

Medical Policy



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Title: Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions

Related Policies:	<ul style="list-style-type: none"> ▪ <i>Meniscal Allografts and Other Meniscal Implants</i> ▪ <i>Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions</i>
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Populations	Interventions	Comparators	Outcomes
Individuals: • With full-thickness articular cartilage lesions of the knee	Interventions of interest are: • Osteochondral autograft	Comparators of interest are: • Marrow stimulation • Autologous chondrocyte implantation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals:	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include:

Populations	Interventions	Comparators	Outcomes
<ul style="list-style-type: none"> • With full-thickness articular cartilage lesions of the knee when autografting would be inadequate 	<ul style="list-style-type: none"> • Fresh osteochondral allograft 	<ul style="list-style-type: none"> • Osteochondral autograft 	<ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
<p>Individuals:</p> <ul style="list-style-type: none"> • With primary full-thickness articular cartilage lesions of the ankle <1.5 cm² 	<p>Interventions of interest are:</p> <ul style="list-style-type: none"> • Osteochondral autograft 	<p>Comparators of interest are:</p> <ul style="list-style-type: none"> • Marrow stimulation 	<p>Relevant outcomes include:</p> <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
<p>Individuals:</p> <ul style="list-style-type: none"> • With large (>1.5 cm²) or cystic (>3.0 cm³) full-thickness articular cartilage lesions of the ankle 	<p>Interventions of interest are:</p> <ul style="list-style-type: none"> • Osteochondral autograft 	<p>Comparators of interest are:</p> <ul style="list-style-type: none"> • Marrow stimulation 	<p>Relevant outcomes include:</p> <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
<p>Individuals:</p> <ul style="list-style-type: none"> • With osteochondral lesions of the ankle that have failed primary treatment 	<p>Interventions of interest are:</p> <ul style="list-style-type: none"> • Osteochondral autograft 	<p>Comparators of interest are:</p> <ul style="list-style-type: none"> • Marrow stimulation 	<p>Relevant outcomes include:</p> <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
<p>Individuals:</p> <ul style="list-style-type: none"> • With primary full-thickness articular cartilage lesions of the ankle <1.5 cm² 	<p>Interventions of interest are:</p> <ul style="list-style-type: none"> • Fresh osteochondral allograft 	<p>Comparators of interest are:</p> <ul style="list-style-type: none"> • Marrow stimulation 	<p>Relevant outcomes include:</p> <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
<p>Individuals:</p> <ul style="list-style-type: none"> • With large (>1.5 cm²) or cystic (>3.0 cm³) cartilage lesions of the ankle when autografting would be inadequate 	<p>Interventions of interest are:</p> <ul style="list-style-type: none"> • Fresh osteochondral allograft 	<p>Comparators of interest are:</p> <ul style="list-style-type: none"> • Osteochondral autograft 	<p>Relevant outcomes include:</p> <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
<p>Individuals:</p> <ul style="list-style-type: none"> • With revision osteochondral lesions of the ankle when autografting would be inadequate 	<p>Interventions of interest are:</p> <ul style="list-style-type: none"> • Fresh osteochondral allograft 	<p>Comparators of interest are:</p> <ul style="list-style-type: none"> • Osteochondral autograft 	<p>Relevant outcomes include:</p> <ul style="list-style-type: none"> • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
<p>Individuals:</p> <ul style="list-style-type: none"> • With full-thickness articular cartilage lesions of the elbow 	<p>Interventions of interest are:</p>	<p>Comparators of interest are:</p> <ul style="list-style-type: none"> • Marrow stimulation 	<p>Relevant outcomes include:</p> <ul style="list-style-type: none"> • Symptoms • Functional outcomes

Populations	Interventions	Comparators	Outcomes
	<ul style="list-style-type: none"> Fresh osteochondral autograft 		<ul style="list-style-type: none"> Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With full-thickness articular cartilage lesions of the shoulder 	Interventions of interest are: <ul style="list-style-type: none"> Osteochondral autograft 	Comparators of interest are: <ul style="list-style-type: none"> Marrow stimulation 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Functional outcomes Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder 	Interventions of interest are: <ul style="list-style-type: none"> Autologous or allogeneic minced or particulated articular cartilage 	Comparators of interest are: <ul style="list-style-type: none"> Marrow stimulation Autologous chondrocyte implantation 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Functional outcomes Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder 	Interventions of interest are: <ul style="list-style-type: none"> Decellularized osteochondral allograft plugs 	Comparators of interest are: <ul style="list-style-type: none"> Marrow stimulation 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Functional outcomes Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder 	Interventions of interest are: <ul style="list-style-type: none"> Reduced osteochondral allograft discs 	Comparators of interest are: <ul style="list-style-type: none"> Marrow stimulation 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Functional outcomes Quality of life Treatment-related morbidity

DESCRIPTION

Osteochondral grafts are used to repair full-thickness chondral defects involving a joint. In the case of osteochondral autografts, 1 or more small osteochondral plugs are harvested from non-weight-bearing sites, usually from the knee, and press fit into a prepared site in the lesion. Osteochondral allografts are typically used for larger lesions. Autologous or allogeneic minced cartilage, decellularized osteochondral allograft plugs, and reduced osteochondral allograft discs are also being evaluated as a treatment of articular cartilage lesions.

OBJECTIVE

The objective of this evidence review is to determine whether the use of osteochondral autografts and allografts improves the net health outcome for individuals who have focal articular cartilage lesions of the knee, ankle, elbow, or shoulder.

BACKGROUND

Articular Cartilage Lesions

Damaged articular cartilage can be associated with pain, loss of function, and disability, and can lead to debilitating osteoarthritis over time. These manifestations can severely impair an individual's activities of daily living and quality of life. The vast majority of osteochondral lesions occur in the knee with the talar dome and capitulum being the next most frequent sites. The most common locations of lesions are the medial femoral condyle (69%), followed by the weight-bearing portion of the lateral femoral condyle (15%), the patella (5%), and trochlear fossa.¹ Talar lesions are reported to be about 4% of osteochondral lesions.²

Treatment

There are 2 main goals of conventional therapy for patients who have significant focal defects of the articular cartilage: symptom relief and articular surface restoration.

First, there are procedures intended primarily to achieve symptomatic relief: debridement (removal of debris and diseased cartilage) and rehabilitation. Second, there are procedures intended to restore the articular surface. Treatments may be targeted to the focal cartilage lesion, and most such treatments induce local bleeding, fibrin clot formation, and resultant fibrocartilage growth. These marrow stimulation procedures include microfracture, abrasion arthroplasty, and drilling, all of which are considered standard therapies.

Microfracture

Microfracture is an arthroscopic procedure in which a small pick creates a network of holes at the base of the articular cartilage lesion, allowing blood into the injured area to form clots and subsequent fibrocartilage growth. Mithoefer et al (2009) examined the efficacy of the microfracture technique for articular cartilage lesions of the knee in a systematic review.³ Twenty-eight studies (N=3122 patients) were selected; 6 studies were randomized controlled trials. Microfracture was found to improve knee function in all studies during the first 24 months after the procedure but the reports on durability were conflicting. Solheim et al (2016) reported on a prospective longitudinal study of 110 patients and found that, at a mean of 12 years (range, 10-14) after microfracture, 45.5% of patients had poor outcomes, including 43 patients who required additional surgery.⁴ The size of the lesion has also been shown to affect outcomes following marrow stimulation procedures.

Abrasion and Drilling

Abrasion and drilling are techniques to remove damaged cartilage. Instead of a drill, high-speed burrs are used in the abrasion procedure.

Fibrocartilage is generally considered to be less durable and mechanically inferior to the original articular cartilage. Thus, various strategies for chondral resurfacing with hyaline cartilage have been investigated. Alternatively, treatments of very extensive and severe cartilage defects may resort to complete replacement of the articular surface either by osteochondral allotransplant or artificial knee replacement.

Osteochondral Grafting

Autologous or allogeneic grafts of osteochondral or chondral tissue have been proposed as treatment alternatives for patients who have clinically significant, symptomatic, focal defects of the articular cartilage. It is hypothesized that the implanted graft's chondrocytes retain features

of hyaline cartilage that are similar in composition and property to the original articulating surface of the joint. If true, the restoration of a hyaline cartilage surface might restore the integrity of the joint surface and promote long-term tissue repair, thereby improving function and delaying or preventing further deterioration.

Both fresh and cryopreserved allogeneic osteochondral grafts have been used with some success. However, cryopreservation decreases the viability of cartilage cells, and fresh allografts may be difficult to obtain and create concerns regarding infectious diseases. As a result, autologous osteochondral grafts have been investigated as an option to increase the survival rate of the grafted cartilage and to eliminate the risk of disease transmission. Autologous grafts are limited by the small number of donor sites; thus, allografts are typically used for larger lesions. In an effort to extend the amount of the available donor tissue, investigators have used multiple, small osteochondral cores harvested from non-weight-bearing sites in the knee for treatment of full-thickness chondral defects. Several systems are available for performing this procedure: the Mosaicplasty System (Smith & Nephew), the OATS (Osteochondral Autograft Transfer System; Arthrex), and the COR and COR2 systems (DePuy Mitek). Although mosaicplasty and autologous osteochondral transplantation may use different instrumentation, the underlying mode of repair is similar (ie, use of multiple osteochondral cores harvested from a non-weight-bearing region of the femoral condyle and autografted into the chondral defect). These terms have been used interchangeably to describe the procedure.

Preparation of the chondral lesion involves debridement and preparation of recipient tunnels. Multiple individual osteochondral cores are harvested from the donor site, typically from a peripheral non-weight-bearing area of the femoral condyle. Donor plugs range from 6 to 10 mm in diameter. The grafts are press fit into the lesion in a mosaic-like fashion into the same-sized tunnels. The resultant surface consists of transplanted hyaline articular cartilage and fibrocartilage, which is thought to provide "grouting" between the individual autografts. Mosaicplasty or autologous osteochondral transplantation may be performed with either an open approach or arthroscopically. Osteochondral autografting has also been investigated as a treatment of unstable osteochondritis dissecans lesions using multiple dowel grafts to secure the fragment. While osteochondral autografting is primarily performed on the femoral condyles of the knee, osteochondral grafts have been used to repair chondral defects of the patella, tibia, and ankle. With osteochondral autografting, the harvesting and transplantation can be performed during the same surgical procedure. Technical limitations of osteochondral autografting are difficulty in restoring concave or convex articular surfaces, the incongruity of articular surfaces that can alter joint contact pressures, short-term fixation strength and load-bearing capacity, donor-site morbidity, and lack of peripheral integration with peripheral chondrocyte death.

Reddy et al (2007) evaluated donor-site morbidity in 11 of 15 patients who had undergone graft harvest from the knee (mean, 2.9 plugs) for treatment of osteochondral lesions of the talus.⁵ At an average 47-month follow-up (range, 7-77), 5 patients were rated as having an excellent Lysholm Knee Scale score (95-100 points), 2 as good (84-94 points), and 4 as poor (≤ 64 points). The reported knee problems were instability in daily activities, pain after walking 1 mile or more, slight limp, and difficulty squatting. Hangody et al (2001) reported that some patients had slight or moderate complaints with physical activity during the first postoperative year but there was no long-term donor-site pain in a series of 36 patients evaluated 2 to 7 years after autologous osteochondral transplantation.⁶

Filling defects with minced or particulated articular cartilage (autologous or allogeneic) is another single-stage procedure being investigated for cartilage repair. The Cartilage Autograft Implantation System (Johnson & Johnson) harvests cartilage and disperses chondrocytes on a scaffold in a single-stage treatment. The Reveille® Cartilage Processor (Exactech Biologics) has a high-speed blade and sieve to cut autologous cartilage into small particles for implantation. BioCartilage® (Arthrex) consists of a micronized allogeneic cartilage matrix that is intended to provide a scaffold for microfracture. DeNovo NT® Graft (Natural Tissue Graft) is produced by ISTO Technologies and distributed by Zimmer. DeNovo NT consists of manually minced cartilage tissue pieces obtained from juvenile allograft donor joints. The tissue fragments are mixed intraoperatively with fibrin glue before implantation in the prepared lesion. It is thought that mincing the tissue helps both with cell migration from the extracellular matrix and with fixation.

A minimally processed osteochondral allograft (Chondrofix®; Zimmer) is now available. Chondrofix is composed of decellularized hyaline cartilage and cancellous bone; it can be used “off the shelf” with precut cylinders (7-15 mm). Multiple cylinders may be used to fill a larger defect in a manner similar to autologous osteochondral transplantation or mosaicplasty.

ProChondrix® (AlloSource) and Cartiform® (Arthrex) are wafer-thin allografts where the bony portion of the allograft is reduced. The discs are laser etched or porated and contain hyaline cartilage with chondrocytes, growth factors, and extracellular matrix proteins. ProChondrix is available in dimensions from 7 to 20 mm and is stored fresh for a maximum of 28 days. Cartiform is cut to the desired size and shape and is stored frozen for a maximum of 2 years. The osteochondral discs are typically inserted after microfracture and secured in place with fibrin glue and/or sutures.

Autologous chondrocyte implantation is another method of cartilage repair involving the harvesting of normal chondrocytes from normal non-weight-bearing articular surfaces, which are then cultured and expanded in vitro and implanted back into the chondral defect.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, title 21, parts 1270 and 1271. Osteochondral grafts are included in these regulations.

DeNovo® ET Live Chondral Engineered Tissue Graft (Neocartilage) is marketed by ISTO Technologies outside of the United States. The FDA approved ISTO’s investigational new drug application for Neocartilage in 2006, which allowed ISTO to pursue phase 3 clinical trials of the product in human subjects. However, ISTO’s clinical trial for Neocartilage was terminated due to poor enrollment as of August 31, 2017.

POLICY

- A. Fresh osteochondral allografting may be considered **medically necessary** as a technique to repair:
1. Full-thickness chondral defects of the knee caused by acute or repetitive trauma when other cartilage repair techniques (e.g., microfracture, osteochondral autografting or autologous chondrocyte implantation) would be inadequate due to the size, location, or depth of the lesion, **OR**
 2. Large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesions of the talus when autografting would be inadequate due to lesion size, depth, or location, **OR**
 3. Revision surgery after failed prior marrow stimulation for large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesions of the talus when autografting would be inadequate due to lesion size, depth, or location.
- B. Osteochondral allografting for all other joints is considered **experimental / investigational**.
- C. Osteochondral autografting, using 1 or more cores of osteochondral tissue, may be considered **medically necessary**:
1. For the treatment of symptomatic full-thickness cartilage defects of the knee caused by acute or repetitive trauma in individuals who have had an inadequate response to a prior surgical procedure, when **ALL** of the following have been met:
 - a. Adolescent individuals should be skeletally mature with documented closure of growth plates. Adult individuals should be too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (e.g., 55 years or younger), **AND**
 - b. Focal, full-thickness (grade III or IV) unipolar lesions on the weight-bearing surface of the femoral condyles, trochlea, or patella that are between 1 and 2.5 cm² in size, **AND**
 - c. Documented minimal to absent degenerative changes in the surrounding articular cartilage (Outerbridge Grade II or less), and normal-appearing hyaline cartilage surrounding the border of the defect, **AND**
 - d. Normal knee biomechanics, or alignment and stability achieved concurrently with osteochondral grafting.
- OR**
2. Large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesions of the talus, **OR**

3. Revision surgery after failed marrow stimulation for osteochondral lesion of the talus.
- D. Osteochondral autografting for all other joints and any indications other than those listed above is considered **experimental / investigational**.
- E. Treatment of focal articular cartilage lesions with autologous minced or particulated cartilage is considered **experimental / investigational**.
- F. Treatment of focal articular cartilage lesions with micronized, minced, or particulated allogeneic cartilage is considered **experimental / investigational**.
- G. Treatment of focal articular cartilage lesions with decellularized osteochondral allograft plugs (e.g., Chondrofix) is considered **experimental / investigational**.
- H. Treatment of focal articular cartilage lesions with reduced osteochondral allograft discs (e.g., ProChondrix, Cartiform) is considered **experimental / investigational**.

POLICY GUIDELINES

- A. If debridement is the only prior surgical treatment, consideration should be given to marrow-stimulating techniques before osteochondral grafting is performed, particularly for lesions less than 1.5 cm² in area or 3.0 cm³ in volume.
- B. Severe obesity (e.g., body mass index greater than 35 kg/m²) may affect outcomes due to the increased stress on weight-bearing surfaces of the joint.
- C. Malalignment and instability of the joint are contraindications. Therefore, additional procedures, such as repair of ligaments or tendons or creation of an osteotomy for realignment of the joint, may be performed at the same time. In addition, meniscal allograft transplantation may be performed in combination, either concurrently or sequentially, with osteochondral allografting or osteochondral autografting.

Outerbridge cartilage grading scale	
Grade I:	softening and swelling of the cartilage
Grade II:	shows fragmentation and fissuring of the superficial cartilage of less than one-half in diameter
Grade III:	fragmentation and deeper fissuring of more than one-half inch
Grade IV:	shows erosion of the cartilage down to the bone

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review was created with searches of the PubMed database. The most recent literature update was performed through February 27, 2023.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

OSTEOCHONDRAL AUTOGRAFT FOR ARTICULAR CARTILAGE LESIONS OF THE KNEE

Clinical Context and Therapy Purpose

The purpose of osteochondral autograft, or autologous osteochondral transplantation, in individuals with full-thickness focal articular cartilage lesions of the knee is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with full-thickness articular cartilage lesions of the knee.

Interventions

The therapy being considered is autologous osteochondral transplantation. The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from another area. It is hypothesized that the implanted graft's chondrocytes retain features of hyaline cartilage that are similar in composition and property to the original articulating surface of the joint, thereby restoring the hyaline cartilage surface.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. Symptom improvements in the knee can be detected using the Lysholm Knee Scale, which consists of 8 items: pain, instability, locking, swelling, limp, stair climbing, squatting, and need for support.

For long-term outcomes, 5- to 15-year follow-up is recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

Zamborsky et al (2020) completed a systematic review and network meta-analysis that evaluated the most appropriate surgical interventions for patients with knee articular cartilage defects.⁷ The authors included a total of 21 articles (from 12 RCTs) in their analysis with a total population of 891 patients. Follow-up varied widely among the included studies, ranging from 12 months to 15 years. Of the surgical interventions evaluated, microfracture was associated with significantly higher failure rates compared to autologous chondrocyte implantation at 10 years of follow-up (relative risk [RR], 0.12; 95% confidence interval [CI]; 0.04 to 0.39). No significant differences in failure rates were seen between microfracture and osteochondral autograft transplantation, matrix-induced autologous chondrocyte implantation, or characterized chondrocyte implantation at 2, 5, and 10 years of follow-up. Osteochondral autograft transplantation was associated with significantly more excellent or good results at >3 years of follow-up as compared to microfracture, whereas microfracture was associated with significantly poorer results as compared to autologous chondrocyte implantation and matrix-induced autologous chondrocyte

implantation. No significant differences between the interventions were noted regarding reintervention, biopsy types, or adverse events. Based on efficacy and safety, autologous chondrocyte implantation was ranked as the best intervention for failure outcome at 10 years of follow-up, followed by osteochondral autograft transplantation, then microfracture. Microfracture was consistently ranked worse than cartilage repair techniques for other outcomes including quality of tissue repair and return-to-activity rates.

Gracitelli et al (2016) wrote a Cochrane review evaluating surgical interventions (microfracture, drilling, autologous osteochondral transplantation, allograft transplantation) for the treatment of isolated cartilage defects of the knee in adults.⁸ Three RCTs compared autologous osteochondral transplantation with microfracture for isolated cartilage defects. The evidence was considered of very low quality with high or unclear risk of bias.

Magnussen et al (2008) showed in their systematic review that, in the short term, neither of the “advanced” cartilage repair techniques (osteochondral transplantation or autologous chondrocyte transplantation) showed superior outcomes compared with traditional abrasive techniques.⁹ Based on evidence from 5 RCTs and a prospective comparative trial, reviewers concluded that no single technique produced superior clinical results for treatment of articular cartilage defects; however, “any differences in outcome based on the formation of articular rather than fibrocartilage in the defect may be quite subtle and only reveal themselves after many years of follow-up. Similarly, complications such as donor-site morbidity in autologous osteochondral transplantation may be late in their presentation and thus not be detected at short follow-up.”

However, Pareek et al (2016) found, in a mid-term meta-analysis that included 5 RCTs, that Tegner Activity Scale scores were higher, and failure rates lower, with autologous osteochondral transplantation than with microfracture.¹⁰ In a subgroup analysis, activity scores were higher in the subset of patients treated with autologous osteochondral transplantation who had lesions greater than 3 cm² at mid-term follow-up.

Harris et al (2011) evaluated in a systematic review whether outcomes from cartilage repair or restoration techniques remained successful if combined with meniscal allograft.¹¹ Six level IV studies (case series) with 110 patients were included in the review. Patients underwent meniscal allograft transplantation with autologous chondrocyte implantation (n=73), osteochondral allograft (n=20), autologous osteochondral transplantation (n=17), or microfracture (n=3). All studies showed improved clinical outcomes at final follow-up compared with the preoperative condition. Outcomes were also compared with historical outcomes of each procedure performed in isolation. Four of the 6 studies found outcomes equivalent to procedures performed in isolation, suggesting that the combined procedures did not result in poorer outcomes.

Observational Studies

While observational studies do not provide evidence of efficacy or comparative efficacy, these studies may provide information about the durability of any observed improvements and potential impact of patient selection factors. Observational studies have reported longer-term outcomes and the impact of sex, age, and size and location of the lesion.

Hangody et al (2008), who first reported the use of the mosaicplasty technique in humans in 1992, has co-authored a number of summaries and case series.^{12,13,14} Hangody et al (2008),

based on their experience with this procedure, considered the optimal indications to be lesions 1 to 4 cm² in diameter; patients 50 years of age or younger (due to decreased repair capacity with aging); and correction of instability, malalignment, and meniscal or ligament tears.¹⁴ Solheim et al (2010, 2013) reported 5- to 9-year (N=69) and 10- to 14-year (N=73) follow-up from patients treated for articular cartilage defects 1 to 5 cm² in area.^{15,16} The Lysholm Knee Scale scores and visual analog scale (VAS) scores for pain improved at mid-term and long-term follow-up. However, a poor outcome, defined as a Lysholm Knee Scale score of 64 or less or subsequent knee replacement, was observed in 40% of the patients by 10 to 14 years. Factors associated with a poor outcome in this series were patient age (≥ 40 years at the time of surgery), female sex, and articular cartilage defects of 3 cm² or more.

The importance of concomitant realignment procedures is addressed by other studies. Marcacci et al (2007) described a 7-year follow-up for 30 patients treated with autologous osteochondral transplantation for symptomatic grade III to IV chondral lesions (average, 1.9 cm; range, 1.0-2.5 cm).¹⁷ Nineteen patients received other procedures (anterior cruciate ligament reconstruction, meniscectomy, medial collateral ligament repair) at the same time. Magnetic resonance imaging (MRI) at 7 years showed complete bone integration in 96% of patients, complete integration of the grafted cartilage in 75% of cases, complete filling of the cartilage defect in 63%, and congruency of the articular surface in "some" patients.

Other publications have reported on improved outcomes following autologous osteochondral transplantation for patellar lesions. Astur et al (2014), for example, conducted a prospective study analyzing 33 patients with symptomatic patellar lesions (diameter, 1-2.5 cm) treated with autologous osteochondral transplantation.¹⁸ At a minimum 2-year follow-up (range, 24-54 months), all patients were reported to have significant improvements in functional scores, as measured by the Lysholm Knee Scale, Kujala, and Fulkerson scores and the 36-Item Short-Form (SF-36) Health Survey quality of life score. In a series of 22 patients (mean lesion size, 1.6 cm²), Nho et al (2008) reported that both the International Knee Documentation Committee Subjective Knee Evaluation Form and the activity of daily living scores increased significantly from preoperatively to 29-month follow-up following patellar resurfacing.¹⁹

Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Knee

Several systematic reviews of RCTs have evaluated autologous osteochondral transplantation for cartilage repair of the knee in the short- and mid-term. The RCTs are not high quality, and not all reviews found a benefit compared with abrasion techniques. However, compared with abrasion techniques (eg, microfracture, drilling), there is evidence that autologous osteochondral transplantation decreases failure rates and improves outcomes in patients with medium-size lesions (eg, 2-6 cm²) when measured at longer follow-up. This is believed to be due to the improved durability of the natural hyaline cartilage compared with the fibrocartilage that is obtained with abrasion techniques. Factors shown to affect success in observational studies are male sex, younger age, and lesions smaller than 3 cm². Thus, there is a relatively narrow range of lesion size for which autologous osteochondral transplantation is most effective. In addition, the best results have been observed with lesions on the femoral condyles, although treatment of trochlea and patella lesions also improves outcomes. Correction of malalignment is important for the success of the procedure.

FRESH OSTEOCHONDRAL ALLOGRAFT FOR ARTICULAR CARTILAGE LESIONS OF THE KNEE

Clinical Context and Therapy Purpose

The purpose of fresh osteochondral allografts in individuals with full-thickness focal articular cartilage lesions of the knee is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with full-thickness articular cartilage lesions of the knee.

Interventions

The therapy being considered is fresh osteochondral allograft. The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from a donor.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. Symptom improvements in the knee can be detected using the Lysholm Knee Scale, which consists of 8 items: pain, instability, locking, swelling, limp, stair climbing, squatting, and need for support.

For long-term outcomes, 5- to 15-year follow-up is recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

A systematic review by Kunze et al (2022) focused solely on potential risk factors for failure after osteochondral allograft transplantation of the knee.²⁰ They included 16 studies consisting of 1401 patients who received an allograft transplant. The pooled prevalence of overall failure was 18.9%. Of the risk factors identified, bipolar chondral defects (odds ratio [OR], 4.20; 95% CI,

1.17 to 15.08; $p=.028$) and male sex (OR, 2.04; 95% CI, 1.17 to 3.55; $p=.012$) were significant risk factors for failure after allograft transplant. Older age (mean difference [MD], 5.06 years; 95% CI, 1.44 to 8.70; $p=.006$) and greater body mass index (MD, 1.75 kg/m²; 95% CI, 0.48 to 3.03; $p=.007$) at the time of surgery were also significant risk failures for failure. There was no statistical significance to support that concomitant procedures, lesion size, or lesion location were associated with an increased risk of failure.

Merkely et al (2021) conducted a systematic review of clinical outcomes after osteochondral allograft transplantation for large chondral defects of the knees.²¹ Their review compared patients receiving a primary allograft transplant ($n=13$) and those receiving allograft transplant as a revision after a failed autologous implant ($n=13$). All patients demonstrated significant improvement in all functional scores after allograft transplant, and there were no significant differences between groups. Authors concluded that revision of prior failed autologous implant with allograft transplant is a viable treatment option with similar clinical outcomes as primary allograft transplant.

Gracitelli et al (2016) published a Cochrane review on surgical interventions (microfracture, drilling, mosaicplasty, and allograft transplantation) for treating cartilage defects of the knees and did not identify any RCTs on fresh allograft transplantation.⁸

De Caro et al (2015) included in their systematic review, 11 articles that had at least 10 patients and were published in the previous 5 years.²² Articles included a total of 374 knees in 358 patients treated with fresh osteochondral allografting. The size of the lesions ranged from 1 to 27 cm². Different outcome measures were used but overall results showed improvement in objective and subjective clinical scores, a high rate of return to some level of sport or active duty, and graft survival rates of 82% at 10 years and 66% at 20 years. Although bony integration was usually achieved, cartilage integration was limited.

Chui et al (2015) stated in their review of indications, techniques, and outcomes that fresh osteochondral allografting would be indicated for lesions greater than 2 cm² for which other techniques such as microfracture, autologous osteochondral transplantation, and autologous chondrocyte implantation are inadequate due to lesion size, location, or depth.²³ Reviewers also considered fresh osteochondral allografting to be a salvage procedure for previously failed restoration treatments of the knee.

Observational Studies

Nielsen et al (2017) identified 149 knees in 142 patients who had participated in a sport or recreational activity before a cartilage injury.²⁴ Following treatment with 1 or more osteochondral allografts (mean size, 8.2 cm²), 112 (75.2%) patients had returned to the sport. Allograft survival was 91% at 5 years and 89% at 10 years; 14 knees (9.4%) were considered failures.

Gracitelli et al (2015) reported on fresh osteochondral allografting for patellar cartilage injury.²⁵ Of 28 knees (27 patients) that had osteochondral transplantation, 8 (28.6%) were considered failures and 9 (45%) required further surgery. Allograft survival was estimated to be 78.1% at 10 years and 55.8% at 15 years. The mean follow-up duration was 9.7 years (range, 1.8-30.1) for the 20 (71.4%) knees with intact grafts.

Section Summary: Fresh Osteochondral Allograft for Articular Cartilage Lesions of the Knee

The evidence on fresh osteochondral allografts for articular cartilage lesions of the knee includes case series and systematic reviews of case series. Due to the lack of alternatives, this fresh allograft procedure may be considered as a salvage operation in younger patients for full-thickness chondral defects of the knee caused by acute or repetitive trauma when other cartilage repair techniques (eg, microfracture, autologous osteochondral transplantation, autologous chondrocyte implantation) would be inadequate due to lesion size, location, or depth.

OSTEOCHONDRAL AUTOGRAFT FOR ARTICULAR CARTILAGE LESIONS OF THE ANKLE LESS THAN 1.5 CM²

Clinical Context and Therapy Purpose

The purpose of autologous osteochondral transplantation in individuals with primary full-thickness focal articular cartilage lesions of the ankle <1.5 cm² is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with primary full-thickness focal articular cartilage lesions of the ankle <1.5 cm².

Interventions

The therapy being considered is autologous osteochondral transplantation. The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from another area.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. There are several symptom measurements for the ankle, such as the Foot and Ankle Ability Measures, in which the patient indicates the ability to perform various walking activities on a scale from "no difficulty" to "unable to do," as well as the American Orthopaedic Foot & Ankle Society Score, and the Foot and Ankle Outcome Score; quality of life can be measured using the Short-Form 12-item (SF-12) or SF-36.

Based on the available literature, follow-up should be 6 months or longer, but longer-term follow-up is recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Osteochondral lesions of the talus are typically associated with an ankle sprain or fracture but comprise a relatively small proportion of lesions (~4%) compared with cartilage lesions of the knee joint.² Therefore, RCTs on autologous osteochondral transplantation for talar lesions may be limited.

REVIEW OF EVIDENCE

Systematic Reviews

Feeney (2022) published a systematic review and meta-analysis that evaluated autologous osteochondral transplantation in the management of osteochondral lesions of the talus.²⁶ A total of 23 studies were included (Table 1), which were assessed to be of poor to average methodological quality using the modified Coleman Methodology Score. The characteristics of the systematic review are summarized in Table 2. The mean area of the lesion, as reported in 13 studies, was $135.5 \pm 45.85 \text{ mm}^2$ (range, 85-249). Across 13 studies, 51% of patients had undergone ankle surgery prior to autologous osteochondral transplantation. More than half of the studies reported preoperative and postoperative VAS scores and American Orthopaedic Foot and Ankle Society (AOFAS) scores. Study results are summarized in Table 3. Donor site pain occurred in 9% of cases. Notably, the systematic review did not limit inclusion of studies based on lesion size (ie, lesions $>1.5 \text{ cm}^2$ were also included) or whether autologous osteochondral transplantation was used as a primary or secondary procedure. Therefore, some of the included studies are also discussed in other sections of this review: Haleem et al (2014)²⁷, Yoon et al (2014)²⁸, Ahmad and Jones (2016)²⁹, Georgiannos et al (2016)³⁰, and Shimozone et al (2018).³¹ A main limitation of this systematic review is the poor methodologic quality of the included studies.

Zengerink et al (2010) published a systematic review on the treatment of osteochondral lesions of the talus.³² Fifty-one nonrandomized and 1 randomized trial (Gobbi et al [2006]³³) were included. Studies described a variety of lesion sizes, some cystic, some as primary treatment, and some after a failed arthroscopic procedure, with follow-up of at least 6 months. Characteristics and results of the systematic review are summarized in Tables 2 and 3. Because of the high cost of autologous chondrocyte implantation and the knee morbidity seen with autologous osteochondral transplantation, reviewers concluded that bone marrow stimulation is the treatment of choice for primary osteochondral talar lesions. However, the analysis was not conducted to assess the relation between lesion characteristics and success rates, limiting the interpretation of these results. Since Zengerink et al (2010) did not list each included study in their publication, these studies are not included in Table 1.

Table 1. Studies Included in Systematic Reviews

Study	Feeney (2022)^{26,}
Emre et al (2012) ^{34,}	●
Haleem et al (2014) ^{27,}	●
Petersen et al (2014) ^{35,}	●
Yoon et al (2014) ^{28,}	●
de L' Escalopier et al (2015) ^{36,}	●
Ahmad and Jones (2016) ^{29,}	●
Flynn et al (2016) ^{37,}	●
Fraser et al (2016) ^{38,}	●
Georgiannos et al (2016) ^{30,}	●
Guney et al (2016) ^{39,}	●
Li et al (2017) ^{40,}	●
Park et al (2018) ^{41,}	●
Shimozono et al (2018) ^{31,}	●
Adanas and Ozkan (2019) ^{42,}	●
Bai et al (2020) ^{43,}	●
Basal and Aslan (2020) ^{44,}	●
Kim and Haskell (2020) ^{45,}	●
Nguyen et al (2020) ^{46,}	●
Sabaghzadeh et al (2020) ^{47,}	●
Toker et al (2020) ^{48,}	●
de L' Escalopier et al (2021) ^{49,}	●
Wan et al (2022) ^{50,}	●
Zhang et al (2022) ^{51,}	●

Table 2. Characteristics of Systematic Reviews

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Feeney (2022) ²⁶ ,	2012-2022	23	Patients who underwent autologous osteochondral transplant; mean age 36.2±7.06 years (range 25.4-55.4); 66.1% male, 33.9% female	797 (NR)	Evidence level I-IV studies (prospective/retrospective cohorts or series, case controls, nonrandomized controlled trials)	Minimum follow-up period of 6 months; mean duration of follow-up, 47.7±32.68 months (range 12-143.5)
Zengerink et al (2010) ³² ,	1966-2006	52	Patients who underwent various treatments for osteochondral lesions of the talus; mean age 31 years (range 18-75); 63% male, 37% female	1361 (NR)	RCTs, quasi-experimental studies (including case series)	Minimum follow-up period of 6 months

NR: not reported; RCT: randomized controlled trial.

Table 3. Results of Systematic Reviews

Study	Aggregate Mean Preoperative VAS Score	Aggregate Mean Postoperative VAS Score	Reduction in VAS Score from Baseline	Aggregate Mean Preoperative AOFAS Score	Aggregate Mean Postoperative AOFAS Score	Reduction in AOFAS Score from Baseline	Average Success Rate (%)
Feeney (2022) ²⁶ ,							
No. of studies assessed	14		7	14		8	
No. of patients			210			224	
Autologous osteochondral	6.47±1.35	1.98±1.18		56.41±8.52	87.14±4.8		

Study	Aggregate Mean Preoperative VAS Score	Aggregate Mean Postoperative VAS Score	Reduction in VAS Score from Baseline	Aggregate Mean Preoperative AOFAS Score	Aggregate Mean Postoperative AOFAS Score	Reduction in AOFAS Score from Baseline	Average Success Rate (%)
transplantation							
MD			-4.22			29.70	
95% CI			-4.54 to -3.90			25.68 to 33.73	
p-value			<.0001			<.0001	
Zengerink et al (2010) ³² ,							
Bone marrow stimulation							85
Osteochondral autografting							87
Autologous chondrocyte implantation							76

AOFAS: American Orthopaedic Foot and Ankle Society; CI: confidence interval; MD: mean difference; VAS: visual analog scale.

Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Ankle Less Than 1.5 cm²

For the use of autologous osteochondral transplantation for repair of articular cartilage lesions of the ankle that are less than 1.5 cm² in area, a systematic review found similar improvements in outcomes following microfracture and autologous osteochondral transplantation. Another systematic review found that autologous osteochondral transplantation reduces pain and improves function in patients with osteochondral lesions of the talus, including lesions <1.5 cm² in area; most included studies performed autologous osteochondral transplantation as a secondary procedure. Given the success of marrow stimulation procedures for smaller lesions (<1.5 cm²) and the increase in donor-site morbidity with graft harvest from the knee, current evidence does not support the use of autologous osteochondral transplantation as a primary treatment for smaller ankle lesions.

Osteochondral Autograft for Larger Lesions or Lesions That Have Failed a Prior Procedure

The following sections review the evidence for lesions that have failed a prior arthroscopic procedure, and for larger lesions, defined as at least 1.5 cm² in size. This size threshold is derived from studies that have determined that bone marrow stimulation procedures for articular cartilage lesions of the talus that are at least 1.5 cm² in area have lower success rates than for those for smaller lesions.^{52,53,54} For lesions less than 1.5 cm² in size, multiple studies have shown

high success rates with marrow stimulation alone.⁵⁵ Because of the increase in morbidity with autologous osteochondral transplantation, marrow stimulation would be the most appropriate treatment for small primary lesions. Of the relatively small number of talar osteochondral lesions, about 20% will be considered too large for marrow stimulation.⁵² A series reported by Choi et al (2009) also estimated that failure rate following marrow stimulation was 10.5% for lesions less than 1.5 cm²; whereas 80% of lesions at least 1.5 cm² failed after a marrow stimulation procedure.⁵²

OSTEOCHONDRAL AUTOGRAFT FOR THE PRIMARY TREATMENT OF LARGE (AREA >1.5 CM²) OR CYSTIC (VOLUME >3.0 CM³) ARTICULAR CARTILAGE LESIONS OF THE ANKLE

Clinical Context and Therapy Purpose

The purpose of autologous osteochondral transplantation in individuals with large (area >1.5 cm²) or cystic (volume >3.0 cm³) full-thickness articular cartilage lesions of the ankle is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with large (area >1.5 cm²) or cystic (volume >3.0 cm³) full-thickness articular cartilage lesions of the ankle.

Interventions

The therapy being considered is autologous osteochondral transplantation. The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from another area.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. There are several symptom measurements for the ankle, such as the Foot and Ankle Ability Measures, in which the patient indicates the ability to perform various walking activities on a scale from "no difficulty" to "unable to do," as well as the American Orthopaedic Foot & Ankle Society Score, and the Foot and Ankle Outcome Score; quality of life can be measured using the SF-12 or SF-36.

Based on the available literature, follow-up should be 6 months or longer, but longer-term follow-up is recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Randomized Controlled Trials

Gobbie et al (2006) conducted the single RCT identified on autologous osteochondral transplantation for articular cartilage lesions of the talus.³³ The study included 32 patients (33 ankles) with large (mean, 4 cm²; range, 1-8) lesions randomized to chondroplasty (n=11 ankles), microfracture (n=10 ankles), or autologous osteochondral transplantation (n=12 ankles). Assessment at 24-month follow-up showed similar improvements for the 3 treatment groups, as measured by the AOFAS Ankle-Hindfoot Scale score (mean baseline scores ranging from 31-37 and mean 24-month scores ranging from 83-85). An AOFAS score of 90 to 100 is considered excellent, 80 to 89 is good, 70 to 79 is fair, and <70 is poor. The Subjective Assessment Numeric Evaluation scores also improved significantly in all treatment groups, from baseline scores of 35 to 36 to 24-month scores of 78 to 82. Complication rates were also similar. Postoperative pain, measured by numeric pain intensity scores, was greater following autologous osteochondral transplantation (5.25) than after chondroplasty (3.3) or microfracture (3.4). Although authors reported following subjects through a mean of 53 months (range, 24-199), durability results after 24 months were not reported. Thus, any potential differences between hyaline and fibrocartilage at longer-term follow-up cannot be determined from this study.

Observational Studies

Hangody et al (2008) reviewed the records of 1097 mosaicplasties for the knee and ankle in a single institution¹⁴. Ninety-eight of the mosaicplasties were for the treatment of talus lesions. Based on an evaluation of clinical scores, good-to-excellent results were reported for 93% of the talar procedures. Durable results were available for 36 patients, with a mean follow-up period of 4.2 years (range, 2-7). In this subset of the population, the average size of the grafts was 1 cm², and an average of 3 osteochondral cores (range, 1-6 cm²) were used. According to the Hanover ankle evaluation, 28 (78%) experienced excellent results, 6 (17%) experienced good results, and 2 (5%) experienced moderate results.

Haleem et al (2014) reported on a minimum 5-year follow-up for autologous osteochondral transplantation for larger lesions of the talus.²⁷ Fourteen patients who had a double-plug graft for a larger lesion (mean, 208 mm²) were matched by age and sex to a cohort of 28 patients who had a single-plug graft for a smaller osteochondral lesion (mean, 74 mm²). Both groups had significant improvements in the Foot and Ankle Outcome Score and SF-12 Health Survey scores, with no significant difference between the single-plug and double-plug groups. In the single-plug group, Foot and Ankle Outcome Score improved from 51.6 at baseline to 87.1 at final follow-up, while in the double-plug group the Foot and Ankle Outcome Score improved from 49.5 to 86.2.

Shimozono et al (2018) conducted a retrospective analysis comparing patients receiving autologous osteochondral transplantation (n=25) with patients receiving osteochondral allografts (n=16) for lesions of the ankle.³¹ Patients in the autograft group had significantly better outcomes as measured by the Foot and Ankle Outcome Score, the Magnetic Resonance Observation of Cartilage Repair Tissue score, and the SF-12 Health Survey. The rate of secondary procedures was also higher in the allograft group (25%) compared with the autograft group (0%).

Section Summary: Osteochondral Autograft for the Primary Treatment of Large (Area >1.5 cm²) or Cystic (Volume >3.0 cm³) Articular Cartilage Lesions of the Ankle

The evidence on autologous osteochondral transplantation for the treatment of large or cystic articular cartilage lesions includes a RCT that found similar efficacy results for autologous osteochondral transplantation, marrow stimulation, and chondroplasty at 2-year follow-up. Longer-term results were not reported in this RCT. However, several observational studies with longer-term follow-up (4 to 5 years) have shown favorable results for patients with large or cystic lesions receiving autologous osteochondral transplantation. Studies on the standard treatment for ankle lesions (marrow stimulation), have reported positive outcomes for patients with small lesions of the ankle (<1.5 cm²) but have generally reported high failure rates for patients with large (>1.5 cm²) lesions.

Osteochondral Autograft For Treatment Of Osteochondral Lesions Of The Ankle That Have Failed A Prior Marrow Stimulation Procedure

Clinical Context and Therapy Purpose

The purpose of autologous osteochondral transplantation in individuals with osteochondral lesions of the ankle that have failed a prior marrow stimulation procedure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with osteochondral lesions of the ankle that have failed a prior marrow stimulation procedure.

Interventions

The therapy being considered is autologous osteochondral transplantation. The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from another area.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. There are several symptom measurements for the ankle, such as the Foot and Ankle Ability Measures, in which the patient indicates the ability to perform various walking activities on a scale from "no difficulty" to "unable to do," as well as the American Orthopaedic Foot & Ankle Society Score, and the Foot and Ankle Outcome Score; quality of life can be measured using the SF-12 or SF-36.

Based on the available literature, follow-up should be at least 6 months, but longer-term follow-up is recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Nonrandomized Comparative Trials

Yoon et al (2014) compared outcomes for 22 patients who underwent autologous osteochondral transplantation with outcomes for 22 patients who underwent repeat arthroscopy using marrow stimulation after failed treatment of osteochondral lesions of the talus.²⁸ The treatment was selected by the patient after discussion with the surgeon about the risks and benefits of the 2 procedures, including possible nonunion of the osteotomy site, donor-site morbidity, and the recovery period. The study included consecutive patients who met study criteria and had failed primary marrow stimulation. Exclusion criteria were diffuse arthritic changes or diffuse fibrillated articular cartilage or axial malalignment or chronic ankle instability. These 44 patients were among 399 patients who received arthroscopic marrow stimulation during the study period, indicating that, for about 90% of patients, primary marrow stimulation was effective. The 2 groups were comparable at baseline. Independent and blinded evaluation showed an excellent or good outcome on AOFAS scores (≥ 80) in 19 (86.4%) patients treated with autologous osteochondral transplantation compared with 12 (54.5%) patients who received repeat marrow stimulation ($p=.021$). All patients showed initial improvement in VAS and AOFAS scores after 6 months, but over a mean follow-up of 50 months, only 7 (31.8%) in the repeat marrow stimulation group achieved excellent or good results, and 14 (63.6%) of this group underwent further revisions. For patients with large lesions who were treated with repeat microfracture, 100% underwent a subsequent procedure. Conversely, a significantly higher proportion of the group treated with autologous osteochondral transplantation (18 [81.8%]) achieved excellent or good results over a mean follow-up of 48 months, and none required further revisions.

Imhoff et al (2011) retrospectively evaluated 26 autologous osteochondral transplantation procedures (25 patients) of the talus at a mean follow-up of 7 years (range, 53-124 months); 9

had failed a prior marrow stimulation procedure.⁵⁶ Two additional patients had undergone a revision procedure and were not included in the follow-up data. The lesion size was less than 3 cm², and an average of 1.5 cylinders was grafted. From baseline to follow-up, for all 26 ankles combined, AOFAS scores improved from 50 to 78 points (p<.01), Tegner Activity Scale scores from 3.1 to 3.7 (p<.05), and VAS scores for pain from 7.8 to 1.5 (p<.01). However, in an analysis between patients undergoing surgery for the first time and patients undergoing revision surgery, outcomes were significantly worse in patients who had undergone a prior marrow stimulation procedure (Table 4).

Table 4. Results at 7-Year Follow-Up

Outcomes	AOFAS Score (SD)	Tegner Activity Scale Score (SD)	VAS Score (SD)
Repeat procedure	62.0 (16.4)	2.0 (1.9)	3 (3.2)
Initial procedure	87.0 (15.0)	4.6 (2.2)	0.6 (1.1)
p-value	<.01	<.01	<.01

Adapted from Imhoff et al (2011).⁵⁶

AOFAS: American Orthopaedic Foot and Ankle Society; SD: standard deviation; VAS: visual analog scale.

Observational Studies

Hangody et al (2001) reported on autologous osteochondral transplantation for osteochondritis dissecans for 36 consecutive patients.⁶ Most patients had previous surgical interventions and presented with stage III or IV lesions (completely detached or displaced fragment). The average size of the defect was 1 cm, and the average number of grafts per patient was 3 (range, 1-6). At a mean follow-up of 4.2 years, ankle function measured using the Hannover scoring system showed good-to-excellent results in 34 (94%) cases. Examination by radiograph, computed tomography, and MRI showed incorporation into the recipient bed and congruency of the articular surface.

Kreuz et al (2006) reported on outcomes from a prospective series of 35 patients who underwent osteochondral grafting from the ipsilateral talar articular facet following failed bone marrow stimulation.⁵⁷ Mean lesion diameter was 6.3 mm. At a mean follow-up of 49 months (range, 33-77), the AOFAS Ankle-Hindfoot Scale score had improved from 54.5 points (range, 47-60) to 89.9 points (range, 80-100).

Georgiannos et al (2016) reported on 5- to 7-year follow-up for a prospective cohort of 46 patients who had failed a prior marrow stimulation procedure.³⁰ Osteochondral plugs, which ranged from 4.75 to 8 mm in diameter, were taken from the talar facet. A temporary block of bone was removed to provide access to the talar dome. At a median follow-up of 5.5 years (range, 52-75 months), AOFAS score had improved from 55 to 90, and the median VAS score improved from 52/100 to 91. All grafts had incorporated and osteotomy sites healed, although 5 patients underwent subsequent surgery for osteophytes.

Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Ankle That Have Failed a Prior Marrow Stimulation Procedure

The evidence for autologous osteochondral transplantation in patients with articular cartilage lesions of the talus that have failed a prior marrow stimulation procedure includes 2 nonrandomized comparative trials and several case series. One nonrandomized comparative

study has suggested improved outcomes with autologous osteochondral transplantation compared with repeat marrow stimulation. Another study compared outcomes among patients receiving autologous osteochondral transplantation as a first treatment with patients receiving autologous osteochondral transplantation as a revision treatment. The study found improvements in both groups compared to baseline measures; however, larger improvements were seen in the group receiving autologous osteochondral transplantation as a first treatment compared with those receiving autologous osteochondral transplantation as a revision procedure. Case series have consistently indicated good-to-excellent results of autologous osteochondral transplantation at mid-term follow-up.

Fresh Osteochondral Allograft for Articular Cartilage Lesions of the Ankle

Use of autologous osteochondral transplantation is limited by the number of cores that can be taken from the non-weight-bearing part of the talus or ipsilateral knee. Autologous osteochondral transplantation may also be inadequate due to lesion depth or location, such as on the talar shoulder. For osteochondral lesions for which autologous osteochondral transplantation would be inadequate due to lesion size, depth, or location, the use of fresh osteochondral allografts has been investigated. Use of fresh allografts for defects of the talus has been reported mainly in case series and a systematic review of these series.⁵⁸ Due to the relatively rare occurrence of this condition, most series have fewer than 20 patients. One RCT was identified that compared autologous osteochondral transplantation with allograft plugs for recurrent cartilage lesions.

Diniz et al (2019) conducted a systematic review on the use of allografts for 10 foot and ankle indications.⁵⁹ A total of 107 studies were identified, 12 of which were related to osteochondral lesions of the ankle (N=125 patients). No meta-analyses were conducted. Summary descriptions were not presented separately by lesion size. Eleven of the studies were considered level IV evidence and 1 study was level V evidence. Within these studies, 6 minor complications and 9 major complications were reported, for an overall complication rate of 12%. The authors concluded that osteochondral allografts for lesions of the ankle can be considered in larger defects that are not amenable to bone marrow stimulation or when donor site morbidity is of concern (grade: C).

Van Dijk (2017) noted that, in addition to the failure rate of autologous osteochondral transplantation, an osteochondral allograft can compromise a future arthrodesis or arthroplasty by the failure of bony ingrowth because the bulk of the graft will consist of dead bone.⁶⁰

The following 3 sections assess the evidence for fresh osteochondral allograft for specific indications involving articular cartilage lesions of the ankle.

FRESH OSTEOCHONDRAL ALLOGRAFT FOR PRIMARY FULL-THICKNESS ARTICULAR CARTILAGE LESIONS OF THE ANKLE LESS THAN 1.5 CM²

Clinical Context and Therapy Purpose

The purpose of fresh osteochondral allograft in individuals with primary full-thickness articular cartilage lesions of the ankle less than 1.5 cm² is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with primary full-thickness articular cartilage lesions of the ankle less than 1.5 cm².

Interventions

The therapy being considered is fresh osteochondral allograft. The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from a donor.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. There are several symptom measurements for the ankle, such as the Foot and Ankle Ability Measures, in which the patient indicates the ability to perform various walking activities on a scale from "no difficulty" to "unable to do," as well as the American Orthopaedic Foot & Ankle Society Score, and the Foot and Ankle Outcome Score; quality of life can be measured using the SF-12 or SF-36.

Based on the available literature, follow-up should be at least 6 months, but longer-term follow-up is recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

The literature on fresh allograft for the treatment of small lesions of the ankle is very limited because this treatment is considered only when there are no other options available to delay arthrodesis or arthroplasty. Because microfracture is effective as a primary treatment in lesions less than 1.5 cm² and autologous osteochondral transplantation is effective as a revision procedure, use of allograft for small lesions has not been reported. Note that other allograft products, such as minced juvenile cartilage and reduced allograft discs, are described in other sections.

Section Summary: Fresh Osteochondral Allograft for Primary Full-Thickness Articular Cartilage Lesions of the Ankle Less Than 1.5 cm²

There is little evidence on fresh osteochondral allografts for the primary treatment of full-thickness articular cartilage lesions of the ankle less than 1.5 cm². Because microfracture is effective as a primary treatment in lesions less than 1.5 cm², autologous osteochondral transplantation is typically considered a revision procedure. Due to the high failure rate of allografts, use of allografts for small primary cartilage lesions is not appropriate.

FRESH OSTEOCHONDRAL ALLOGRAFT FOR LARGE (AREA >1.5 CM²) OR CYSTIC (VOLUME >3.0 CM³) CARTILAGE LESIONS OF THE ANKLE

Clinical Context and Therapy Purpose

The purpose of fresh osteochondral allograft in individuals with large (area >1.5 cm²) or cystic (volume >3.0 cm³) cartilage lesions of the ankle for which autografting would be inadequate is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with large (area >1.5 cm²) or cystic (volume >3.0 cm³) cartilage lesions of the ankle for which autografting would be inadequate.

Interventions

The therapy being considered is fresh osteochondral allograft: The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from a donor.

Comparators

The comparator of interest is autologous osteochondral transplantation. The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from another area.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. There are several symptom measurements for the ankle, such as the Foot and Ankle Ability Measures, in which the patient indicates the ability to perform various walking activities on a scale from "no difficulty" to "unable to do," as well as the American Orthopaedic Foot & Ankle Society Score, and the Foot and Ankle Outcome Score; quality of life can be measured using the SF-12 or SF-36.

Based on the available literature, follow-up should be at least 3 to 5 years.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

Migliorini et al (2022) conducted a systematic review and meta-analysis of 40 studies (1174 procedures) to compare osteochondral allograft versus autologous osteochondral transplantation for osteochondral lesions of the talus.⁶¹ The included studies (35 retrospective, 4 prospective, and 1 RCT by Ahmad and Jones [2016]²⁹, summarized in detail below) evaluated the outcomes of allograft and/or autograft osteochondral transplant for management for talar osteochondral defects. At baseline, the length of follow-up, male to female ratio, mean age, body mass index, lesion size, VAS score, and AOFAS score were all comparable between the groups ($p > .1$). The mean follow-up was 46.5 ± 25 months. The mean lesion size was 1.8 ± 0.8 cm² and 2.6 ± 4.3 cm² in the allograft and autograft groups, respectively. At the last follow-up, the Magnetic Resonance Observation of Cartilage Repair Tissue score (MD, 10.5; $p = .04$) and AOFAS score (MD, 4.8; $p = .04$) were better in the autograft group, while the VAS score was similar between the 2 groups ($p = .4$). At the last follow-up, autografts demonstrated lower rate of revision surgery (OR, 7.2; $p < .0001$) and failure (OR, 5.1; $p < .0001$). One main study limitation is the retrospective design of most included studies. Most study authors did not clarify the type of allograft used. Primary and revision surgeries were often mixed, and some authors combined the surgeries with other procedures.

Pereira et al (2021) published a systematic review including 12 studies (7 retrospective case series and 5 prospective case series) in 191 patients who received a fresh osteochondral allograft for osteochondral lesions of the talus ($n = 194$ ankles; mean lesion size range, 1.21 to 3.8 cm²).⁵⁸ The average patient follow-up was 56.8 months (range, 6 to 240). Results revealed that aggregate mean preoperative and postoperative AOFAS scores ($n = 8$ studies) were 49.6 (range, 38-61) preoperatively and 80.4 (range, 72.8-84) postoperatively. All studies reporting both pre- and postoperative AOFAS scores showed significant improvements from the preoperative values ($p < .05$). Five studies evaluated the VAS pain score, with significant decreases pre- to postoperatively ($p < .05$). Overall, 21.6% of patients required subsequent surgical interventions such as arthroscopic debridement and hardware removal. The overall graft survival rate was 86.6%; 26 graft failures were recorded across the included studies.

Van Tienderen et al (2017) included in a systematic review, 5 studies with a total of 90 patients (91 ankles) who received a fresh osteochondral allograft for large or cystic osteochondral lesions of the talus.⁶² Studies selected reported at least 1 outcome of interest, including AOFAS score, Foot Functional Index score, VAS score, reoperation rate, or rate of allograft collapse. The mean lesion volume was 3.7 cm³ (range, 1.0-10.9) and the number of prior procedures ranged from 1 to 4. At a mean follow-up of 45 months (range, 6-91), mean AOFAS scores of the combined studies improved from 48 to 80 and mean VAS scores of the combined studies improved from 7.1 to 2.7. However, some failures occurred: 23 (25.3%) patients required at least 1 reoperation and 12 (13.2%) patients were considered failures, defined as postoperative graft nonunion or resorption or persistence of symptoms leading to arthrodesis or arthroplasty.

Randomized Controlled Trials

Ahmad and Jones (2016) conducted a RCT comparing autologous osteochondral transplantation with fresh allograft plugs for the treatment of large (area >1.5 cm², n=9) or recurrent (volume >3.0 cm³; n=27) cartilage lesions of the talus.²⁹ The majority of the study participants had recurrent osteochondral lesions. Only 5 patients with large primary osteochondral lesions were in the autograft treatment group, and 4 patients with large primary osteochondral lesions were in the allograft treatment group. Subgroup analyses on these patients with primary lesions were not conducted.

Section Summary: Fresh Osteochondral Allograft for Large (Area >1.5 cm²) or Cystic (Volume >3.0 cm³) Cartilage Lesions of the Ankle

The evidence for fresh osteochondral allografts for the treatment of large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesions of the ankle includes a small number of patients in a RCT and systematic reviews of mainly case series. The majority of patients in the RCT were patients with revision osteochondral lesions, so conclusions about the few patients with primary lesions could not be made. The systematic reviews of case series reported improvements in ankle scores and decreases in pain scores, though 25% of patients needed additional surgery and 13% experienced either graft nonunion, resorption, or symptom persistence in 1 systematic review. A recent systematic review compared allografts and autografts for osteochondral lesions of the talus, and found that talar osteochondral transplant using allografts was associated with higher rates of failure and revision compared with autografts at midterm follow-up. Also, the use of allografts may have a negative impact on any future arthroplasty or arthrodesis. For particularly large lesions, marrow stimulation techniques have been found to be ineffective and obtaining an adequate volume of autograft may cause significant morbidity. For these reasons, osteochondral allografts may be a considered option for large lesions of the ankle.

FRESH OSTEOCHONDRAL ALLOGRAFT FOR REVISION OF OSTEOCHONDRAL LESIONS OF THE ANKLE

Clinical Context and Therapy Purpose

The purpose of fresh osteochondral allograft as a revision procedure in individuals with recurrent osteochondral lesions of the ankle for which autografting would be inadequate is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with recurrent osteochondral lesions of the ankle for which autografting would be inadequate.

Interventions

The therapy being considered is fresh osteochondral allograft. The injured area of cartilage and underlying bone is removed and replaced with a graft of cartilage and bone harvested from a donor.

Comparators

The comparator of interest is autologous osteochondral transplantation: The injured area of cartilage and underlying bone are removed and replaced with a graft of cartilage and bone harvested from another area.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity. There are several symptom measurements for the ankle, such as the Foot and Ankle Ability Measures, in which the patient indicates the ability to perform various walking activities on a scale from "no difficulty" to "unable to do," as well as the American Orthopaedic Foot & Ankle Society Score, and the Foot and Ankle Outcome Score; quality of life can be measured using the SF-12 or SF-36.

Based on the available literature, follow-up should be 5 years or longer.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Randomized Controlled Trial

Ahmad and Jones (2016; discussed above) included in their study, 9 large and 27 recurrent osteochondral lesions of the talus.²⁹ Most patients had failed a prior microfracture. The study randomized 20 patients to autologous osteochondral transplantation and 20 patients to plugs taken from a size-matched donor talus. Four patients from the allograft group had significant damage to the shoulder of the talar dome. These 4 patients received a hemi-talus allograft and were subsequently excluded from the study. Comparative analyses combined the patients with primary and recurrent lesions. Foot and Ankle Ability Measures and VAS scores were similar in the 2 groups. In the allograft group, the mean Foot and Ankle Ability Measures score increased from 55.2 to 80.7, and the mean VAS score decreased from 7.8 to 2.7 at final follow-up. These outcomes were reported as being lower than those reported for the autograft group, but the differences were not statistically significant. However, more patients in the allograft group had graft nonunion (3/16 [18.8%] patients vs. the autograft group 2/20 [10%] patients), consistent with the systematic review by VanTienderen et al (2017; described above).

Observational Study

Gaul et al (2019) presented a case series of 19 patients (20 ankles) who received osteochondral allografts for osteochondral lesions of the ankle, 19 of which had prior surgical procedures (drilling, osteotomy, microfracture).⁶³ Five of the 20 ankles required further surgery, 3 of which were considered allograft failures. The mean time to failure was 3.5 years. Of the 17 nonfailed ankles, the median follow-up was 9.7 years. Mean Olerud-Molander Ankle Score improved

significantly following the procedure. Of the 15 patients who answered the follow-up survey, 14 reported less pain and better function.

Section Summary: Fresh Osteochondral Allograft for Revision of Osteochondral Lesions of the Ankle

The evidence on fresh osteochondral allografts for revision of osteochondral lesions of the ankle includes a RCT that compared outcomes between patients receiving autografts versus allografts. Most of the patients had failed a prior microfracture. The RCT found that outcomes were statistically similar with osteochondral allografts compared with autografts. However, failure rates due to nonunion were higher in patients in the allograft group compared with patients in the autograft group. For particularly large lesions, marrow stimulation techniques have been found to be ineffective, and obtaining an adequate volume of autograft may cause significant morbidity. For these reasons, osteochondral allografts may be an option for revision of large lesions of the ankle.

OSTEOCHONDRAL AUTOGRAFT FOR ARTICULAR CARTILAGE LESIONS OF THE ELBOW

Clinical Context and Therapy Purpose

The purpose of autologous osteochondral transplantation in individuals with full-thickness articular cartilage lesions of the elbow is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with full-thickness articular cartilage lesions of the elbow.

Interventions

The therapy being considered is autologous osteochondral transplantation. The injured area of cartilage and underlying bone is removed and replaced with a graft of cartilage and bone harvested from another area.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity.

Based on the available literature, follow-up should be 6 months or longer, or until patients can return to their previous activity level, but longer-term follow-up is recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

A systematic review of 71 case series or case reports (N=934) by Sayani et al (2021) investigated patient-reported functional outcomes, range of motion, and return to sports after treatment (autologous osteochondral transplantation [n=427], fixation [n=141], debridement and microfracture [n=136], and nonsurgical or nonoperative management [n=230]) for osteochondritis dissecans of the capitulum.⁶⁴ Subgroup analysis according to treatment type was possible for 30 studies, including 14 studies on autologous osteochondral transplantation. Autologous osteochondral transplant groups demonstrated significant improvements in postoperative functional scores and range of motion, but when standardized, there was no significant differences between treatment types (debridement, fixation, or autograft transplant) in magnitude of outcomes. The overall return to sports was 94% of patients treated surgically. In larger lesions, there was a significantly lower return to sports rate when nonoperative treatment was used compared to surgical intervention (20% vs. 96.3%, respectively; n=114; p<.001). There was no significant difference in return to sports rates between baseball and gymnastics for lesions managed surgically. The highest proportion of return to sports rates was with debridement (100%), followed by autologous osteochondral transplantation (95.9%), and then fixation (83.1%).

Westermann et al (2016) included in their systematic review, 24 case series (N=492 patients) that assessed return to sports after operative treatment (autologous osteochondral transplantation [n=164], microfracture and debridement [n=236], and fixation [n=92]) for osteochondritis dissecans of the capitulum.⁶⁵ The most common primary sport was baseball (371/464) followed by gymnastics (35/464). Quality of the evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation system. None of the studies were randomized or controlled, but rather mostly level 4 evidence, retrospective, and from single institutions. The overall return to sports rate was 86% at a mean of 5.6 months. Average lesion size was similar for the different treatments among 8 studies with information available. Among all 24 studies, patients were more likely to return to their preoperative sport at any level after autologous osteochondral transplantation (0.95; 95% CI, 0.89 to 0.99) compared with debridement and microfracture (0.62; 95% CI, 0.46 to 0.77; p<.001) or fixation with pins, wires, or screws (0.72; 95% CI, 0.51 to 0.89; p=.01). Grafts were taken from the lateral femoral condyle or ribs. The percentages returning to their preoperative sport at their previous level were 94% (autologous osteochondral transplantation), 71% (microfracture and debridement), and 64% (fixation). Adverse events from the surgical procedures were rare; however, patients considering autologous osteochondral transplantation need to consider donor site morbidity.

Kirsch et al (2017) conducted a systematic review of the literature through July 2016 of case series evaluating return to play after autologous osteochondral transplantation for the treatment of osteochondritis dissecans of the capitellum.⁶⁶ Seven case series (N=126) met the inclusion criteria and were rated as moderate quality using the Methodological Index for Non-Randomized Studies. A total of 119 (94%) of the patients undergoing autologous osteochondral transplantations successfully returned to competitive sports. The mean time to unrestricted return was 5.6 months (range, 3 to 14).

Observational Study

Sato et al (2018) presented a case series of 72 patients receiving autologous osteochondral transplantation for advanced (stage III and IV) osteochondritis dissecans of the humeral capitellum in young athletes, who were followed for at least 3 years.⁶⁷ The Timmerman and Andrews clinical rating score, which incorporates subjective measures (such as pain, swelling, and activity level) and objective measures (such as flexion and arc of elbow motion) improved significantly from 101 to 190 following the procedure. Seventy of the patients returned to their sport without restrictions by 5.8 months. Subsequent surgeries included additional grafting (n=2), delayed medial ligament reconstruction (n=1), and arthroscopic removal of loose bodies (n=2).

Donor-Site Morbidity

Bexkens et al (2017) conducted a meta-analysis of case series that assessed donor-site morbidity after autologous osteochondral transplantation for osteochondritis dissecans of the capitulum.⁶⁸ Reviewers included 11 studies with 190 patients (range, 11-33 patients per series); most patients were adolescents. Grafts were harvested from the femoral condyle in 8 studies and from the costal-osteochondral junction in 3 studies. With donor-site morbidity defined as persistent symptoms of at least 1 year or that required intervention, morbidity was reported in 10 (7.8%) of 128 patients from the knee-to-elbow group and 1 (1.6%) of 62 patients in the rib-to-elbow group. A limitation of this meta-analysis was its incomplete assessment and reporting of outcomes for the donor site in the primary publications.

Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Elbow

Osteochondritis dissecans of the elbow typically occurs in patients who play baseball or do gymnastics. The literature on autologous osteochondral transplantation for advanced osteochondritis dissecans of the elbow consists of case series, primarily from Europe and Asia, and systematic reviews of case series. Although a meta-analysis suggested a benefit of autologous osteochondral transplantation compared with debridement or fixation, additional prospective comparative studies are needed to determine the effects of the procedure with greater certainty.

Osteochondral Autograft for Articular Cartilage Lesions of the Shoulder Clinical Context and Therapy Purpose

The purpose of autologous osteochondral transplantation in individuals with full-thickness articular cartilage lesions of the shoulder is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with full-thickness articular cartilage lesions of the shoulder.

Interventions

The therapy being considered is autologous osteochondral transplantation. The injured area of cartilage and underlying bone is removed and replaced with a graft of cartilage and bone harvested from another area.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity.

The limited available literature indicates a follow-up of 9 years; however, shorter follow-up would be acceptable.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Kircher et al (2009) reported on 9-year follow-up after autologous osteochondral transplantation for cartilage defects of the shoulder in 7 patients from a European study.⁶⁹ One additional patient was reported to have had donor-site morbidity at the knee and chose not to return for follow-up. All plugs showed full integration with the surrounding bone, and 6 of 7 patients showed a congruent joint surface. The Constant score improved from 76 points preoperatively to 90 points at 33 months and remained at 91 points at the 9-year follow-up. Subscores for pain and activities of daily living showed significant improvement at 33-month follow-up, with a very slight nonsignificant decline at 9-year follow-up. None of the patients required additional shoulder surgery.

Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Shoulder

The evidence on osteochondral autografting for the shoulder is very limited and therefore does not allow conclusions about the efficacy of this treatment.

MINCED OR PARTICULATED CARTILAGE FOR ARTICULAR CARTILAGE LESIONS

Clinical Context and Therapy Purpose

The purpose of autologous or allogeneic minced or particulated articular cartilage transplantation in individuals with full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder.

Interventions

The therapy being considered is autologous or allogeneic minced or particulated articular cartilage transplantation. In these procedures, pieces of cartilage are mechanically minced into 1- to 2-mm pieces, allowing chondrocytes to be released from the extracellular matrix, migrate to surrounding tissues, and form a new cartilage tissue matrix.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity.

Based on the available literature, follow-up should be 1 to 2 years or longer.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

AUTOLOGOUS MINCED CARTILAGE

Randomized Controlled Trial

Cole et al (2011) reported on a multicenter trial with 29 patients (of 582 screened) randomized in a 1:2 ratio to microfracture or Cartilage Autograft Implantation System.⁷⁰ In the single-stage

Cartilage Autograft Implantation System procedure, autologous hyaline cartilage was harvested, minced, affixed to a synthetic absorbable scaffold, and fixed on the lesion site with absorbable staples. At baseline, there were no significant differences between groups in the duration of symptoms, International Cartilage Repair Society grade, and area and depth of the chondral defect. There was a difference in the sex and work status of the 2 groups. At 3-week and 6-month follow-ups, there were no significant differences in outcomes between the 2 groups, but at later follow-up, there were differences reported. The International Knee Documentation Committee Form score was significantly higher in the Cartilage Autograft Implantation System group compared with the microfracture group at both 12 (73.9 vs. 57.8) and 24 (83.0 vs. 59.5) months. All subdomains of the Knee injury and Osteoarthritis Outcome Score symptoms and stiffness, pain, activities of daily living, sports and recreation, knee-related quality of life were significantly increased at 24 months in the Cartilage Autograft Implantation System group compared with microfracture patients. Qualitative analysis of MRI at 3 weeks and 6, 12, and 24 months showed no differences in the fill of the graft bed, tissue integration, or presence of subchondral cysts. Adverse events were similar for the groups.

ALLOGENEIC JUVENILE MINCED CARTILAGE

KNEE

Case Reports and Series

Evidence on the efficacy of DeNovo NT is limited to case reports and small case series. Farr et al (2014) conducted an industry-sponsored prospective study, the largest series identified, which included 25 patients with cartilage lesions of the femoral condyle or trochlea.⁷¹ Patients had symptomatic, focal, contained chondral lesions of the femoral condyles or trochlea with defect areas ranging between 1 cm² and 5 cm² (mean, 2.7 cm²; range 1.2-4.6). Mean number of prior surgeries was 1.1, with 18 patients reporting prior debridement and/or microfracture. Patients returned for follow-up at 3, 6, 12, 18, and 24 months for radiographs, International Knee Documentation Committee examination, and completion of questionnaires. Outcomes included the Knee injury and Osteoarthritis Outcome Score, International Knee Documentation Committee, Marx Activity Scale, and 100-mm VAS score for pain. International Knee Documentation Committee score improved over the 24 months of follow-up. At 24 months, International Knee Documentation Committee score had improved from 45.7 preoperatively to 73.6 of 100. There were also significant improvements in Knee injury and Osteoarthritis Outcome Score subscores ($p < .001$) and VAS pain score (from 43.7/100 at baseline to 11.1 at 24 months; $p < .001$). MRI showed a mean lesion fill of 109.7%, with mild graft hypertrophy identified in 20.7% of patients. Of 11 elective second-look arthroscopies at 24 months, 2 grafts (18%) showed either partial or complete delamination. Histology from 8 patients with biopsy showed a mixture of hyaline and fibrocartilage; areas with hyaline cartilage varied across sections. There was good integration with the surrounding native cartilage.

Tompkins et al (2013) included in their study, 13 patients (15 knees) who received particulated juvenile allograft to the patella.⁷² Ten of the 15 knees underwent concomitant procedures, limiting interpretation of functional outcomes. Cartilage repair, assessed at a mean of 28.8 months, was reported to be nearly normal in 73% of knees while 27% of knees had evidence of graft hypertrophy.

A retrospective review by Dawkins et al (2021) included 34 patients (36 knees) who received particulated juvenile allograft to the patellofemoral joint.⁷³ Return to sport rate among patients who participated in a sport preoperatively was 100% (n=30 patients, 31 knees). After allograft, independent MRI assessment concluded that 67% of patients achieved an overall grade of normal or nearly normal. In terms of defect fill, 78% had majority defect fill. Primary graft failure occurred in 2 cases and 1 patient experienced surgical complication.

Ankle

One proposed advantage of particulated articular cartilage for osteochondral lesions of the talus is that it is not always necessary to perform an osteotomy to access the lesion. At this time, use of DeNovo NT for the talus has been reported in case reports, small case series, and a systematic review of these studies.

Systematic Reviews

Saltzman et al (2017) reported on a descriptive systematic review of published case reports and case series.⁷⁴ Included were data on 33 ankles from 2 case reports, a series of 7 patients by Bleazey and Brigido (2012)⁷⁵, and a series of 24 ankles by Coetzee et al (2013)⁷⁶.

Case Reports and Series

Coetzee et al (2013) published a preliminary report that described 24 ankles (23 patients) with osteochondral lesions of the talus (mean lesion size, 125 mm²) that were treated with DeNovo NT.⁷⁶ Fourteen (58%) of the ankles had failed at least 1 prior bone marrow stimulation procedure. At an average follow-up of 16.2 months, 78% of ankles had good-to-excellent scores on the AOFAS Ankle-Hindfoot Scale score, with a final mean VAS score of 24 out of 100. However, 18 (76%) ankles had at least 1 concomitant procedure (hardware removal and treatment for impingement, synovitis, instability, osteophytes, malalignment), limiting interpretation of the functional results. One treatment failure was caused by partial graft delamination.

Saltzman et al (2017), in addition to their systematic review of the literature, reported on 6 patients who had been treated at their institution with particulated juvenile articular cartilage for articular cartilage lesions of the talus.⁷⁴ Lesion size ranged from 96 to 308 mm². Two of the 6 patients underwent a medial malleolar osteotomy to access the lesion. Implantation procedures included debridement, marrow stimulation, and fixation of the particulated cartilage with fibrin glue. At a mean 13-month follow-up, all 6 patients reported subjective improvements in pain and function. However, for all 3 patients who had MRIs between 3 months and 2 years postoperatively, there was persistent subchondral edema and nonuniform chondral surface.

Dekker et al (2018) conducted a retrospective review of patients receiving particulated juvenile cartilage allograft transplantation for osteochondral lesions of the talus (N=15).⁷⁷ Twelve of the 15 patients had undergone a prior microfracture procedure and 3 patients received the transplant as a primary procedure. A successful procedure was defined as an improvement in pain and no subsequent cartilage procedures. After at least 1 year of follow-up, 9 (60%) cases were considered successful, with 3 patients needing additional cartilage procedures and 3 reporting continued pain. Predictors of failure were larger lesions and male sex.

DiSandis et al (2018) reported on a series of 46 patients receiving particulated juvenile cartilage allograft transplantation and autologous bone marrow aspirate concentration for osteochondral

lesions of the talus.⁷⁸ Only 24 patients had pre- and post-Foot and Ankle Outcome Score and SF-12 Health Survey data. Almost all subscale scores were significantly improved after the procedure; however, MRI showed inhomogeneous repair tissue structure, persistent bone marrow edema, and moderately hyperintense tissue.

Section Summary: Minced or Particulated Cartilage for Articular Cartilage Lesions

The evidence on autologous minced or particulated cartilage includes a small RCT from 2011. The evidence on allogeneic minced cartilage includes case reports and case series. The case series have suggested an improvement in outcomes compared with baseline, but there is also evidence of subchondral edema, nonuniform chondral surface, graft hypertrophy, and delamination. For articular cartilage lesions of the knee, further evidence, preferably from RCTs, is needed to evaluate the effect on health outcomes compared with other available procedures. For articular cartilage lesions of the ankle, there are few treatment options and, in the largest case series, over half of the patients had failed prior marrow stimulation. However, the concomitant procedures performed in that study limited the interpretation of its results. Randomized comparisons with microfracture in patients who have not received prior treatment would permit greater certainty about the effectiveness of this procedure.

DECELLULARIZED OSTEOCHONDRAL ALLOGRAFT PLUGS

Clinical Context and Therapy Purpose

The purpose of decellularized osteochondral allograft plugs in individuals with full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder.

Interventions

The therapy being considered is decellularized osteochondral allograft plugs. For decellularized osteochondral allograft plugs, allografts undergo a procedure that extracts lipids. The graft is then inactivated and sterilized in order to extend shelf life.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity.

Based on the available literature, follow-up should be 1 to 2 years or longer.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Case Series

Case series have suggested high failure rates for decellularized osteochondral allograft plugs (Chondrofix). Farr et al (2016) reviewed records of 32 patients and identified failure in 23 (72%) patients when failure was defined as structural damage of the graft identified by MRI or arthroscopy, or any reoperation resulting in the removal of the allograft.⁷⁹ Johnson et al (2017) examined records from an institutional registry of 34 patients who, following discussion of alternative cartilage repair options, chose treatment with a decellularized osteochondral allograft plug.⁸⁰ Patient-reported outcomes along with MRI results were recorded at 6 months, 1 year, and 2 years by independent observers. At a mean follow-up of 15.5 months (range, 6-24), 10 (29%) patients required revision surgery with removal of the implant. Failure rates were higher for females and larger lesions (hazard ratio, 1.9 per 1 cm² increase; 95% CI, 1.2 to 3.1; p=.005).

Section Summary: Decellularized Osteochondral Allograft Plugs

The evidence on decellularized osteochondral allograft plugs has reported delamination of the implants and high failure rates.

REDUCED OSTEOCHONDRAL ALLOGRAFT DISCS

Clinical Context and Therapy Purpose

The purpose of reduced osteochondral allograft discs in individuals with full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder.

Interventions

The therapy being considered is reduced osteochondral allograft discs. For reduced osteochondral allograft discs, the discs are laser etched and contain hyaline cartilage with chondrocytes, growth factors, and extracellular matrix proteins.

Comparators

To restore articular surface, standard therapies of marrow stimulation currently in use include microfracture, abrasion arthroplasty, and drilling. Microfracture involves debridement of the damaged area and puncturing of the underlying bone to allow bleeding of the bone, stimulating the formation of new joint surface cartilage.

Outcomes

The general outcomes of interest are improvements in symptoms, functional outcomes, quality of life, and treatment-related morbidity.

Literature describing appropriate follow-up is not available, but based upon other allograft procedures, a minimum of 1 to 2 years would be considered appropriate.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Case Reports and Series

The evidence on reduced osteochondral allograft discs is limited to case reports and small case series.

The largest case series, published by Mehta et al (2022), assessed short-term clinical outcomes in 18 patients (8 males, 10 females) with isolated articular cartilage lesions who were treated with marrow stimulation followed by placement of ProChondrix.⁸¹ Mean patient age at surgery was 32.39 years and mean lesion size was 3.86 cm². Study characteristics and results are summarized in Tables 5 and 6. There were 2 failures requiring reoperation. Study limitations included small sample size and follow-up period. In addition, the procedure was performed by a single surgeon, who also collected, compiled, and analyzed the data. The defects treated in the study were relatively small, focal, contained lesions.

Table 5. Summary of Key Case Series Characteristics

Study	Country	Participants	Treatment	Follow-Up
Mehta (2022) ⁸¹ ,	U.S.	Patients (N=18) with symptomatic, full-thickness, articular cartilage lesions of the knee smaller than 30 x 30 mm in size	Marrow stimulation followed by placement of ProChondrix	2.5 years (range, 6-43 months)

Table 6. Summary of Key Case Series Results

Study	Treatment	VAS score	IKDC Score ^a	KOOS ^b - Sports and Recreational Activity Function	KOOS ^b - QOL	SF-36 Physical Functioning	SF-36 Energy / Fatigue	SF-36 Social Functioning	SF-36 Bodily Pain
Mehta (2022) ^{81,}	Marrow stimulation followed by placement of ProChondrix (N=18)	Decreased from 6.55 to 2.55	Increased from 37.61 to 59.65	Increased +26.04	Increased +18.76	Increased +25.20	Increased +16.50	Increased +11.79	Increased +25.18
p-value		.02	.02	.04	.007	.04	.02	.04	.04

^a Patient-completed tool that contains sections on knee symptoms, function, and sports activities. Scores range from 0 points (lowest level of function or highest level of symptoms) to 100 points (highest level of function and lowest level of symptoms).

^b The KOOS evaluates consequences of knee injury. It includes 5 separately scored subscales (pain, other symptoms, function in daily living, function in sport and recreation, and quality of life), and the final score is a percentage score from 0 (extreme problems) to 100 (no problems).

IKDC: International Knee Documentation Committee; KOOS: Knee Injury and Osteoarthritis Outcome Score; SF-36: Short Form-36; VAS: visual analog scale.

Section Summary: Reduced Osteochondral Allograft Discs

The evidence on reduced osteochondral allograft discs consists only of small case series and is insufficient to draw conclusions about treatment efficacy.

SUMMARY OF EVIDENCE

Knee Lesions

For individuals who have full-thickness articular cartilage lesions of the knee who receive an osteochondral autograft, the evidence includes randomized controlled trials (RCTs), systematic reviews of RCTs, and longer-term observational studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Several systematic reviews have evaluated osteochondral autografting for cartilage repair in the short- and mid-term. Compared with abrasion techniques (eg, microfracture, drilling), there is evidence that osteochondral autografting decreases failure rates and improves outcomes in patients with medium-size lesions (eg, 2-6 cm²) when measured at longer follow-up. This is believed to be due to the higher durability of hyaline cartilage compared with fibrocartilage from abrasion techniques. There appears to be a relatively narrow range of lesion size for which osteochondral autografting is most effective. The best results have also been observed with lesions on the femoral condyles, although treatment of lesions on the trochlea and patella may also improve outcomes. Correction of malalignment is important for the success of the procedure. The evidence suggests that osteochondral autografts may be considered an option for moderate-

sized, symptomatic, full-thickness, chondral lesions of the femoral condyle, trochlea, or patella. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have full-thickness articular cartilage lesions of the knee when autografting would be inadequate due to lesion size, location, or depth who receive a fresh osteochondral allograft, the evidence includes case series and systematic reviews of case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Due to the lack of alternatives, this procedure may be considered a salvage operation in younger patients for full-thickness chondral defects of the knee caused by acute or repetitive trauma when other cartilage repair techniques (eg, microfracture, osteochondral autografting, autologous chondrocyte implantation) would be inadequate due to lesion size, location, or depth. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Ankle Lesions

For individuals who have primary full-thickness articular cartilage lesions of the ankle less than 1.5 cm² who receive an osteochondral autograft, the evidence includes observational studies and systematic reviews of these studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A systematic review found similar improvements in outcomes following microfracture and autologous osteochondral transplantation. Another systematic review found that autologous osteochondral transplantation reduces pain and improves function in patients with osteochondral lesions of the talus, including lesions less than 1.5 cm²; most included studies performed autologous osteochondral transplantation as a secondary procedure. Given the success of marrow stimulation procedures for smaller lesions (<1.5 cm²) and the increase in donor-site morbidity with graft harvest from the knee, current evidence does not support the use of autologous osteochondral transplantation as a primary treatment for smaller articular cartilage lesions of the ankle. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have large (area >1.5 cm²) or cystic (volume >3.0 cm³) full-thickness articular cartilage lesions of the ankle who receive an osteochondral autograft, the evidence includes a RCT and several observational studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A RCT in patients with large lesions found similar efficacy for autologous osteochondral transplantation, marrow stimulation, and arthroplasty at 2-year follow-up. Longer-term results were not reported in the RCT. However, observational studies with longer-term follow-up (4-5 years) have shown favorable results for patients with large or cystic lesions receiving osteochondral autograft transplantation. Limitations of the published evidence preclude determining the effects of the technology on health outcomes. Studies on the standard treatment for ankle lesions, marrow stimulation, have reported positive outcomes for patients with small lesions of the ankle (<1.5 cm²), but have generally reported high failure rates for patients with large (>1.5 cm²) lesions. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have osteochondral lesions of the ankle that have failed primary treatment who receive an osteochondral autograft, the evidence includes 2 nonrandomized comparative trials and several case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The best evidence for revision autologous osteochondral

transplantation comes from a nonrandomized comparative study that found better outcomes with autologous osteochondral transplantation than with repeat marrow stimulation. This finding is supported by case series that have indicated good-to-excellent results at mid-term and longer-term follow-up with revision autologous osteochondral transplantation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have primary full-thickness articular cartilage lesions of the ankle less than 1.5 cm² who receive a fresh osteochondral allograft, there is little evidence. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Because microfracture is effective as a primary treatment for lesions less than 1.5 cm² and autologous osteochondral transplantation is effective as a revision procedure, use of allograft for small primary cartilage lesions has not been reported. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have large (area >1.5 cm²) or cystic (volume >3.0 cm³) cartilage lesions of the ankle when autografting would be inadequate, who receive a fresh osteochondral allograft, the evidence includes a small number of patients in a RCT and systematic reviews of mainly case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The majority of patients in the RCT were patients with revision osteochondral lesions, so conclusions about the few patients with primary lesions could not be made. The systematic reviews of case series reported improvements in ankle scores and decreases in pain scores, though 25% of patients needed additional surgery and 13% experienced either graft nonunion, resorption, or symptom persistence in 1 systematic review. A recent systematic review compared allografts and autografts for osteochondral lesions of the talus, and found that talar osteochondral transplant using allografts was associated with higher rates of failure and revision compared with autografts at midterm follow-up. For particularly large lesions, marrow stimulation techniques have been found to be ineffective, and obtaining an adequate volume of autograft may cause significant morbidity. For these reasons, osteochondral allografts may be a considered option for large lesions of the ankle. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have revision osteochondral lesions of the ankle when autografting would be inadequate, who receive a fresh osteochondral allograft, the evidence includes a RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Most of the patients in the RCT had failed a prior microfracture. The RCT found that outcomes were statistically similar with osteochondral allografts compared with autografts. However, failure rates due to nonunion were higher in patients in the allograft group compared with patients in the autograft group. For particularly large lesions, marrow stimulation techniques have been found to be ineffective, and obtaining an adequate volume of autograft may cause significant morbidity. For these reasons, osteochondral allografts may be a considered option for revision of large lesions of the ankle. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Elbow Lesions

For individuals who have full-thickness articular cartilage lesions of the elbow who receive an osteochondral autograft, the evidence includes a meta-analysis of case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Osteochondritis dissecans of the elbow typically occurs in patients who play baseball or do

gymnastics. Although the meta-analysis suggested a benefit of osteochondral autografts compared with debridement or fixation, RCTs are needed to determine the effects of the procedure with greater certainty. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Shoulder Lesions

For individuals who have full-thickness articular cartilage lesions of the shoulder who receive an osteochondral autograft, the evidence includes a case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Evidence on osteochondral autografting for the shoulder is very limited. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Knee, Ankle, Elbow, or Shoulder Lesions

For individuals who have full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder who receive autologous or allogeneic minced or particulated articular cartilage, the evidence includes a small RCT and small case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The evidence on autologous minced cartilage includes a small RCT. The evidence on allogeneic juvenile minced cartilage includes a few small case series. The case series have suggested an improvement in outcomes compared with preoperative measures, but there is also evidence of subchondral edema, nonhomogeneous surface, graft hypertrophy, and delamination. For articular cartilage lesions of the knee, further evidence, preferably from RCTs, is needed to evaluate the effect on health outcomes compared with other procedures. There are fewer options for articular cartilage lesions of the ankle. However, further study in a larger number of patients is needed to assess the short- and long-term effectiveness of this technology. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder who receive decellularized osteochondral allograft plugs, the evidence includes small case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The case series reported delamination of the implants and high failure rates. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder who receive reduced osteochondral allograft discs, the evidence includes small case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A prospective case series assessed ProChondrix for treatment of articular cartilage lesions of the knee and found sustained positive results out to a mean follow-up of 2.5 years, with a low failure rate. However, larger prospective studies with longer follow-up are necessary to further elucidate the safety and efficacy of reduced osteochondral allograft discs. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2017 Input

In response to requests, clinical input on osteochondral autografts for treating focal articular cartilage lesions in the ankle and elbow was received from 3 respondents, including 2 specialty society-level responses and 1 physician from 1 health system, while this policy was under review in 2017.

Input obtained in 2017 supports the following indications:

- Use of osteochondral autograft for:
 - Primary treatment of large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesion of the talus.
 - Revision surgery after failed marrow stimulation for osteochondral lesion of the talus.
- Use of fresh osteochondral allograft for:
 - Primary treatment of large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesion of the talus when autografting would be inadequate due to lesion size, depth, or location.
 - Revision surgery for osteochondral lesions of the talus when autografting would be inadequate due to lesion size, depth, or location.

Thus, the above indications may be considered medically necessary considering the suggestive evidence and clinical input support.

However, the clinical input does not support whether the following indication provides a clinically meaningful improvement in the net health outcome or is consistent with generally accepted medical practice.

- Use of osteochondral grafts in the elbow.

Thus, the above indication may be considered investigational.

2011 Input

In response to requests, input was received from 3 academic medical centers while this policy was under review in 2011. Input generally agreed with the stated criteria for osteochondral grafting, except the following: Input was mixed on the requirement for an inadequate response to a prior surgical procedure, the size of the lesion, and the requirement for an absence of meniscal pathology. Input was also mixed on the investigational status of osteochondral grafts in other joints, including the patellar and talar joints, and for the use of autologous minced cartilage.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given

to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

ANKLE

American Orthopaedic Foot and Ankle Society

In 2018, the American Orthopaedic Foot and Ankle Society (AOFAS) issued a position statement on the use of osteochondral transplantation for the treatment of osteochondral lesions of the talus.⁸² In the statement, the Society "endorses the use of osteochondral autograft and allograft transplantation for the treatment of osteochondral lesion of the talus, especially large diameter lesions, cystic lesions, and those that have failed previous surgical treatment. AOFAS does not consider these procedures to be experimental in a patient population that has failed nonoperative management."

International Consensus Group on Cartilage Repair of the Ankle

In 2017, the International Consensus Group on Cartilage Repair of the Ankle convened to review the best available evidence and develop consensus statements to guide management of patients needing cartilage repair of the ankle.⁸³ The Consensus Group, consisting of 75 experts from 25 countries, acknowledged that evidence in the field of cartilage repair of the ankle is both low quality and at low levels. One topic addressed by the Consensus Group was the use of osteochondral allografts. Through a process based on the Delphi method of achieving consensus, the following recommendations were issued:

- Osteochondral allograft plugs may be preferred over autografts in the following conditions: lesions >1.5 cm; knee osteoarthritis; history of knee infection; patients expressing concern of donor site morbidity of the knee. (grade of evidence: prospective cohort study)
- The source of osteochondral allograft plugs for the ankle should come from the ankle, not the knee. (grade of evidence: basic science)
- There is an absence of clinical evidence and clinical experience for the use of decellularized osteochondral allograft plugs.
- The preferred type of allograft for the ankle is fresh, not frozen. (grade of evidence: basic science)

ELBOW

American Academy of Orthopaedic Surgeons

In 2010, the American Academy of Orthopaedic Surgeons (AAOS) released guidelines on the diagnosis and treatment of osteochondritis dissecans. In the guidelines, AAOS was unable to recommend for or against a specific cartilage repair technique in symptomatic skeletally immature or mature patients with an unsalvageable osteochondritis dissecans lesion.^{84,85}

In 2010, an AAOS review of articular cartilage restoration methods stated that "osteochondral autografting is generally used for smaller focal lesions of the femoral condyle no greater than 1.5 to 2 cm."⁸⁶

KNEE

National Institute for Health and Care Excellence

In 2018, the NICE issued a new guidance on mosaicplasty for symptomatic articular cartilage defects of the knee (IPG607).⁸⁷ The guidance states that the evidence for safety and efficacy of mosaicplasty for knee cartilage defects is adequate to support the use of the procedure.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 7.

Table 7. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT03873545 ^a	A Prospective, Multi-Center Study Evaluating ProChondrix® CR for the Repair of Focal Articular Cartilage Defects in the Knee	80	Dec 2026
NCT05391841 ^a	Prospective, Non-interventional Study to Evaluate the Efficacy and Safety of NOVOCART Inject for the Treatment of Cartilage Defects in the Knee in Pediatric Patients With Closed Epiphyses	30	Jul 2030
NCT04744402 ^a	A Multi-Center, Active-Controlled, Open-Label, Phase 2 Trial to Compare the Efficacy and Safety of CartiLife®, and Microfracture for Patients With Articular Cartilage Defects in the Knee	25	Dec 2023
NCT04296487	Introduction of Autologous Chondrocyte Implantation Procedure for the Treatment of Chondral Defect in the Knee	100	Sep 2025
NCT03219307 ^a	Safety and Efficacy of NOVOCART 3D in the Treatment of Articular Cartilage Defects Following Failure on Microfracture	30	Dec 2028
NCT01656902 ^a	A Prospective Randomized Controlled Multicenter Phase-III Clinical Study to Evaluate the Safety and Effectiveness of NOVOCART® 3D Plus Compared to the Standard Procedure Microfracture in the Treatment of Articular Cartilage Defects of the Knee	263	Jun 2023
<i>Unpublished</i>			
NCT01329445 ^a	Post Market, Longitudinal Data Collection Study of DeNovo NT for Articular Cartilage Defects of the Knee	160	Dec 2021 (unknown)
NCT01670617 ^a	A Stratified, Post-Market Study of DeNovo NT for the Treatment of Femoral and Patellar Articular Cartilage Lesions of the Knee	90	Dec 2021 (unknown)
NCT01347892 ^a	Post Market, Longitudinal Data Collection Study of Articular Cartilage Lesions in the Ankle Treated With DeNovo(R) NT	205	Sep 2019 (unknown)

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
27415	Osteochondral allograft, knee, open
27416	Osteochondral autograft(s), knee, open (e.g., mosaicplasty) (includes harvesting of autograft[s])
28446	Open osteochondral autograft, talus (includes obtaining graft[s])
29866	Arthroscopy, knee, surgical; osteochondral autograft(s) (e.g., mosaicplasty) (includes harvesting of the autograft[s])
29867	Arthroscopy, knee, surgical; osteochondral allograft (e.g., mosaicplasty)

REVISIONS	
04-02-2015	<p>A stand-alone policy entitled "Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions" was created from the "Transplantation for Chondral Defects" medical policy.</p> <p>Updated Description section.</p> <p>In Policy section:</p> <ul style="list-style-type: none"> ▪ In Item B, removed "including patellar and talar, and any indications other than those listed above," to read, "Osteochondral allografting for all other joints is considered experimental / investigational." ▪ In Item C. 2., removed "or" and "or patella" to read, "Focal, full-thickness (grade III or IV) unipolar lesions on the weight-bearing surface of the femoral condyles, trochlea, or patella that are between 1 and 2.5 cm² in size. (Outerbridge cartilage grading scale: Grade III has fragmentation and deeper fissuring of more than one-half inch and grade IV shows erosion of the cartilage down to the bone) AND" ▪ In Item C, removed "5. Absence of meniscal pathology, 6. Non-repairable stage III or IV, 7. Otherwise healthy non-elderly patient who can comply with the post-operative regiment including physical therapy, 8. Body mass index (BMI) less than 30" ▪ In Item D, removed "patellar and" to read, "Osteochondral autografting for all other joints, including talar, and any indications other than those listed above, is considered experimental / investigational." <p>Updated Rationale section.</p> <p>In Coding section:</p> <ul style="list-style-type: none"> ▪ Removed CPT and HCPCS codes 27412, 29870, 29871, 29873, 29874, 29875, 29876, 29877, J7330, and S2112 ▪ Removed ICD-9 codes 717.7 and 732.7. ▪ Removed ICD-10 codes S89.90xA, S89.90xD, and S89.90xS.

REVISIONS	
	Updated Revision section.
	Updated References section.
09-01-2015	Updated Description section.
	In Policy section: <ul style="list-style-type: none"> ▪ In Item A, removed "large (e.g., 10 cm²)" and added "when other cartilage repair techniques (e.g., microfracture, osteochondral autografting or autologous chondrocyte implantation) would be inadequate due to the size, location, or depth of the lesion", to read "Osteochondral allografting may be considered medically necessary as a technique to repair full-thickness chondral defects of the knee caused by acute or repetitive trauma when other cartilage repair techniques (e.g., microfracture, osteochondral autografting or autologous chondrocyte implantation) would be inadequate due to the size, location, or depth of the lesion."
	Updated Rationale section.
	Updated References section.
02-17-2017	Updated Description section.
	In Policy section: <ul style="list-style-type: none"> ▪ In Item C, added "of the knee" to read, "Osteochondral autografting, using 1 or more cores of osteochondral tissue, may be considered medically necessary for the treatment of symptomatic full-thickness cartilage defects of the knee caused by acute or repetitive trauma in patients who have had an inadequate response to a prior surgical procedure, when ALL of the following have been met:" ▪ In Item C 1, added "or younger" and removed "younger than" to read, "Adolescent patients should be skeletally mature with documented closure of growth plates (e.g., 15 years or older). Adult patients should be too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (e.g., 55 years or younger), AND" ▪ Added Item G, "Treatment of focal articular cartilage lesions with decellularized osteochondral allograft plugs (e.g., Chondrofix) is considered experimental / investigational." ▪ Added Item H, "Treatment of focal articular cartilage lesions with reduced osteochondral allograft discs (e.g., ProChondrix, Cartiform) is considered experimental / investigational."
	Updated Rationale section.
	Updated References section.
07-11-2017	Updated Description section.
	In Policy section: <ul style="list-style-type: none"> ▪ Added new Item A 2, "Large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesions of the talus when autografting would be inadequate due to lesion size, depth, or location, OR" ▪ Added new Item A 3, "Revision surgery after failed prior marrow stimulation for large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesions of the talus when autografting would be inadequate due to lesion size, depth, or location." ▪ In Item C 1 a, removed "(e.g., 15 years or older)" to read, "Adolescent patients should be skeletally mature with documented closure of growth plates." ▪ Added new Item C 2, " Large (area >1.5 cm²) or cystic (volume >3.0 cm³) osteochondral lesions of the talus, OR" ▪ Added New Item C 3, "Revision surgery after failed marrow stimulation for osteochondral lesion of the talus." ▪ In Item D, removed "including talar" to read, "Osteochondral autografting for all other joints, including talar, and any indications other than those listed above, is considered experimental / investigational."

REVISIONS	
	<ul style="list-style-type: none"> ▪ In Policy Guidelines, added "particularly for lesions less than 1.5 cm² in area or 3.0 cm³ in volume" to Item 1.
	Updated Rationale section.
	In Coding section:
	<ul style="list-style-type: none"> ▪ Added coding bullet.
	Updated References section.
07-06-2018	Policy published to the bcbsks.com website on June 6, 2018, with an effective date of July 6, 2018.
	Updated Description section.
	In Policy section:
	<ul style="list-style-type: none"> ▪ In Item A, added "fresh" to read, "Fresh osteochondral allografting may be considered medically necessary as a technique to repair:" ▪ In Item E, added "or particulated" to read, "Treatment of focal articular cartilage lesions with autologous minced or particulated cartilage is considered experimental / investigational." ▪ In Item F, added "or particulated" to read, "Treatment of focal articular cartilage lesions with allogeneic minced or particulated cartilage is considered experimental / investigational."
	Updated Rationale section.
	In Coding section:
	<ul style="list-style-type: none"> ▪ Removed ICD-9 codes.
	Updated References section.
02-18-2021	Updated Description section.
	Updated Rationale section.
	Updated References section.
06-16-2021	Updated Description section.
	Updated Rationale section.
	Updated References section.
06-01-2022	Updated Description Section
	Updated Policy Section <ul style="list-style-type: none"> ▪ Added "micronized" to statement: Treatment of focal articular cartilage lesions with micronized, minced, or particulated allogeneic cartilage is considered experimental / investigational.
	Updated Rationale Section
	Updated Coding Section <ul style="list-style-type: none"> ▪ Convert ICD-10 codes to code ranges
	Updated References Section
05-23-2023	Updated Description Section
	Updated Rationale Section
	Updated Coding Section <ul style="list-style-type: none"> ▪ Removed ICD-10 codes
	Updated References Section

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