery. The effectiveness of the two surgical procedures in treating valgus knee OA has been proven. Open lateral wedge osteotomy takes a long time to heal, and bone grafting may be needed during surgery.

Evidence from the literature: Chahla *et al.*[28] systematically evaluated the related research on medial closed wedge DFO and lateral open wedge DFO for the treatment of lateral unicompartmental knee OA; they pointed out that the mean survival rate of the two osteotomy procedures at 10 years after surgery was 80%, and the incidence of complications was low; thus, DFO could effectively delay TKA. Zhang *et al.*[29] retrospectively analyzed 50 patients who underwent DFO using lateral open wedge osteotomy and medial closed wedge osteotomy of the distal femur and examined the Knee Injury and Osteoarthritis Outcome Score (KOOS), subjective satisfaction index, femorotibial angle, knee joint range of motion, fracture healing time, surgical complications, and other indexes. The results showed that the fracture healing time of lateral open wedge osteotomy of the distal femur was longer, whereas the other indexes did not differ according to the approach. Therefore, it was considered that both surgical procedures could achieve ideal treatment outcomes. Wylie *et al.*[30] systematically evaluated the treatment outcomes and complications of the two osteotomy procedures and pointed out that there was no difference in the postoperative quality of life score, complications, or risk of revision between the two procedures for valgus knee OA.

Clinical Question 8: Is it Effective to Use Dual-Site Osteotomy for Unicompartmental Knee OA Originating from Dual-Site Deformities of the Femur and Tibia?

Recommendation 8: Dual-site periarticular knee osteotomy is a safe and effective method for the treatment of unicompartmental knee OA with femoral and tibial deformities (evidence level and recommendation strength: 1D).

Lower extremity alignment abnormalities in some patients with knee OA are not caused by a single deformity; two or even three deformities are common. The most common clinical deformity combination is distal femur

deformity plus proximal tibia deformity. If only one of the deformities has been identified before surgery, correction according to the predetermined target alignment may be achieved; however, the abnormally inclined joint line will often remain, or the original normal joint line will be excessively inclined after surgery, which will lead to increased horizontal shear stress between the articular cartilage, secondary chronic joint instability, or even subluxation, ultimately affecting the long-term outcome of osteotomy.

Evidence from the literature: Ji *et al.*[31] retrospectively analyzed the clinical outcomes in 15 patients with knee OA accompanied by dual-site deformity treated using dual-site osteotomy of the distal femur and proximal tibia. No complications such as perioperative infections, nerve and blood vessel injury, postoperative joint stiffness, and deep vein thrombosis of the lower extremities occurred. The HSS score, VAS score, femorotibial angle, inclination of the joint line, as well as the position of the intersection point between the mechanical axis of the lower extremity and the tibial plateau were improved. Therefore, they believed that dual-site periarticular knee osteotomy is safe and effective for unicompartmental knee OA with femoral and tibial deformities. Schröter *et al.*[32] retrospectively analyzed 33 patients with severe genu varus (medial proximal tibial angle <87° and lateral distal femoral angle >90°) who underwent dual-site osteotomy with an average follow-up period of 18 months. At the last follow-up, the medial proximal tibial angle increased from 84° ± 3° before surgery to 89° ± 2°, and the lateral distal femoral angle decreased from 92° ± 2° to 87° ± 2°. The Lysholm score and International Knee Documentation Committee (IKDC) score were significantly improved. Therefore, dual-site osteotomy was considered to effectively correct lower extremity alignment in patients with severe genu varus and improve knee joint function. Nakayama *et al.*[33] retrospectively analyzed 33 patients who underwent dual-site osteotomy. On arthroscopic exploration, more than 90% of the medial femoral condyles and medial tibial plateaus and 12.8% of patellofemoral joints had cartilage repair to some extent, and the KOOS and IKDC scores were significantly improved compared with those before surgery. This suggests that dual-site osteotomy can improve the cartilage repair of the affected compartment. At present, dual-site osteotomy still has some problems, such as preoperative planning (it is difficult to harmonize the alignment correction and joint line balance) and is a challenging surgical procedure. In the future, further research on preoperative planning should be performed to simplify the dual-site osteotomy procedure and improve the accuracy of the deformity correction.

Clinical Question 9: What Are the Outcomes of PFO for the Treatment of Varus Unicompartmental Knee OA?

Recommendation 9: The short-term treatment outcomes of PFO for varus unicompartmental knee OA are positive, whereas the long-term treatment outcomes still need to be verified (evidence level and recommendation strength: 1D).

In recent years, with the concept of "knee preservation" being put forward, periarticular knee osteotomy for lower extremity alignment correction has been increasingly applied in the treatment of knee OA. HTO is a convenient surgical procedure, and its treatment outcomes are positive; this has been verified by clinical studies in China and other countries. PFO is a surgical method proposed by Chinese scholars. PFO can reduce the pressure in the medial compartment to delay the progression of OA. Although the theory underlying PFO is widely accepted, it has been performed for a short time in clinical practice; thus, its treatment outcomes and adverse reactions have not been widely clinically verified.

Evidence from the literature: To study the mechanism of PFO in the treatment of medial compartment knee OA and the related factors affecting the clinical treatment outcomes, Qin *et al.*[34] retrospectively analyzed 45 patients with medial compartment knee OA accompanied by varus deformity, all of whom were treated with PFO. The results showed that the HSS score, VAS score, and knee joint range of motion were significantly improved at 6 weeks, and 3, 6, 12, 18, 24, and 36 months after surgery. Multiple linear regression was used to screen for factors related to clinical treatment outcomes after PFO. The results showed that five factors (the change in vertical distance between the fibular head and tibial plateau, the K-L grading of tibiofibular arthritis, BMI, tibiofibular joint inclination, and preoperative HSS score) were correlated with the HSS score after PFO. To compare the clinical treatment outcomes of PFO and HTO for medial compartment knee OA, Guo *et al.*[35] retrospectively analyzed 52 patients with medial compartment knee OA, among whom, 23 patients were treated with medial open wedge HTO and 29 patients with PFO. The results showed that the HSS score was higher and the VAS score lower in the HTO group at 12 months after surgery; thus, the postoperative treatment outcomes of HTO were considered to be better than those of PFO. To compare the clinical outcomes of the two surgical procedures for the treatment of unicompartmental knee OA, Qiu *et al.*[36] retrospectively analyzed the data of 63 patients undergoing osteotomy, including 37 patients undergoing HTO and 26 patients undergoing PFO. The results suggested that the Lysholm score and Western Ontario and McMaster Universities Arthritis Index (WOMAC) of HTO at 12 months after surgery were significantly better than those of PFO. Therefore, HTO is considered to result in better knee joint function.

Although PFO causes less trauma, during weight-bearing after surgery, the degree of lateral shift of the main weight-bearing area of the knee joint is less than that after HTO, and the center of gravity still tends to the medial compartment. If medial meniscus and cartilage injuries are present, the corresponding symptoms will still exist after the surgery. Considering that patients with varus knee OA can achieve better knee joint function after HTO, it is suggested that patients with varus knee OA without serious medical contraindications should first undergo HTO.

Clinical Question 10: Can Computer Navigation Assist in Improving the Treatment Outcomes of Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 10: The alignment accuracy of periarticular knee osteotomy assisted by computer navigation is better than that of traditional osteotomy (evidence level and recommendation strength: 1C).

Determining the osteotomy line in periarticular knee osteotomy for lower extremity alignment correction mainly depends on preoperative planning, and the correction angle and dimensions of opening or closing are adjusted according to intraoperative fluoroscopy assisted by grid lines, alignment rods, etc. However, these methods are affected by the patient's position, viewing angle of fluoroscopy, measurement error, and other factors, and are thus inherently unreliable. Computer navigation-assisted osteotomy can improve the accuracy of the correction angle and opening or closing dimensions.

Evidence from the literature: To compare the accuracy and treatment outcomes of traditional osteotomy and navigation-assisted osteotomy, a meta-analysis by Kim *et al.*,[37] which included seven clinical studies that compared computer navigation-assisted and traditional medial open HTO, confirmed that the rates of satisfaction with imaging alignment correction were 83.7% and 62.1% in the navigation and traditional groups, respectively. KSS score, Lysholm score, or the risk of complications were not significantly different between the two groups. A meta-analysis by Shi *et al.*[38] showed that compared with the traditional group, lower extremity alignment in the navigation group was closer to the Fujisawa point after surgery, the increase in the degree of posterior inclination of the tibial plateau was smaller, and the mechanical femorotibial angle was more accurate after surgery, with statistical significance. However, there was no statistically significant difference between the two groups in Lysholm score, knee joint range of motion, incidence of delayed healing of tibial osteotomy, or incidence of surgical site infection.

Therefore, at present, evidence shows that computer-assisted osteotomy can improve the accuracy of osteotomy, but the long-term treatment outcomes and imaging results of the two methods still need to be further clarified by randomized controlled studies with large sample sizes and long-term follow-up.

Clinical Question 11: Can Tranexamic Acid Reduce Blood Loss during the Perioperative Period?

Recommendation 11: The combined use of tranexamic acid through multiple routes can significantly reduce perioperative blood loss during periarticular knee osteotomy for lower extremity alignment correction (evidence level and recommendation strength: 1D).

Knee OA occurs mostly in older patients with poor bone marrow hematopoietic function, and intraoperative and postoperative bleeding often affect the postoperative recovery of patients. Therefore, the application of safe and effective hemostatic drugs is particularly important. Tranexamic acid is widely used in orthopaedic surgeries because of its good hemostatic effect. Its mechanism of action involves inhibiting the fibrinolytic system to stop bleeding.

Evidence from the literature: To evaluate the hemostatic effect of tranexamic acid in HTO, Chen *et al.*[39] retrospectively analyzed 100 patients who underwent open wedge HTO. The length of hospital stay (days), hemoglobin level, and blood transfusion rate in the group receiving an intravenous infusion of 1 g of tranexamic acid during surgery plus local application of 1 g of tranexamic acid before the end of the surgery were better than those in the group without tranexamic acid during surgery. Therefore, the intraoperative use of tranexamic acid is considered to have a definite hemostatic effect during HTO. To confirm the safety of the perioperative use of tranexamic acid in HTO, Ma *et al.*[40] conducted a systematic review and meta-analysis. The results showed that the risk of postoperative thrombotic complications such as deep vein thrombosis and pulmonary embolism, as well as infectious complications, after using tranexamic acid was the same as that of the control group. However, considering postoperative immobilization, combining tranexamic acid with low-molecular-weight heparin sodium is recommended to reduce the influence of tranexamic acid on thrombosis. At present, the routes of administration and dosage of tranexamic acid remain controversial; thus, multi-center and high-quality randomized controlled trials with large sample sizes are needed to confirm its efficacy and safety. Clinically, we can refer to the following protocol for the intraoperative use of tranexamic acid in TKA: intravenous tranexamic acid once intraoperatively or combined with local application, or intravenous tranexamic acid at least once after surgery.

Clinical Question 12: Does the Healing of Allogeneic Bone Graft and Autogenous Iliac Bone Graft Osteotomy Differ?

Recommendation 12: The healing of allogeneic bone graft and autogenous iliac bone graft in medial open wedge HTO is similar (evidence level and recommendation strength: 2D).

Generally, bone grafting is not needed for medial open wedge HTO. However, when the medial opening height is large (>12 mm), there is a fracture at the lateral "hinge," or the patient has high-risk factors for fracture nonunion (e.g. obesity, smoking), bone grafting should be performed at the same time as rigid internal fixation to ensure fracture healing, reduce the loss of orthopaedic angle, and promote early postoperative functional recovery. Because wedge bone defects will be present after medial osteotomy, the larger the opening angle, the larger the volume of bone defects, and the higher the possibility of potential nonunion. The nonunion rate of the osteotomy site in HTO is reportedly 0%–35%,[41] and bone grafting is an effective method to fill bone defects and reduce the nonunion rate in HTO.

Evidence from the literature: To compare the differences between autologous bone graft and allogeneic bone graft, Kuremsky *et al.*[42] compared 19 HTO patients with allogeneic bone graft and 51 cases of autologous iliac bone graft and analyzed the healing rate of the broken end and the risk of postoperative complications. The above indexes were similar between the two groups, with the same healing effect; however, the length of hospital stay of patients undergoing allogeneic bone grafting was significantly shorter than that of patients undergoing autologous bone grafting. To compare the treatment outcomes of the two bone grafting methods, Ren *et al.*[43] included three randomized controlled trials and seven observational studies in a meta-analysis. The results showed that the duration of surgery in patients undergoing allogeneic bone graft during HTO was shorter; however, the risk of postoperative complications, the osteotomy correction angle, and the healing rate did not differ between the two groups, and both methods of bone implantation were safe and reliable. Cho *et al.*[44] followed up 29 patients with autologous bone grafting and 23 patients with allogeneic bone grafting for 2 years and found that postoperative imaging indicators or clinical outcomes were not significantly different between the two bone grafting methods; however, allogeneic bone grafting could avoid the trauma caused by iliac bone grafting. At present, there are no high-quality literature reports on the effect of various artificial bone graft materials in osteotomy, and related basic and clinical studies are needed.

Clinical Question 13: What Type of Steel Plate Should Be Selected for Fixation in Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 13: The clinical outcome of the anatomical locking plate in periarticular knee osteotomy for lower extremity alignment correction is better than that of the compression plate (evidence level and recommendation strength: 1D).

The screw control force of the compression plate is limited; thus, achieving stable fixation is difficult when used in periarticular knee osteotomy for lower extremity alignment correction. The angular stability of the anatomical locking plate depends on the special locking mechanism of the locking screws. This greatly simplifies the internal fixation surgery, better matches the shape of the proximal lateral tibia, does not require bending of the plate during surgery, and has the advantages of high strength and good stability; therefore, the anatomical locking plate can maximally maintain the correction effect after osteotomy.

Evidence from the literature: To compare the biomechanical characteristics of the anatomical locking and compression plates, Raja *et al.*[45] used DICOM data of patients' postoperative CT scans to simulate osteotomy and fixed models for finite element analysis and collected the simulation data produced by fretting, displacement, and implant stress. The results showed that under specific loads, the maximum displacement of the compression plate was higher than that of the anatomical locking plate, and the average stress was significantly lower than that of the anatomical locking plate; thus, it was considered that the stability of the compression plate is worse than that of the anatomical locking plate. To compare the treatment outcomes of the anatomical locking and compression plates in open wedge HTO, the meta-analysis of Han *et al.*[46] revealed that the osteotomy healing rate of the two plates was similar, but the correction retention rate of the compression plate was lower and the angle of correction loss was larger, whereas the improvement of knee joint function with the anatomical locking plate was more significant. Therefore, the biomechanical performance of the anatomical locking plate is better than that of the compression plate, and better clinical outcomes can be obtained with reduced loss of the long-term correction angle.

Clinical Question 14: Should Negative Pressure Drainage Be Routinely Inserted after Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 14: Negative pressure drainage after periarticular knee osteotomy for lower extremity alignment correction has no significant effect on postoperative blood loss and early complications (evidence level and recommendation strength: 2D).

Blood loss and early complications after osteotomy are common in the clinical setting, and whether to place a drainage tube during surgery is generally decided by the surgeon based on experience. Previous research has shown that drainage in the surgical field can drain hematomas; however, it also eliminates the tamping effect of the hematoma, which can increase the risk of postoperative blood loss. Although the overt blood loss of patients without drainage is reduced, it is necessary to correctly estimate the hidden blood loss and replenish blood volume timeously after surgery to prevent anemia.

Evidence from the literature: To analyze the influence of negative pressure drainage on postoperative blood loss, Xu *et al.*[47] included patients with medial compartment knee OA undergoing HTO to conduct a retrospective study on whether to place drainage. The results showed that hemoglobin, hematocrit, and total blood loss were not different, and knee joint function or pain improvement also did not differ between the groups with and without negative pressure drainage. Li *et al.*[48] conducted a randomized controlled trial on whether to insert negative pressure drainage in patients undergoing HTO. The results showed that total blood loss and hemoglobin after surgery were similar between the groups with and without negative pressure drainage; however, knee joint range of motion was higher, and the incidence of incision complications was lower after inserting drainage.

With the improvement of surgical techniques, as well as the application of hemostatic drugs and ERAS in the perioperative period, not inserting drainage after alignment correction has been gradually accepted. However, the influence

of drainage on joint function after surgery remains controversial, and high-quality, multi-center randomized controlled trials are needed to provide further evidence.

Clinical Question 15: Is Analgesic Therapy Required after Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 15: Early application of multi-mode combined analgesia after periarticular knee osteotomy for lower extremity alignment correction can significantly relieve pain and reduce the use of opioids in the perioperative period (evidence level and recommendation strength: 1D).

Although alignment correction can significantly relieve the pain associated with knee OA, restore the function of the knee joint, and improve the quality of life, patients may experience pain caused by the osteotomy in the early postoperative period. Multi-mode analgesia refers to the combination of analgesic methods and drugs with different mechanisms of action that result in a synergistic or additive analgesic effect. At the same time, the dosage of each drug can be reduced and, correspondingly, the adverse reactions can be reduced to achieve the best analgesic effect. Perioperative analgesia can reduce postoperative complications, relieve pain, and facilitate early functional exercise, which is especially important for the rehabilitation of orthopaedic patients.

Evidence from the literature: To study the treatment outcomes of multi-mode combined analgesia in periarticular knee osteotomy for lower extremity alignment correction, Jung *et al.*[49] conducted a randomized controlled trial on multi-mode combined analgesia (periarticular cocktail injection therapy: bupivacaine 200 mg, morphine hydrochloride 10 mg, epinephrine 200 mg, and 0.9% sodium chloride 19.8 mL). The results showed that the application of this analgesic therapy could significantly relieve pain and reduce morphine use. Besides, it is easy to administer. Clinicians can master it with little training, leading to a new concept in postoperative preemptive analgesia. However, the best formulation of the "cocktail" remains controversial, and the best drug types, concentrations, and proportions need to be verified. To evaluate the application value of femoral nerve block in multi-mode combined analgesia, Ren *et al.*[50] conducted a randomized controlled trial on femoral nerve block based on epidural analgesia, and the results showed that femoral nerve block could significantly relieve patients' perioperative pain. Sim *et al.*[51] observed the analgesic effect of ultrasound-guided adductor canal block in patients undergoing HTO under the condition of postoperative morphine analgesia; they achieved a good analgesic effect and could reduce the dose of morphine used in the perioperative period. Therefore, "cocktail" therapy and multi-mode analgesia mainly based on block therapy are considered to be effective for pain management after HTO. In the future, a horizontal comparison of various multi-mode analgesia therapies is needed, and the best analgesia scheme for periarticular knee osteotomy for lower extremity alignment correction needs to be determined using larger-scale research and multi-dimensional comprehensive evaluations.

Clinical Question 16: What Are the Adverse Effects of Periarticular Knee Osteotomy for Lower Extremity Alignment Correction on Subsequent TKA?

Recommendation 16: The difficulty of performing TKA and the risk of revision after periarticular knee osteotomy for lower extremity alignment correction are significantly higher, and the function of the knee joint will be decreased (evidence level and recommendation strength: 1C).

Although HTO can restore normal lower extremity alignment, relieve knee joint pain, and improve knee joint function, approximately 60% of patients still require TKA 10–15 years after surgery. In patients with HTO failure, it becomes more difficult to perform subsequent TKA because of problems such as low patella position, shortening of the patellar ligament, change in the Q angle, internal and external rotation of the tibial tubercle, reduced posterior tibial slope, and contracture or relaxation of the soft tissue.

Evidence from the literature: To evaluate TKA after the failure of HTO, Sun *et al.*[54] conducted a meta-analysis. The results showed that TKA after HTO required a longer duration of surgery, with a higher postoperative infection rate and reduced knee flexion angle. A meta-analysis by Chen *et al.*[55] showed that the complexity of TKA and the revision rate after HTO were higher, and the loosening and impingement rates of the tibial prosthesis were higher after surgery. Therefore, although HTO provides satisfactory pain relief and functional improvement for patients with a high activity demand, the technical requirements of TKA after HTO failure are more complex, and the risk is significantly higher than when TKA is performed as the initial surgery.

Clinical Question 17: When Can Partial Weight-Bearing Be Performed after Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 17: Early partial weight-bearing after periarticular knee osteotomy for lower extremity alignment correction will not affect postoperative recovery or increase the risk of complications (evidence level and recommendation strength: 2C).

Early weight-bearing after osteotomy is an important part of postoperative rehabilitation; however, the best time for weight-bearing remains controversial among orthopaedic surgeons. Early postoperative weight-bearing can promote lower extremity movement and muscle strength recovery and reduce the risk of thrombosis. However, fracture and lower extremity correction angle loss may occur in the weak area of the osteotomy site. With the continuous improvement of rigid internal fixation materials and the quality of perioperative management, it is possible to further advance the timing of postoperative weight-bearing.

Evidence from the literature: To explore the effect of different timings of weight-bearing on the postoperative

outcomes of HTO, Lansdaal *et al.*[56] randomly divided 48 patients into two groups after HTO: early partial weight-bearing (the day after surgery) and delayed weight-bearing (2 months after surgery). At the 2-month follow-up, IKDC score, imaging parameters, or pain degree were not significantly different between the two groups; thus, it was considered that partial weight-bearing as early as possible after surgery would not affect functional recovery. Moreover, the postoperative complications of the two groups were compared, which proved that partial weight-bearing as early as possible after osteotomy would not increase the risk of postoperative complications. To evaluate the safety of early weight-bearing after bilateral HTO, Takeuchi *et al.*[57] analyzed 10 patients who underwent bilateral HTO at the same time. They started active and passive training for lower extremity muscle strength on the second day after surgery. The patients were able to stand up and walk with partial weight-bearing 1 week after surgery and started full weight-bearing 3 weeks after surgery. No complications such as delayed union of fracture, infections, or loosening of the prosthesis were found after surgery. Therefore, it was considered that early postoperative weight-bearing can promote postoperative rehabilitation without increasing the risk of adverse events. Lee *et al.*[58] evaluated six clinical controlled trials related to early complete weight-bearing (2 weeks after surgery) and delayed complete weight-bearing (6–8 weeks after surgery) after HTO in a meta-analysis, which showed that Lysholm score, femorotibial angle, and the incidence of postoperative complications did not differ between the two groups.

Therefore, for patients with reliable bone grafting, reliable internal fixation, and no hinge fracture, early partial weight-bearing can be considered. Immediately after recovery from anesthesia, the patients were instructed to carry out ankle joint dorsiflexion and plantarflexion of the affected limb. On the second day after surgery, knee joint flexion and extension of the affected limb as well as standing on the affected limb without weight-bearing with bedside assistance were allowed. Usually, patients can bear some weight with crutches on the third day after surgery and gradually increase the weight at 4 weeks after surgery. At 6–8 weeks postoperatively, they are allowed to walk without crutches with weight-bearing depending on X-ray findings. Many factors may affect the weight-bearing timing after surgery, such as age, internal comorbidities, and types of internal fixation. Therefore, the extensive promotion of early postoperative partial weight-bearing needs further study.

Clinical Question 18: What Are the Risk Factors for Infections after Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 18: Male sex, old age (>65 years), smoking, diabetes, long anesthesia time (>3.5 hours), oblique skin incision, and artificial bone grafting materials may be risk factors for infections after periarticular knee osteotomy for lower extremity alignment correction (evidence level and recommendation strength: 1C).

Infections are a common and serious complication after periarticular knee osteotomy for lower extremity alignment correction. According to reports, the incidences of superficial and deep infections after HTO were 1%–9.6% and 0.5%–4.7%, respectively, and some patients needed multiple surgical interventions. The methods to treat postoperative infections include dressing change, debridement, and removal of internal fixation, which not only affect the postoperative outcome but also increase the hospital stay and costs. Therefore, determining the high-risk factors leading to infections is important for guiding infection prevention and treatment.

Evidence from the literature: To evaluate the risk factors for surgical site infection after HTO, Kawata *et al.*[59] retrospectively analyzed the data of 12,853 patients undergoing HTO from 2010 to 2017 in a Japanese national database and found that 195 patients had surgical site infections, and 50 patients had deep infections. Male sex, old age (>50 years), long anesthesia time (>3.5 hours), and the use of artificial bone graft materials were independent risk factors for postoperative infections of HTO. Anagnostakos *et al.*[60] systematically reviewed 26 clinical research articles and concluded that the type of skin incision, specifically oblique incision, was significantly correlated with postoperative infections. Liu *et al.*[61] followed up 59 patients for 4 years after medial HTO and found that age >65 years and previous diabetes history were risk factors for surgical site infections after HTO. Although a high BMI is considered to be a risk factor for postoperative infections after various orthopaedic operations, literature to support that it is a risk factor for postoperative infections at the surgical site after HTO is not available. Because of the small sample size and low research quality of most studies, the evidence of risk factors for infections after periarticular knee osteotomy for lower extremity alignment correction is insufficient at present. However, most scholars still suggest that antibiotics should be routinely used in the perioperative period of HTO to prevent postoperative infections[62].

Clinical Question 19: Which Measures during HTO Are Beneficial for Knee Cartilage Regeneration?

Recommendation 19: Moderate lateral displacement of the alignment and inclination of the joint line <4° are beneficial for cartilage regeneration of the knee joint after HTO (evidence level and recommendation strength: 2D).

With the popularization of the concept of knee preservation, periarticular knee osteotomy for lower extremity alignment correction has been widely used in clinical practice. For a long time, it was thought that articular cartilage lacks regeneration ability; however, recent research has found that osteotomy can not only delay TKA but also result in the regeneration of the cartilage in the worn compartment to some extent. Therefore, clarifying the factors related to

postoperative cartilage regeneration is of great significance for clinical treatment.

Evidence from the literature: Kim *et al.*[63] analyzed 104 patients with lower extremity alignment corrected from 6.0° ± 2.2° varus preoperatively to 1.8° ± 3.2° valgus after HTO and classified them by knee arthroscopy examination of the cartilage status combined with the International Cartilage Repair Society Hyaline Cartilage Lesion Classification System (four-grade method). The results showed that 51.9% of medial femoral condyle and 34.6% of medial tibial plateau cartilage injuries were improved; thus, accurate valgus correction was beneficial for cartilage regeneration. Koshino *et al.*[64] treated 115 patients (146 knees) with HTO. At 2 years postoperatively, arthroscopy confirmed that 46 out of the 132 knees with a valgus angle ≥5° after surgery showed complete cartilage regeneration, whereas only one out of the 14 knees with a valgus angle ≤4° showed complete cartilage regeneration. Therefore, the authors speculated that correction to valgus >5° after HTO is of great significance for cartilage regeneration after surgery. To determine whether the inclination of the articular line caused by unilateral osteotomy will affect the regeneration of cartilage after HTO, Kim *et al.*[65] retrospectively analyzed the data of 61 patients (62 knees) who underwent HTO and measured the inclination of the articular line at the follow-up 22 months on average after surgery. Knee arthroscopy showed that the knee joints with an inclination of the articular line <5° showed better cartilage regeneration. It is unclear whether age and sex will affect cartilage regeneration after HTO.

Clinical Question 20: What Is the Effect of Periarticular Knee Osteotomy for Lower Extremity Alignment Correction on Inflammatory Factors in the Joint?

Recommendation 20: Periarticular knee osteotomy for lower extremity alignment correction can reduce the level of inflammatory factors in the joint and provide a good internal environment for cartilage regeneration (evidence level and recommendation strength: 2D).

The pathogenesis of OA is considered to be a complicated and multifactorial process caused by genetic, mechanical, and environmental factors, and the disorder of inflammatory factors and the pathogenesis at a molecular level have attracted increasing attention.

Evidence from the literature: Inflammatory factors can disrupt the balance of chondrocyte synthesis and decomposition. Interleukin (IL)-1β, IL-6, and IL-17 can damage the articular cartilage, and their levels in the plasma and knee joint synovial fluid of patients with knee OA are significantly higher than those in healthy people. Bai *et al.*[66] treated 26 patients with HTO and detected the levels of IL-1β, IL-6, and IL-17 in the plasma and synovial fluid of the affected knee joint before surgery and 6 months postoperatively and compared them with those in normal people. The results showed that the level of inflammatory factors was significantly higher before surgery in patients than in normal people, and although it had decreased significantly at 6 months postoperatively, the level was still higher than that in normal people. Nevertheless, proteoglycan epitope, fibroblast growth factor-2, and procollagen peptide in the knee joint increased after HTO, and these factors are beneficial for cartilage regeneration[67]. At the molecular level, microRNAs are a type of non-coding ribonucleic acid that can regulate gene expression after transcription and are correlated with cartilage degeneration. Kwak *et al.*[68] found that the expression of two microRNAs (microR-30c-5p and microR-23a-3p) in the synovial fluid of patients after HTO was different from that before surgery, and both microRNAs were correlated with the progression of OA. Therefore, changes in the intraarticular environment after HTO may play a positive role in cartilage regeneration.

Clinical Question 21: What Are the Indications for Knee Arthroscopic Exploration and Cleaning in Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 21: If symptomatic meniscus injury (tear), intraarticular loose bodies, or intercondylar fossa stenosis are definitively diagnosed before periarticular knee osteotomy for lower extremity alignment correction, knee arthroscopy is recommended (evidence level and recommendation strength: 1D).

Arthroscopy has important application value in the diagnosis and treatment of knee OA. Arthroscopy can repair the damaged meniscus and remove unstable cartilage and loose bodies. Drilling into the subchondral sclerotic bone can effectively relieve intraosseous pressure. Under the arthroscope, all types of impurities and pain-causing factors can be removed from the joint, and synovium with significant inflammation or thickening can be removed, which can effectively relieve joint pain. Therefore, it is suggested that arthroscopic exploration should be routinely performed for patients who are definitively diagnosed with symptomatic meniscus injury (tear), intraarticular loose bodies, or intercondylar fossa stenosis before operation[69,70].

Evidence from the literature: To analyze the treatment outcomes of arthroscopy combined with HTO for the treatment of medial compartment knee OA, Yoo and Shin[71] retrospectively analyzed the data of patients with varus knee OA before and after surgery. The results showed that the hip-knee-ankle angle, femorotibial angle, and medial proximal tibial angle were significantly improved postoperatively. The Lysholm score, AKS score, and knee joint range of motion were also significantly improved. Therefore, knee arthroscopy combined with HTO is an effective method for the treatment of medial compartment knee OA. Kim *et al.*[72] retrospectively analyzed 88 patients with varus knee OA who were divided into two groups: the single treatment group (HTO) and the combined treatment group (knee arthroscopy + HTO), according to different surgical procedures. The postoperative imaging results and pain score did not differ between the two groups. Therefore, both surgical schemes could improve the symptoms and signs of patients in a short

time. Moreover, HTO combined with arthroscopic surgery could simultaneously treat intraarticular lesions, and the postoperative pain relief and joint function improvement were better than with HTO alone.

Clinical Question 22: Can the Application of a 3D-Printed Corrective Osteotomy Guide Improve the Accuracy of Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 22: A 3D-printed corrective osteotomy guide has the functions of guiding, osteotomy, and correction and can improve the accuracy of lower extremity alignment correction (evidence level and recommendation strength: 1D).

During periarticular knee osteotomy for lower extremity alignment correction, repeated adjustments relying on the surgeon's operating experience and multiple fluoroscopies by C-arm X-ray machine are often needed to obtain the ideal osteotomy position, which may lead to more bone loss, a prolonged duration of surgery, increased intraoperative blood loss, and an increased risk of postoperative complications. In addition, intraoperative fluoroscopy is unreliable because of the influences of body position, the viewing angle of fluoroscopy, and measurement error, which reduces the accuracy of alignment correction, while accurate control of the target alignment is key to the success of osteotomy. Preoperative planning error or intraoperative surgical error may lead to poor lower extremity alignment. 3D-printed individualized corrective osteotomy can utilize DICOM data of preoperative CT scans to create the knee joint model, simulate the opening after osteotomy during surgery, correct the alignment, and accurately locate the Fujisawa point; it can use 3D printing technology to print out an individualized corrective osteotomy guide plate, assist in intraoperative osteotomy and correction, predict the correction results, and reduce intraoperative fluoroscopy, which helps to reduce the duration of surgery and complications.

Evidence from the literature: Ma *et al.* retrospectively analyzed 241 patients who underwent medial open HTO with 3D-printed individualized corrective osteotomy guide and 100 patients undergoing traditional medial open HTO. The former group underwent an average of 2.8 fluoroscopies, which was 75% less than that of the traditional medial open HTO group. The average duration of surgery in the 3D-printed group (24 min) was 63% shorter than that in the traditional medial open HTO group. The risks of osteotomy-related fractures and implant-related infections after surgery with a 3D-printed individualized corrective osteotomy guide were lower. Therefore, compared with traditional osteotomy, the application of a 3D-printed individualized corrective osteotomy guide significantly reduces the number of fluoroscopies by C-arm X-ray machine, shortens the duration of surgery, reduces intraoperative blood loss, and improves the accuracy of alignment control and the safety of the surgery.

Clinical Question 23: Which Measures Promote Postoperative Rehabilitation of Patients during the Perioperative Period?

Recommendation 23: ERAS can promote the rehabilitation of patients after periarticular knee osteotomy for lower extremity alignment correction. Postoperative rehabilitation measures include physical therapy, cold compression, lymphatic return manipulation, muscle strength training, joint loosening manipulation, and continuous passive functional training (evidence level and recommendation strength: 1C).

The concept of ERAS was introduced in the late 1990s. It is a multi-mode and multi-system intervention measure based on evidence-based medicine. It can alleviate the physiological and psychological stress responses of patients during the perioperative period and achieve the goals of rapid postoperative rehabilitation, pain relief, and early recovery of normal life. At present, ERAS is widely used in all subspecialties of orthopaedics. Periarticular knee osteotomy for lower extremity alignment correction combined with ERAS can not only relieve pain symptoms on the premise of preserving the knee but also greatly shorten the average hospital stay and improve patient satisfaction.

Evidence from the literature: Early rehabilitation therapy adopted by Wang *et al.*[73] included physical therapy, cold compression, lymphatic return manipulation, muscle strength training, joint loosening manipulation, and continuous passive functional training. The results confirmed that early rehabilitation therapy based on ERAS could effectively improve the joint range of motion after HTO, relieve pain, and promote the recovery of the overall function of the knee joint. Yu *et al.*[74] selected patients with knee OA accompanied by varus deformity and anterior cruciate ligament injury who underwent arthroscopic anterior cruciate ligament reconstruction combined with HTO and provided them with routine nursing and ERAS-based nursing interventions, respectively. The results showed that the VAS score of the routine nursing group at each time point after surgery was higher than that of the ERAS group; the time required for active flexion and extension to 30°, 45°, 60°, 90°, and 120° was longer than that of the ERAS group; and the patient satisfaction was worse. Therefore, nursing interventions based on ERAS can alleviate pain after arthroscopic anterior cruciate ligament reconstruction combined with HTO, shorten the time required for active knee flexion to reach the same angle after surgery, and accelerate the rehabilitation process.

Clinical Question 24: What Are the Key Factors of the Perioperative Management of Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 24: Nutritional support, anemia management, postoperative blood glucose monitoring, and thrombus management are key factors that should be managed during the perioperative period of periarticular knee osteotomy for lower extremity alignment correction (evidence level and recommendation strength: 1D).

Periarticular knee osteotomy for lower extremity alignment correction is mostly used in middle-aged and older patients who often have cardiovascular and cerebrovascular diseases, diabetes, and other underlying diseases. Moreover, older patients have a poor tolerance for surgery, the hematopoietic reserve capacity of their bone marrow is reduced, and postoperative complications such as malnutrition, anemia, and poor wound healing can easily occur. Good perioperative management is essential to improve the surgery outcome and reduce the risk of complications.

Evidence from the literature: A preoperative diet high in protein and vitamins combined with a high-nutrition elemental diet if necessary could rapidly increase the level of plasma albumin to over 35 g/L. On the basis of adequate nutritional support, patients with postoperative anemia should be treated with erythropoietin combined with iron to correct anemia. The specific method for patients with hemoglobin <95 g/L is as follows: subcutaneous injection of 10,000 units of erythropoietin and intravenous infusion of 100–200 mg of iron sucrose, once every day or every other day; patients with hemoglobin >95 g/L can be given 300 mg/day of oral iron only.[75] Based on a preoperative blood glucose control program for patients with diabetes, blood glucose should be monitored every 2–4 hours on the day of surgery; it should be monitored on an empty stomach and 2 hours after the three meals on the first day after surgery, and the glucose-lowering program should be adjusted according to the blood glucose level to control the blood glucose at 6.0–11.1 mmol/L. Postoperative thrombus management should follow the basic principles in the Chinese Guidelines for Prevention of Venous Thromboembolism in Major Orthopaedic Surgery and adopt physical preventive measures (e.g. plantar venous pump and intermittent inflation pressure device) to reduce the incidence of postoperative deep vein thrombosis of the lower extremities; if there are no contraindications, it is recommended to use physical preventative measures in combination with prophylactic medication.[76]

Clinical Question 25: Which Factors Should Be Evaluated in the Follow-Up of Periarticular Knee Osteotomy for Lower Extremity Alignment Correction?

Recommendation 25: Healing of the osteotomy site, lower extremity alignment, joint function, and cartilage regeneration should be evaluated regularly, and follow-up results should be combined to guide subsequent treatment and rehabilitation (evidence level and recommendation strength: 1D).

Follow-up is one of the postoperative steps of periarticular knee osteotomy for lower extremity alignment correction. Postoperative follow-up includes the evaluation of the surgical outcome, the necessary intervention measures for the problems that have occurred, and guiding patients to perform rehabilitation training. Postoperative recovery of patients with osteotomy is a staged process; thus, regular postoperative follow-up, detailed medical history collection, physical examination, and imaging examination are necessary. (i) Follow-up time: The recommended follow-up times for rigid internal fixation are 6 weeks, 3 months, and 6 months after surgery; the recommended follow-up times for internal fixation are 2 weeks, 6 weeks, 3 months, and 9 months after surgery. (ii) Imaging examination: Except for 2 weeks after surgery, at all follow-up time points, patients should be examined using local and full-length X-rays of the lower extremities to understand the status of fracture healing, measure lower extremity alignment, and determine whether osteotomy angle loss or joint deformity has occurred. If necessary, CT scanning and 3D reconstruction can be performed to evaluate the joint space between the medial and lateral compartments to indirectly evaluate cartilage regeneration and OA progression, and, if necessary, magnetic resonance examination can be performed. (iii) Functional evaluation: At present, quantitative evaluation methods such as HSS, KSS, KOOS, and the WOMAC osteoarthritis index can be used to evaluate knee joint function after knee osteotomy for alignment correction.[77-79] (iv) Guiding rehabilitation exercise: Postoperative rehabilitation focuses on improving lower extremity muscle strength, training for normal walking, and increasing the knee joint range of motion. (v) If the patient requires removal of the internal fixation, local and full-length X-ray films of both lower extremities should be taken 12–18 months after surgery. If lower extremity alignment has been corrected accurately and the fracture is completely healed, the internal fixation can be removed at a scheduled time point.[80,81]

Formulation Methods of these Guidelines

Methodology

The formulation of these guidelines conforms to the concept and process framework of clinical practice guidelines established by the Institution of Medicine (IOM), the Appraisal of Guidelines Research and Evaluation (AGREE II), and the World Health Organization Handbook for Guideline Development. The formulation process of these guidelines is strictly in accordance with the pre-established plan, and the reporting process of these guidelines refers to the Reporting Items for Practice Guidelines in Healthcare (RIGHT) (Supplemental Table 1).

Populations Indicated for these Guidelines

These guidelines are suitable for patients with unicompartmental knee OA and poor alignment but not for patients with multicompartmental end-stage knee OA, knee OA with normal alignment, and inflammatory arthritis.

Users of these Guidelines

Specialized medical personnel in secondary and tertiary medical institutions in China, including orthopaedic doctors, pain management doctors, rehabilitation doctors, and specialized nurses.

Initiators of these Guidelines

These guidelines were initiated and formulated by the Clinical New Technology Application Committee of the Chinese Hospital Association, the Joint Surgery Study Group of the Chinese Orthopaedic Association of the Chinese Medical Association, and the Osteoarthritis Study Group of the Chinese Association of Orthopaedic Surgeons of the Chinese Medical Doctor Association. The editorial department of the Chinese Journal of Orthopaedics organized methodological experts in the field of orthopaedics to provide guideline formulation methodology and evidence evaluation support. The starting time was November 27, 2020, and the finalization time was November 10, 2021.

Registration of the Plan and Guidelines

These guidelines have been posted on the Practice Guidelines Registration Platform (www.guidelines-registry.cn; IPGRP-2021CN309). The compilation of the plan was completed before the formulation of these guidelines.

Statement and Handling of Conflicts of Interest

All the members who participated in the formulation of these guidelines made a statement regarding any relationships related to these guidelines and completed the conflicts of interest statement form.

Identification and Evaluation of the Importance of Clinical Questions

The process of formulating the clinical questions was performed in strict accordance with the methods for formulating clinical questions of guidelines and combined with evidence-based thinking using the Delphi method. The main steps include drawing up consultation items and outlines, determining the members of the expert group, consulting by letter and revising the items multiple times, and statistical analysis and feedback of the survey results.

The working group of these guidelines collected 25 questionnaires with 78 clinical questions in the first round of the open questionnaire survey, and the survey respondents were doctors at all levels in hospitals of various grades in several provinces and cities in China. Then, the collected clinical questions were summarized, and 36 clinical questions were finally obtained. Next, the second round of investigation was conducted to evaluate the importance of the clinical questions (the importance of each clinical question was divided into five levels, namely, very important, relatively important, generally important, not very important, and uncertain). By assigning values to and summarizing each level of importance, 30 clinical questions were finally ranked in terms of importance. Subsequently, in the third round of discussion, the important clinical questions were deconstructed, deleted, and synthesized again, and the final 25 clinical questions to be included in these guidelines were determined (Supplemental Figure 1).

Clinical Question Selection and Evidence Retrieval

The clinical questions were deconstructed according to the evidence-based medical literature retrieval format (i.e. the PICO principle: populations, intervention measures, controls, and outcome indicators) (Supplemental Table 2). According to the deconstructed clinical questions, evidence retrieval was carried out. (i) The databases and platforms searched included PubMed, Embase, the Cochrane Library, CNKI, and Wanfang database. (ii) Types of studies searched: the retrieval of systematic reviews, meta-analyses, and randomized controlled trials published within 5 years was prioritized, and the retrieval of related studies published more than 5 years ago was increased when the latest evidence was insufficient or the level of evidence was low. (iii) The retrieval time was from the establishment of the database to December 25, 2020. (iv) Further searches of recently published evidence were performed before drafting the main body of these guidelines, and the updated final date for searching was July 31, 2021.

Evaluation of Evidence Quality and Formation of Recommendation Opinions

For systematic reviews and meta-analyses, the methodological quality evaluation tool for systematic reviews was used to evaluate methodological quality[82]; the Cochrane risk bias evaluation tool was used to evaluate randomized controlled trials[83]; for observational research, the Newcastle–Ottawa

TABLE 1 Classification and definition of evidence quality in these guidelines

Evidence level	Definition
High (A)	It is quite certain that the observed value is close to the true value
Moderate (B)	Moderate confidence in the observed value: the observed value may be close to the true value, but it may also be quite different
Low (C)	Limited grasp of the observed value: the observed value may be quite different from the true value
Very low (D)	There is little certainty about the observed value: there may be a great difference between the observed value and the true value

TABLE 2 Recommendation strength classification and definition in these guidelines

Recommendation strength	Definition
Strong (1)	Clearly show that the benefits of intervention outweigh the disadvantages
Weak (2)	The advantages and disadvantages are uncertain, or the advantages of intervention measures may outweigh the disadvantages
Good practice statement (3)	Recommendations based on indirect evidence or expert opinions and experience

TABLE 3 List of recommendations in the clinical guidelines for the treatment of knee osteoarthritis by periarticular knee osteotomy for lower extremity alignment correction in China

Recommendation number	Content	Evidence level and recommendation strength
Recommendation 1	Patients undergoing periarticular knee osteotomy for lower extremity alignment correction should be <65 years for men and <60 years for women	1C
Recommendation 2	The body mass index of patients undergoing periarticular knee osteotomy for lower extremity alignment correction should be <27.5 kg/m^2	1D
Recommendation 3	The Kellgren–Lawrence classification of the affected knee joint compartment of patients undergoing periarticular knee osteotomy for lower extremity alignment correction should be below Grade III, and the joint space of the contralateral compartment should be relatively normal	1D
Recommendation 4	Periarticular knee osteotomy for lower extremity alignment correction is indicated for patients with a varus deformity >5° or a valgus deformity >10°	1D
Recommendation 5	For patients undergoing periarticular knee osteotomy for lower extremity alignment correction, the preoperative knee joint range of motion should be >100°, and flexion contracture should be <15°	1D
Recommendation 6	Lateral closed wedge high tibial osteotomy (HTO) and medial open wedge HTO have similar imaging correction, postoperative joint function, and risk of complications in the treatment of varus knee osteoarthritis. Medial open wedge osteotomy may reduce the patella height and increase the tibial plateau declination, whereas lateral closed wedge HTO takes a long time to heal and reduces the posterior inclination of the tibial plateau. Therefore, the osteotomy method should be selected according to the actual needs and comprehensively judged according to the lengths of both lower extremities	1D
Recommendation 7	Medial closed wedge and lateral open wedge distal femoral osteotomy (DFO) have similar effects in the treatment of valgus knee osteoarthritis. The healing time of the stump of medial closed wedge DFO is shorter than that of lateral open wedge DFO	2D
Recommendation 8	Dual-site periarticular knee osteotomy is a safe and effective method for the treatment of unicompartmental knee osteoarthritis with femoral and tibial deformities	1D
Recommendation 9	The short-term treatment outcomes of proximal fibular osteotomy (PFO) for varus unicompartmental knee osteoarthritis are positive, whereas the long-term treatment outcomes still need to be verified	1D
Recommendation 10	The alignment accuracy of periarticular knee osteotomy assisted by computer navigation is better than that of traditional osteotomy	1C
Recommendation 11	The combined use of tranexamic acid through multiple routes can significantly reduce perioperative blood loss during periarticular knee osteotomy for lower extremity alignment correction	1D
Recommendation 12	The healing of allogeneic bone graft and autogenous iliac bone graft in medial open wedge HTO is similar	2D
Recommendation 13	The clinical outcomes of the anatomical locking plate in periarticular knee osteotomy for lower extremity alignment correction are better than those of the compression plate	1D
Recommendation 14	Negative pressure drainage after periarticular knee osteotomy for lower extremity alignment correction has no significant effect on postoperative blood loss and early complications	2D
Recommendation 15	Early application of multi-mode combined analgesia after periarticular knee osteotomy for lower extremity alignment correction can significantly relieve pain and reduce the use of opioids in the perioperative period	1D
Recommendation 16	Total knee arthroplasty after periarticular knee osteotomy for lower extremity alignment correction is significantly more difficult to perform and results in a higher risk of revision and reduced function of the knee joint	1C
Recommendation 17	Early partial weight-bearing after periarticular knee osteotomy for lower extremity alignment correction will not affect postoperative recovery or increase the risk of complications	2C
Recommendation 18	Male sex, old age (>65 years), smoking, diabetes, long anesthesia time (>3.5 hours), oblique skin incision, and artificial bone grafting materials may be risk factors for infections after periarticular knee osteotomy for lower extremity alignment correction	1C
Recommendation 19	Moderate lateral displacement of the alignment and inclination of the joint line <4° are beneficial for cartilage regeneration of the knee joint after HTO	2D
Recommendation 20	Periarticular knee osteotomy for lower extremity alignment correction can reduce the level of inflammatory factors in the joint and provide a good internal environment for cartilage regeneration	2D
Recommendation 21	If symptomatic meniscus injury (tear), intraarticular loose bodies, or intercondylar fossa stenosis are definitively diagnosed before periarticular knee osteotomy for lower extremity alignment correction, knee arthroscopy is recommended	1D
Recommendation 22	The 3D-printed corrective osteotomy guide assists with guiding, osteotomy, and correction and can improve the accuracy of lower extremity alignment correction	1D
Recommendation 23	Enhanced recovery after surgery can promote the rehabilitation of patients undergoing periarticular knee osteotomy for lower extremity alignment correction. The postoperative rehabilitation measures include physical therapy, cold compression, lymphatic return manipulation, muscle strength training, joint loosening manipulation, and continuous passive functional training	1C
Recommendation 24	Nutritional support, anemia management, postoperative blood glucose monitoring, and thrombus management are recommended during the perioperative period of periarticular knee osteotomy for lower extremity alignment correction	1D
Recommendation 25	Healing of the osteotomy site, lower extremity alignment, joint function, and cartilage regeneration should be evaluated regularly, and follow-up results should be combined to guide subsequent treatment and rehabilitation	1D

scale was used to evaluate the methodological quality of corresponding types of research.[84] The literature rating standards adopted in these guidelines refer to the relevant methods of the working group of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) and other working groups to evaluate the quality of the research.[85,86] The evidence level (Table 1) and recommendation strength (Table 2) of the research were comprehensively judged by combining the research design and other evidence features. The directions and strength of the recommendations were established using the three-round Delphi method. These guidelines contain 25 questions, and 25 recommendations were formulated. See Table 3 for a summary of the recommendations.

External Review of these Guidelines

Before the publication of these guidelines, peer review was conducted; review comments were replied to, and revisions were made accordingly.

Release and Updating of these Guidelines

The full text of these guidelines was first published in the Chinese Journal of Orthopaedics. The guideline formulation team plans to update these guidelines every 2–3 years.

Implementation and Dissemination of these Guidelines

After publication, these guidelines will be disseminated through academic conferences or workshops. Specific ways of dissemination include (i) dissemination for 1–2 years at orthopaedic conferences and knee preservation training classes; (ii) publication and dissemination of the text in newspapers, periodicals, pamphlets, manuals, and other forms of media; and (iii) publication in both Chinese and English and dissemination on Orthonline, AllinMD Orthopaedics, and other websites. (4) Regarding the implementation and evaluation of these guidelines, the implementation of these guidelines will be further promoted by publishing relevant interpretation articles of these guidelines.

List of Names of Consultant Specialists

Xin-long Ma, Yong-cheng Hu, Kun-zheng Wang, Lun-hao Bai, Li Cao, De-sheng Chen, Wei-min Fan, Jing-min Huang, Wei Huang, Qun-hua Jin, Qi Liao, Ai-feng Liu, Guang-yao Liu, Jun Liu, Wei Liu, Song-cen Lv, Tie-bing Qu, Bin Shen, Zhan-jun Shi, Jie Sun, Shui Sun, Xiao-bin Tian, Jian-zhong Xu, Jin-li Zhang, Qiu-jian Zheng, Zong-ke Zhou.

Supporting Information

Additional Supporting Information may be found in the online version of this article on the publisher's web-site:

Supplemental Figure 1 The selection process of important clinical questions

Supplemental Table 1 The checklist of RIGHT

Supplemental Table 2 The 25 deconstructed important clinical questions (PICO principle)

References

1. Safiri S, Kolahi AA, Smith E, Hill C, Bettampadi D, Mansournia MA, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. Ann Rheum Dis. 2020;79:819–28.
2. Sun X, Zhen X, Hu X, Li Y, Gu S, Gu Y, et al. Osteoarthritis in the middle-aged and elderly in China: prevalence and influencing factors. Int J Environ Res Public Health. 2019;16:4701.
3. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet. 2019;393:1745–59.
4. Kim C, Linsenmeyer KD, Vlad SC, Guermazi A, Clancy MM, Niu J, et al. Prevalence of radiographic and symptomatic hip osteoarthritis in an urban United States community: the Framingham osteoarthritis study. Arthritis Rheumatol. 2014;66:3013–7.
5. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of hip symptoms and radiographic and symptomatic hip osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. J Rheumatol. 2009;36:809–15.
6. Barg A, Pagenstert GI, Hügle T, Gloyer M, Wiewiorski M, Henninger HB, et al. Ankle osteoarthritis: etiology, diagnostics, and classification. Foot Ankle Clin. 2013;18:411–26.
7. Long HB, Zeng XY, Liu Q, Wang H, Vos T, Hou Y, et al. Burden of osteoarthritis in China, 1990-2017: findings from the global burden of disease study 2017. Lancet Rheumatol. 2020;2:e164–72.
8. Prieto-Alhambra D, Judge A, Javaid MK, Cooper C, Diez-Perez A, Arden NK. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. Ann Rheum Dis. 2014;73:1659–64.
9. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the Management of Osteoarthritis of the hand, hip, and knee. Arthritis Rheumatol. 2020;72:220–33.
10. Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthr Cartil. 2019;27:1578–89.
11. Brown GA. AAOS clinical practice guideline: treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. J Am Acad Orthop Surg. 2013;21:577–9.
12. Coventry MB. Osteotomy of the upper portion of the tibia for degenerative arthritis of the knee. A preliminary report. J Bone Joint Surg Am. 1965;47:984–90.
13. Trieb K, Grohs J, Hanslik-Schnabel B, Stulnig T, Panotopoulos J, Wanivenhaus A. Age predicts outcome of high-tibial osteotomy. Knee Surg Sports Traumatol Arthrosc. 2006;14:149–1452.
14. Bonasia DE, Dettoni F, Sito G, et al. Medial opening wedge high tibial osteotomy for medial compartment overload/arthritis in the varus knee: prognostic factors. Am J Sports Med. 2014;42:690–8.
15. Flecher X, Parratte S, Aubaniac JM, Argenson JN. A 12-28-year followup study of closing wedge high tibial osteotomy. Clin Orthop Relat Res. 2006;452:91–6.
16. Goshima K, Sawaguchi T, Sakagoshi D, Shigemoto K, Hatsuchi Y, Akahane M. Age does not affect the clinical and radiological outcomes after open-wedge high tibial osteotomy. Knee Surg Sports Traumatol Arthrosc. 2017;25:918–23.
17. Akizuki S, Shibakawa A, Takizawa T, Yamazaki I, Horiuchi H. The long-term outcome of high tibial osteotomy: a ten- to 20-year follow-up. J Bone Joint Surg Br. 2008;90:592–6.
18. Giagounidis EM, Sell S. High tibial osteotomy: factors influencing the duration of satisfactory function. Arch Orthop Trauma Surg. 1999;119:445–9.
19. Yokoyama M, Nakamura Y, Onishi T, Hirano K, Doi M. Healing period after open high tibial osteotomy and related factors: can we really say that it is long? Springerplus. 2016;5:123.
20. Efe T, Ahmed G, Heyse TJ, Boudriot U, Timmesfeld N, Fuchs-Winkelmann S, et al. Closing-wedge high tibial osteotomy: survival and risk factor analysis at long-term follow up. BMC Musculoskelet Disord. 2011;12:46.
21. Sohn S, Koh IJ, Kim MS, Kang BM, In Y. What factors predict patient dissatisfaction after contemporary medial opening-wedge high Tibial osteotomy? J Arthroplasty. 2020;35:318–24.
22. Kuwashima U, Iwasaki K, Kurakazu I, Akasaki Y, Nakashima Y, Itoh M, et al. Effect of osteoarthritis severity on survival and clinical outcomes after high tibial osteotomy. Knee. 2021;29:441–7.

23. Rudan JF, Simurda MA. High tibial osteotomy. A prospective clinical and roentgenographic review. Clin Orthop Relat Res. 1990;255:251–6.
24. Na YG, Lee BK, Hwang DH, Choi ES, Sim JA. Can osteoarthritic patients with mild varus deformity be indicated for high tibial osteotomy? Knee. 2018;25: 856–65.
25. Naudie D, Bourne RB, Rorabeck CH, Bourne TJ. The install award. Survivorship of the high tibial valgus osteotomy. A 10- to −22-year followup study. Clin Orthop Relat Res. 1999;367:18–27.
26. Smith TO, Sexton D, Mitchell P, Hing CB. Opening- or closing-wedged high tibial osteotomy: a meta-analysis of clinical and radiological outcomes. Knee. 2011;18:361–8.
27. Sun H, Zhou L, Li F, Duan J. Comparison between closing-wedge and opening-wedge high Tibial osteotomy in patients with medial knee osteoarthritis: a systematic review and meta-analysis. J Knee Surg. 2017;30:158–65.
28. Chahla J, Mitchell JJ, Liechti DJ, Moatshe G, Menge TJ, Dean CS, et al. Opening- and closing-wedge distal femoral osteotomy: a systematic review of outcomes for isolated lateral compartment osteoarthritis. Orthop J Sports Med. 2016;4:1807697325.
29. Zhang FJ, Liu CH, Fang LM, Ling HG, Ye ZL. Comparison of open-wedge osteotomy and close-wedge osteotomy for valgus knee. Chin J Bone Joint Injury. 2016;31:149–52.
30. Wylie JD, Jones DL, Hartley MK, Kapron AL, Krych AJ, Aoki SK, et al. Distal femoral osteotomy for the valgus knee: medial closing wedge versus lateral opening wedge: a systematic review. Art Ther. 2016;32:2141–7.
31. Ji ZW, Kai X, Peihui W, et al. Linical study of double level osteotomy in knee osteoarthritis with complex deformity. J Pract Orthop. 2020;26:1087–92.
32. Schröter S, Nakayama H, Yoshiya S, Stöckle U, Ateschrang A, Gruhn J. Development of the double level osteotomy in severe varus osteoarthritis showed good outcome by preventing oblique joint line. Arch Orthop Trauma Surg. 2019; 139:519–27.
33. Nakayama H, Kanto R, Onishi S, Kambara S, Ukon R, Amai K, et al. Cartilage repair examined by second-look arthroscopy following double-level osteotomy performed for osteoarthritic knees with severe varus deformity. Knee. 2021;29: 411–7.
34. Qin D, Chen W, Wang J, Lv H, Ma W, Dong T, et al. Mechanism and influencing factors of proximal fibular osteotomy for treatment of medial compartment knee osteoarthritis: a prospective study. J Int Med Res. 2018;46: 3114–23.
35. Guo HH, Tian YJ, An L, Liu G, Guang T. Comparison of arthroscopy combined with proximal fibula osteotomy and high tibial osteotomy for medial compartment knee osteoarthritis. Chin J Bone Joint Injury. 2020;35:1076–8.
36. Qiu HY, Feng ZQ, Wang WG. Comparison of high tibial osteotomy and fibula osteotomy in treatment of knee osteoarthritis. Chin J Joint Surg (Electronic Edition). 2018;12:676–80.
37. Kim HJ, Yoon JR, Choi GW, Yang JH. Imageless navigation versus conventional open wedge high Tibial osteotomy: a meta-analysis of comparative studies. Knee Surg Relat Res. 2016;28:16–26.
38. Shi JH, Zhong DG, Hong WW, Huang YQ. Meta‐analysis of clinical outcomes of computer‐navigated versus conventional opening wedge high tibial osteotomy. J Clin Rehabil Tis Eng Res. 2018;22:5077–84.
39. Chen DS, Zhu JW, Wang TF, Zhu B, Feng CH. Tranexamic acid is beneficial to patients undergoing open-wedge high Tibial osteotomy. Biomed Res Int. 2020; 2020:2514207.
40. Ma JM, Lu HL, Chen XX, Wang DS, Wang Q. The efficacy and safety of tranexamic acid in high tibial osteotomy: a systematic review and meta-analysis. J Orthop Surg Res. 2021;16:373.
41. van den Bekerom MP, Patt TW, Kleinhout MY, van der Vis HM, Albers GH. Early complications after high tibial osteotomy: a comparison of two techniques. J Knee Surg. 2008;21:68–74.
42. Kuremsky MA, Schaller TM, Hall CC, Roehr BA, Masonis JL. Comparison of autograft vs allograft in opening-wedge high tibial osteotomy. J Arthroplasty. 2010;25:951–7.
43. Ren YM, Duan YH, Sun YB, Yang T, Hou W-Y, Zhu R-S, et al. Opening-wedge high Tibial osteotomy using autograft versus allograft: a systematic review and meta-analysis. J Knee Surg. 2020;33:565–75.
44. Cho SW, Kim DH, Lee GC, Lee SH, Park SH. Comparison between autogenous bone graft and Allogenous cancellous bone graft in medial open wedge high Tibial osteotomy with 2-year follow-up. Knee Surg Relat Res. 2013; 25:117–25.
45. Raja IR, Abdul KM, Abdul RA, Hossain MG, Kamarul T. Finite element analysis of Puddu and Tomofix plate fixation for open wedge high tibial osteotomy. Injury. 2012;43:898–902.
46. Han JH, Kim HJ, Song JG, Yang JH, Nakamura R, Shah D, et al. Locking plate versus non-locking plate in open-wedge high tibial osteotomy: a meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2017;25:808–16.
47. Xu KS, Zhang Y, Shen YL, et al. Postoperative blood loss and joint function after high tibial osteotomy with or without drainage tube. Chin J Bone Joint Injury. 2020;35:581–4.
48. Li S, Yang J, Watson C, Lu Q, Zhang M, Miao Z, et al. Drainage relieves pain without increasing post-operative blood loss in high tibial osteotomy: a prospective randomized controlled study. Int Orthop. 2020;44:1037–43.
49. Jung WH, Takeuchi R, Chun CW, Lee J-S, Ha J-H, Kim J-H, et al. Efficacy of periarticular multimodal drug injection after medial opening-wedge high tibial osteotomy: a randomized, controlled study. Art Ther. 2014;30:1261–8.
50. Ren YM, Tian MQ, Duan YH, Sun Y-B, Yang T, Hou W-Y, et al. Was femoral nerve block effective for pain control of medial opening-wedge high tibial osteotomy?: A single blinded randomized controlled study. Medicine (Baltimore). 2021;100:e23978.
51. Sim JA, Lee MG, Jung WS, Lee BK, Lee BH. Clinical efficacy of adductor canal block in medial open wedge high tibial osteotomy. Knee. 2021;26:9–14.
52. Lee DC, Byun SJ. High tibial osteotomy. Knee Surg Relat Res. 2012;24: 61–9.
53. Coventry MB, Ilstrup DM, Wallrichs SL. Proximal tibial osteotomy. A critical long-term study of eighty-seven cases. J Bone Joint Surg Am. 1993;75:196–201.
54. Sun XD, Wang J, Su Z. A meta-analysis of total knee arthroplasty following high tibial osteotomy versus primary total knee arthroplasty. Arch Orthop Trauma Surg. 2020;140:527–35.
55. Chen X, Yang Z, Li H, Zhu S, Wang Y, Qian W. Higher risk of revision in total knee arthroplasty after high tibial osteotomy: a systematic review and updated meta-analysis. BMC Musculoskelet Disord. 2020;21:153.
56. Lansdaal JR, Mouton T, Wascher DC, Demey G, Lustig S, Neyret P, et al. Early weight bearing versus delayed weight bearing in medial opening wedge high tibial osteotomy: a randomized controlled trial. Knee Surg Sports Traumatol Arthrosc. 2017;25:3670–8.
57. Takeuchi R, Aratake M, Bito H, Saito I, Kumagai K, Ishikawa H, et al. Simultaneous bilateral opening-wedge high tibial osteotomy with early full weight-bearing exercise. Knee Surg Sports Traumatol Arthrosc. 2008;16:1030–7.
58. Lee OS, Ahn S, Lee YS. Effect and safety of early weight-bearing on the outcome after open-wedge high tibial osteotomy: a systematic review and meta-analysis. Arch Orthop Trauma Surg. 2017;137:903–11.
59. Kawata M, Jo T, Taketomi S, Inui H, Yamagami R, Matsui H, et al. Type of bone graft and primary diagnosis were associated with nosocomial surgical site infection after high tibial osteotomy: analysis of a national database. Knee Surg Sports Traumatol Arthrosc. 2021;29:429–36.
60. Anagnostakos K, Mosser P, Kohn D. Infections after high tibial osteotomy. Knee Surg Sports Traumatol Arthrosc. 2013;21:161–9.
61. Liu TW, Chiu CH, Chen AC, Chang SS, Chan YS. Risk factor analysis for infection after medial open wedge high Tibial osteotomy. J Clin Med. 2021; 10:1767.
62. Niemeyer P, Stöhr A, Köhne M, Hochrein A. Medial opening wedge high tibial osteotomy. Oper Orthop Traumatol. 2017;29:294–305.
63. Kim KI, Seo MC, Song SJ, Bae DK, Kim DH, Lee SH. Change of chondral lesions and predictive factors after medial open-wedge high Tibial osteotomy with a locked plate system. Am J Sports Med. 2017;45:1615–21.
64. Koshino T, Wada S, Ara Y, Saito T. Regeneration of degenerated articular cartilage after high tibial valgus osteotomy for medial compartmental osteoarthritis of the knee. Knee. 2003;10:229–36.
65. Kim CW, Seo SS, Lee CR, Gwak HC, Kim JH, Jung SG. Factors affecting articular cartilage repair after open-wedge high tibial osteotomy. Knee. 2017;24: 1099–107.
66. Bai YM, Zhang HS, Liu C, Jin S, Su K, Liu Y, et al. Change of inflammatory cytokines levels in both synovial fluid and plasm of patients with primary knee medical osteoarthritis after high tibial osteotomy. Chin J Reparative Reconstr Surg. 2017;31:422–6.
67. Rutgers M, Saris DB, Yang KG, Dhert WJ, Creemers LB. Joint injury and osteoarthritis: soluble mediators in the course and treatment of cartilage pathology. Immunotherapy. 2009;1:435–45.
68. Kwak YH, Kwak DK, Kim NY, Kim YJ, Lim JS, Yoo JH. Significant changes in synovial fluid microRNAs after high tibial osteotomy in medial compartmental knee osteoarthritis: identification of potential prognostic biomarkers. PLoS One. 2020;15:e227596.
69. Huang JM, Yang JY, Wu J, Chen X, Zhao Q, Ren F, et al. Short-term clinical outcomes and second-look arthroscopic findings of high tibial osteotomy combined with medial meniscus posterior root repair. Chin J Orthop. 2019;39: 675–82.
70. Huang JM, Zhang Z, Hu WJ, Wu J, Chen X, Zhao Q. Tibial osteotomy combined with arthroscopic condylar notch plasty to treat flexion deformity of knee varus osteoarthritis. Chin J Orthop. 2017;37:848–55.
71. Yoo MJ, Shin YE. Open wedge high Tibial osteotomy and combined arthroscopic surgery in severe medial osteoarthritis and Varus malalignment: minimum 5-year results. Knee Surg Relat Res. 2016;28:270–6.
72. Kim CW, Lee CR, Seo SS, Gwak HC, Kim JH, Jeong JW. Clinical efficacy of an arthroscopic surgery in open wedge high Tibial osteotomy. J Knee Surg. 2017;30: 352–8.
73. Wang H, Wang CX, Wang J, et al. Early rehabilitation based on ERAS concept for patients with medial compartment knee osteoarthritis after high tibial osteotomy. Chin J Clin. 2021;34:937–41.
74. Yu RX, Lu H, Han RJ, Li S, Yang QQ. Effect of nursing interventions based on enhanced recovery after surgery on postoperative pain and functional rehabilitation of patients undergoing arthroscopic anterior cruciate ligament reconstruction and high tibial osteotomy. Nursing of Integr Tradit Chin Western Med. 2019;5:21–5.

75. Committee Of Musculoskeletal Rehabilitation Technology Transformation Of China Association Of Rehabilitation Technology Transformation And Promotion, Joint Diseases Prevention And Treatment Branch Of China International Exchange And Promotion Association For Medical And Healthcare, Joint Surgery Committee Of Chinese Research Hospital Association. Guidelines for diagnosis and treatment of anemia during perioperative period of orthopedic surgery in China. Chin J Bone Joint Surg. 2019;12:833–40.
76. Chinese Orthopaedic Association. Guidelines for prevention of venous thromboembolism in major orthopedic surgery in China. Chin J Orthop. 2016;36:65–71.
77. Goshima K, Sawaguchi T, Shigemoto K, Iwai S, Fujita K, Kataoka T, et al. Factors associated with patient satisfaction after opening-wedge high Tibial osteotomy. Orthop J Sports Med. 2020;8:1812015388.
78. Lee OS, Lee SH, Mok SJ, Lee YS. Comparison of the regeneration of cartilage and the clinical outcomes after the open wedge high tibial osteotomy with or without microfracture: a retrospective case control study. BMC Musculoskelet Disord. 2019;20:267.
79. He M, Zhong X, Li Z, Shen K, Zeng W. Progress in the treatment of knee osteoarthritis with high tibial osteotomy: a systematic review. Syst Rev. 2021; 10:56.
80. Diermeier T, Imhoff AB, Beitzel K. Flexion and extension osteotomy of the knee. Oper Orthop Traumatol. 2017;29:330–8.
81. Wade R, Shah S, Sujith BS, Shah K, Raj A, Marathe N. High tibial osteotomy in a lax knee: a review of current concepts. J Orthop. 2020;19:67–71.
82. Shea BJ, Hamel C, Wells GA, Bouter LM, Kristjansson E, Grimshaw J, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. J Clin Epidemiol. 2009;62:1013–20.
83. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
84. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25:603–5.
85. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ. 2004;328:1490.
86. Atkins D, Eccles M, Flottorp S, Guyatt GH, Henry D, Hill S, et al. Systems for grading the quality of evidence and the strength of recommendations I: critical appraisal of existing approaches the GRADE working group. BMC Health Serv Res. 2004;4:38.