Original Research

Characteristics and Clinical Outcomes After Osteochondral Allograft Transplantation for Treating Articular Cartilage Defects

Systematic Review and Single-Arm Meta-analysis of Studies From 2001 to 2020

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Background: Osteochondral allograft transplantation (OCA) treats symptomatic focal cartilage defects with satisfactory clinical results.

Purpose: To comprehensively analyze the characteristics and clinical outcomes of OCA for treating articular cartilage defects.

Study Design: Systematic review; Level of evidence, 4.

Methods: We searched Embase, PubMed, Cochrane Database, and Web of Science for studies published between January 1, 2001, and December 31, 2020, on OCA for treating articular cartilage defects. Publication information, patient data, osteochondral allograft storage details, and clinical outcomes were extracted to conduct a comprehensive summative analysis.

Results: In total, 105 studies involving 5952 patients were included. The annual reported number of patients treated with OCA increased from 69 in 2001 to 1065 in 2020, peaking at 1504 cases in 2018. Most studies (90.1%) were performed in the United States. The mean age at surgery was 34.2 years, and 60.8% of patients were male and had a mean body mass index of 26.7 kg/m^2. The mean lesion area was 5.05 cm^2, the mean follow-up duration was 54.39 months, the mean graft size was 6.85 cm^2, and the number of grafts per patient was 54.7. The failure rate after OCA was 18.8%, and 83.1% of patients reported satisfactory results. Allograft survival rates at 2, 5, 10, 15, 20, and 25 years were 94%, 87.9%, 80%, 73%, 55%, and 59.4%, respectively. OCA was mainly performed on the knee (88.9%). The most common diagnosis in the knee was osteochondritis dissecans (37.9%), and the most common defect location was the medial femoral condyle (52%). The most common concomitant procedures were high tibial osteotomy (28.4%) and meniscal allograft transplantation (24.7%). After OCA failure, 54.7% of patients underwent revision with primary total knee arthroplasty.

Conclusion: The annual reported number of patients who underwent OCA showed a significant upward trend, especially from 2016 to 2020. Patients receiving OCA were predominantly young male adults with a high body mass index. OCA was more established for knee cartilage than an injury at other sites, and its best indication was osteochondritis dissecans. This analysis demonstrated satisfactory long-term postoperative outcomes.

Keywords: osteochondral allograft transplantation; articular cartilage defect; cartilage repair; systematic review

Articular cartilage covers the ends of the connected bones in joints. It lubricates the joint surface, reducing the joint surface friction and buffering against shocks and impacts during movement.[23] Articular cartilage lacks nerves and a vascular supply; therefore, its nutrition is supplied by

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the synovial fluid and arterial branches around the synovial membrane layer of the articular capsule.[31,33,106] Once the articular cartilage is damaged or degraded, its capacity to repair and heal is limited.[114,120,121] Articular cartilage defects can be caused by various causes, such as trauma, degeneration, avascular necrosis, osteochondritis dissecans, or osteoarthritis.[86] Studies have shown the prevalence of cartilage damage to be as high as 66%,[123] leading to a range of symptoms including swelling, pain, and limited mobility.[28,94] Cartilage damage may eventually lead to accelerated cartilage wear, increased pain, impaired joint stability, and further development into diffuse osteoarthritis, with ultimate loss of joint function.[46,62,86,99] At the same time, unstable injuries may cause progressive degeneration of the surrounding normal cartilage due to load transfer.[28] Since articular cartilage has limited inherent capacity for spontaneous healing after injury, symptomatic articular cartilage defects benefit from cartilage repair treatment. Therefore, it is necessary to study patients undergoing cartilage repair therapy with symptomatic articular cartilage injuries.

To delay the progression of osteoarthritis and obviate the implementation of arthroplasty, an appropriate cartilage repair protocol can be selected according to the characteristics of the cartilage injury.[94] Traditionally, surgical methods for treating cartilage injuries can be divided into palliative, reparative, and restorative treatments. Palliative treatments include chondral debridement and chondroplasty. Reparative and restorative treatments include marrow stimulation techniques (MSTs; subchondral drilling and microfracture), autologous chondrocyte implantation (ACI), osteochondral autograft transfer (OAT), and osteochondral allograft transplantation (OCA).[46,62,86] Although many factors should be considered in selecting appropriate cartilage repair surgery, research has shown that a small area of cartilage damage is more suitable for MST and OAT. In addition, the treatment effect was even more satisfactory than that of other cartilage repair surgery. In contrast, large cartilage defects >4 cm^2 are more suitable for ACI or OCA treatment.[86,94]

OCA is a restorative cartilage procedure for symptomatic focal cartilage defects that involves transplanting surviving mature hyaline cartilage and supporting subchondral bone into the area of the cartilage defect.[20,75,93,108] As a well-developed, single-stage restorative cartilage procedure, OCA has increasingly become the preferred treatment after cartilage repair surgery failures. OCA has many advantages compared with other cartilage repair techniques, such as simultaneously repairing the cartilage and subchondral bone, treating large or multisite cartilage defects, and supporting early weight-bearing.[46,108] Two studies have shown satisfactory long-term clinical results after OCA, with allograft survival rates at 10 to 25 years postoperatively as high as 59% to 91%.[86,136]

The extensive application of OCA has rendered it 1 of the most common cartilage repair procedures in the United States.[75] However, the availability of allograft is limited because of the scarcity of donor grafts and duration of graft preservation.[48,116,119] Furthermore, there have not been any studies describing the use of OCA at different locations and the demographic data of patients undergoing this procedure. Therefore, we aimed to conduct a comprehensive systematic review and single-arm meta-analysis of the characteristics and clinical outcomes of OCA in treating articular cartilage defects over the past 2 decades (2001-2020) to better understand its research status in different countries, clarify the trends and clinical results of OCA in different sites, and provide clarification and data support for the clinical application of OCA.

METHODS

Search Strategy

A comprehensive systematic literature search was completed per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[105] The literature retrieval was conducted in October 2021 using the Embase, PubMed, Cochrane Database, and Web of Science databases for all the relevant English articles. The following search terms were used: ("osteochondral" or "cartilage" or "cartilages") and ("allograft" or "allogeneic transplants" or "allogeneic transplant" or "transplant, allogeneic" or "transplants, allogeneic" or "allogeneic grafts" or "allogeneic graft" or "graft, allogeneic" or "grafts, allogeneic" or "homografts" or "homograft" or "homologous transplants" or "homologous transplant" or "transplant, homologous" or "transplants, homologous"). We searched the publication date range from January 1, 2001, to December 31, 2020.

Study Selection

The obtained studies were screened and selected using the following inclusion criteria: (1) the participants included were patients of all ages with a definite diagnosis of osteochondral injury, (2) all publicly published clinical studies

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were written in English and involved OCA for cartilage defects, and (3) the patients were evaluated at minimum 2-year follow-up. The exclusion criteria were as follows: (1) revision OCA procedures; (2) chondral defects treated with particulate juvenile articular allograft cartilage; and; (3) duplicate articles, literature reviews, meta-analyses, case reports, technical notes, editorial commentaries, expert consensus statements, conference abstracts and presentations, animal studies, biomechanical studies, and other nonclinical studies.

The references for all included studies were assessed and screened to ensure integrity and thoroughness. Two authors (X.W. and Z.R.) independently reviewed the literature to determine the final inclusion criteria, and any disagreements were resolved between them or discussed with a third author (W.D.).

Data Extraction

All relevant study data were extracted by 2 independent reviewers (X.W. and Y.L.). The extracted data included publication information, sample size, patient characteristics (mean age, sex, mean body mass index (BMI), smoking, mean symptom duration, mean follow-up time), defect size and location, size and number of grafts, storage details of osteochondral allografts, mechanism of injury, previous and concomitant surgeries, failures, reoperations, survival of grafts, and satisfaction. Allograft failure was defined as the removal or revision of the primary OCA, conversion to any arthroplasty, or gross appearance of graft failure on second-look arthroscopy.[39,46,91,93] Any inconsistencies were discussed or resolved with a third author (W.D.).

Statistical Analysis

All extracted data were analyzed using SPSS (Version 19.0; IBM) and Stata/SE 12.0 (StataCorp). Continuous variable data were reported as means and standard deviations, whereas categorical variable data were reported as frequencies and percentages. If partial continuous variables were raw data, the calculation was converted into means and standard deviations to summarize the results consistently. If the mean or standard deviation was not given, it was calculated from the median, minimum, and maximum values.[64,134] Continuous variables were pooled by calculating the mean and 95% CIs, and dichotomous variables were pooled by calculating the proportion and 95% CI. The I^2 statistic was used to measure the heterogeneity among the included studies. The statistical heterogeneity between the studies was considered low, medium, and high when the I^2 thresholds were <25%, 25-75%, and >75%, respectively. The pooled analysis results were deemed statistically significant at $P < .05$.

RESULTS

Search Results

A total of 1389 relevant articles were identified using the electronic database and search strategy. Of these, 798 were excluded after removing duplicates, and 591 articles remained for screening. Of these, 469 were excluded based on the exclusion criteria. We closely reviewed the full texts of the remaining 122 articles, of which 17 were excluded, leaving 105 studies[§] included in this review (Figure 1).

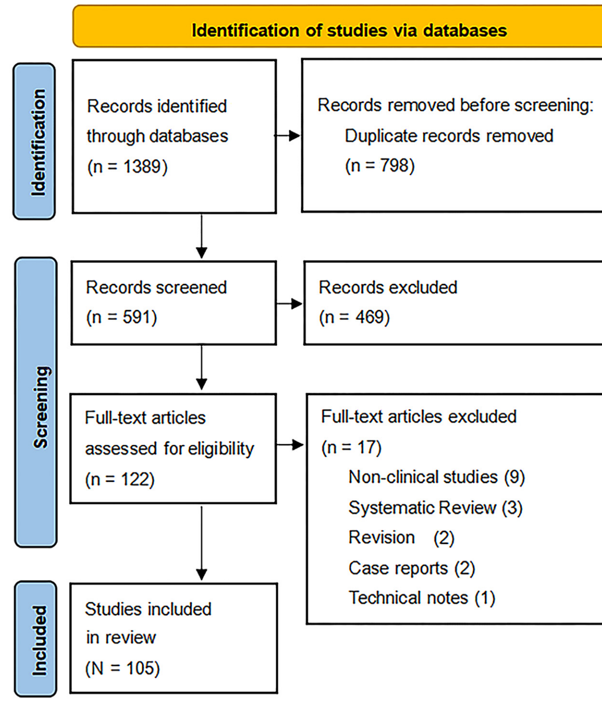

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of study inclusion.

Overall Characteristics and Clinical Outcomes of OCA

Temporal Trends and Country and Injury Site Distributions. The 105 studies included a total of 5952 patients. The annual reported number of patients treated with OCA showed a significant upward trend, from 69 patients in 2001 to 1065 cases in 2020, peaking in 2018 with 1504 cases. No cases were reported in 2002, 2003, and 2006 (Figure 2A). The country distribution of OCA procedures is summarized in Figure 2B. These studies were conducted in 8 countries, the majority of which were performed in the United States (90.12%), followed by Canada (6.23%). The most common location OCA was performed was the knee (88.9%), followed by the ankle (9.73%), shoulder (0.66%), hip (0.59%), and elbow (0.15%) (Figure 2C).

Patient Characteristics. The characteristics of the patients are summarized in Table 1. The mean age of the

[§]References 1-19, 21, 22, 25, 26, 29, 30, 32, 34, 36-45, 47, 49-53, 55-59, 63, 65-68, 70-74, 76-81, 83, 87-92, 95-98, 100-104, 107, 109-113, 115, 117, 118, 127-132, 135, 137-145.

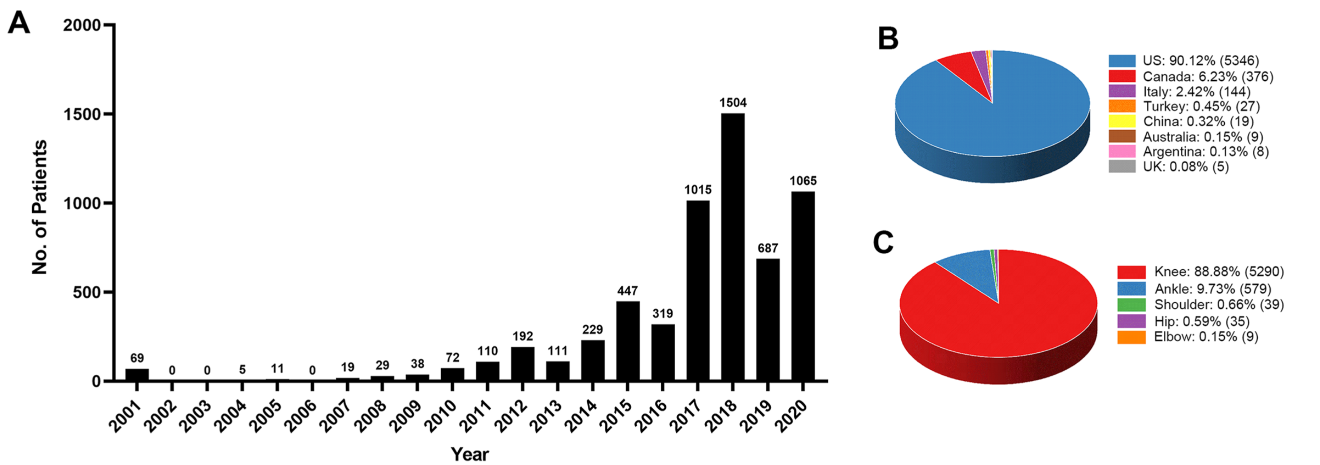

Figure 2. Overall temporal trends, country and injury site distribution of osteochondral allograft transplantation. (A) Annual number of cases reported in studies. (B) The proportion and number of cases reported in studies in different countries. (C) The proportion and number of cases reported in studies in different injury sites.

TABLE 1
Characteristics of the Patients in the Included Studies (N = 5952)

Characteristic	Patients, n	Mean or Proportion (95% CI)	*P*	I^2, %
Age, y	5938	34.2 (32.3-36.0)	<.001	98.8
Sex, %				
Male	5854	60.8 (58.2-63.4)	<.001	74.9
Female	5854	39.2 (36.6-41.8)	<.001	74.9
Body mass index, kg/m^2	4320	26.7 (26.4-27.1)	<.001	85.5
Smoker, %	1149	21.1 (13.4-28.9)	<.001	92.3
Side affected, %				
Left	1108	47.0 (43.7-50.2)	.221	15
Right	1108	53.0 (49.8-56.3)	.221	15
Defect size, cm^2	1872	5.05 (4.45-5.64)	<.001	98.9
Symptom duration, mo	419	38.0 (28.6-47.3)	<.001	96.6
Time to follow-up, mo	4268	54.4 (50.1-58.7)	<.001	99.6
Previous procedure on affected joint, %	2717	77.4 (73.0-81.7)	<.001	90.7
No. of previous surgeries	2788	1.93 (1.75-2.1)	<.001	91.7
Concomitant procedure, %	3318	39.9 (33.9-45.8)	<.001	93.7

patients at the time of surgery was 34.2 years. Most of the patients were male (60.8%). The mean BMI was 26.7 kg/m^2, and 21.1% of the patients were smokers. Right-sided surgery accounted for 53% of all patients. The mean lesion area was estimated at 5.05 cm^2. The mean symptom duration was 38.0 months, and the mean follow-up duration was 54.4 months. Most patients (77.4%) underwent ≥1 operation at the same surgical site before OCA surgery. The affected joints underwent a mean of 1.93 procedures before OCA surgery. OCA was performed alone in most patients (60.1%).

Allograft Characteristics. The graft size was reported in 27 studies[‖] (n = 2244), with a mean graft size of 6.85 cm^2 (95% CI, 6.16-7.54 cm^2). The mean number of grafts used per patient was 1.49 (95% CI, 1.41-1.57) in the 2655 patients reported. Additionally, 57 studies[¶] (n = 2648) mentioned allograft storage temperatures; 40 studies[#] (n = 2026) indicated a preservation temperature of 4°C, 4 studies[6,7,57,103] (n = 47) mentioned temperatures between 2°C and 4°C, and 9 studies[12,104,109,135,137-141] (n = 524) described cold storage. Only 3 studies[63,144,145] (n = 36) used freezing for osteochondral allograft preservation. Furthermore, the details of the storage solution and type

‖References 4, 5, 15, 16, 18, 21, 29, 40, 41, 49-53, 59, 65, 79, 90, 97, 102, 113, 115, 128, 129, 130-132.

¶References 1, 4, 6, 7, 10-12, 15-17, 19, 21, 34, 39-45, 47, 49, 53, 55, 57, 63, 72, 73, 76, 78, 79, 87, 88, 90, 95, 97, 100, 103, 104, 107, 109, 110, 113, 115, 128-131, 135, 137-142, 144, 145.

#References 1, 4, 10, 11, 15-17, 19, 21, 34, 39-45, 47, 49, 53, 55, 72, 73, 76, 78, 79, 87, 88, 90, 97, 100, 107, 110, 113, 115, 128-131, 142.

TABLE 2
Overall Clinical Outcomes of OCA[a]

Characteristic	Patients, n	Mean or Proportion (95% CI)	P	I^2, %
Failure rate, %	4355	18.8 (16.3-21.3)	<.001	81.6
Time to failure, y	2825	4.48 (3.9-5.0)	<.001	99.5
Reoperation rate, %	3094	35.5 (32.5-38.4)	<.001	65.9
Patient satisfaction, %	2355	83.1 (79.7-86.4)	<.001	84.8

[a]OCA, osteochondral allograft transplantation.

of media were examined in 18 studies.[**] Seven studies[1,11,55,72,73,78,110] (n = 325) from Canada reported that osteochondral allografts were stored in Ringer's lactate solution containing 1 g cefazoline and 50,000 units bacitracin per liter. Four studies[15,79,88,115] (n = 238) from the United States reported that grafts were stored in Ringer's lactate solution containing 1 g/L cefazolin and 10 g/mL gentamicin. Four studies[42-45] (n = 113) from Italy reported that grafts were immersed in a solution containing L-glutamine, sodium bicarbonate, and antibiotics. Modified Eagle's medium with different nutrients was included in 3 studies[47,67,142] (n = 45). Among 54 studies[††] mentioning graft preservation duration, except for 3 studies[100,109,142] indicating that the maximum graft preservation duration was 34, 35, and 42 days, all other studies used grafts for <30 days, most of which were between 2 and 4 weeks.

Overall Clinical Outcomes of OCA. In 68 studies[‡‡] (n = 4355) that discussed failure rates, 18.8% of patients had a failed OCA. In total, 35.5% of 3094 patients returned to the operating room at least once for further treatment. The mean time to failure was 4.48 years (Table 2). The Kaplan-Meier survival analysis demonstrated an allograft survival rate of 94% (95% CI, 90.4%-97.5%) of 259 patients 2 years post-transplantation, 87.9% (95% CI, 85.4%-90.5%) of 2114 patients at 5 years, 80% (95% CI, 75.4%-84.6%) of 1860 patients at 10 years, 73% (95% CI, 68.1%-77.9%) of 639 patients at 15 years, 55% (95% CI, 41.3%-68.7%) of 387 patients at 20 years, and 59.4% (95% CI, 50.5%-68.3%) of 118 patients at 25 years (Figure 3A). A total of 33 studies[§§] (n = 2355) had available data regarding patient satisfaction with the results of the OCA procedure. Overall, 83.1% of patients reported being somewhat satisfied with the OCA results (Table 2). Overall trends for annual failures, reoperations, and satisfaction of patients treated with OCA showed no significant trend from 2001 to 2020 (Figure 3, B-D).

**References 1, 11, 15, 42-45, 47, 55, 67, 72, 73, 78, 79, 88, 110, 115, 142.

††References 4, 6-8, 10-13, 15, 17, 19, 21, 39-45, 47, 51, 57, 58, 67, 68, 71, 76, 78, 79, 83, 87, 88, 90, 91, 95, 97, 98, 100, 104, 107, 109, 110, 113, 115, 128, 131, 135, 137-142, 144.

‡‡References 1, 3, 6, 8-13, 15, 19, 21, 25, 26, 32, 34, 36-45, 47, 49-53, 57, 59, 65, 68, 70, 77-79, 88-92, 95, 97, 98, 100-103, 109, 111-113, 115, 118, 127, 129-131, 137-142.

§§References 2, 8, 15, 19, 21, 25, 34, 39-41, 44, 45, 49-53, 65, 68, 71, 90, 97, 107, 111-113, 115, 129-132, 143, 145.

OCA of the Knee

Patient Characteristics and Allograft Details of Knee OCA. Overall, 74 studies[‖‖] reported 5290 patients who underwent knee OCA surgery. The mean age of the patients at the time of surgery was 33.7 years. Most patients were male (60.6%). The patients' mean BMI was 26.7 kg/m^2, and the mean lesion area was estimated at 4.81 mm^2. The mean symptom duration was 28.2 months, and the mean follow-up duration was 58.4 months. Graft size was reported in 25 studies[¶¶] (n = 2213), with a mean graft size of 7.07 cm^2. The mean number of grafts per patient was 1.51 in 2630 patients (Table 3). The most common diagnosis that led to OCA treatment was osteochondral dissecans (37.9%), followed by focal degeneration (22.7%) and acute trauma (20.7%) (Figure 4A).

The most common defect location was the medial femoral condyle (52%), followed by the lateral femoral condyle (27.5%), trochlea (6.9%), patella (6.9%), and tibial plateau (6.8%) (Figure 4B). Most patients (77.3%) underwent a mean of 1.96 procedures on the same knee before OCA surgery (Table 3). The surgical procedures included MST (27%), chondral debridement (17.1%), open reduction and internal fixation (12.2%), loose body removal (9.5%), meniscectomy (7.8%), ligament reconstruction (4.1%), osteotomy (3.9%), meniscal repair (2.9%), chondroplasty (2.4%), ACI (2.2%), OAT (1.7%), OCA (1.7%), hardware removal (1.7%), and others (5.8%) (Table 4).

The most common concomitant procedures were high tibial osteotomy (HTO; 29.4%) and meniscal allograft transplantation (MAT; 25.6%), followed by distal femoral osteotomy (7.9%), tibial tubercle osteotomy (7.0%), ligament reconstruction (7.7%), meniscectomy (6.2%), hardware removal (3.4%), lateral release (3.0%), loose body removal (2.6%), arthroscopy (2.6%), and others (5.7%) (Table 5).

Clinical Outcomes of Knee OCA. According to our analysis, 16.8% of patients failed after OCA of the knee in the 49 included studies (n = 3849); the mean time to failure was 4.53 years (Table 6). Of all failures (n = 472), 258 patients (54.7%) underwent total knee arthroplasty, 133 (28.2%) underwent revision OCA, and 39 (8.3%) underwent

‖‖References 1-5, 8, 10-12, 15-18, 21, 25, 26, 29, 30, 32, 36-38, 41, 44, 47, 50-53, 56, 59, 63, 65, 70, 71, 74, 76-81, 83, 87, 89-92, 95, 97, 98, 101, 102, 104, 109-111, 113, 115, 117, 127-132, 135, 137-143.

¶¶References 4, 5, 15, 16, 18, 21, 29, 41, 50-53, 59, 65, 79, 90, 97, 102, 113, 115, 128, 129, 130-132.

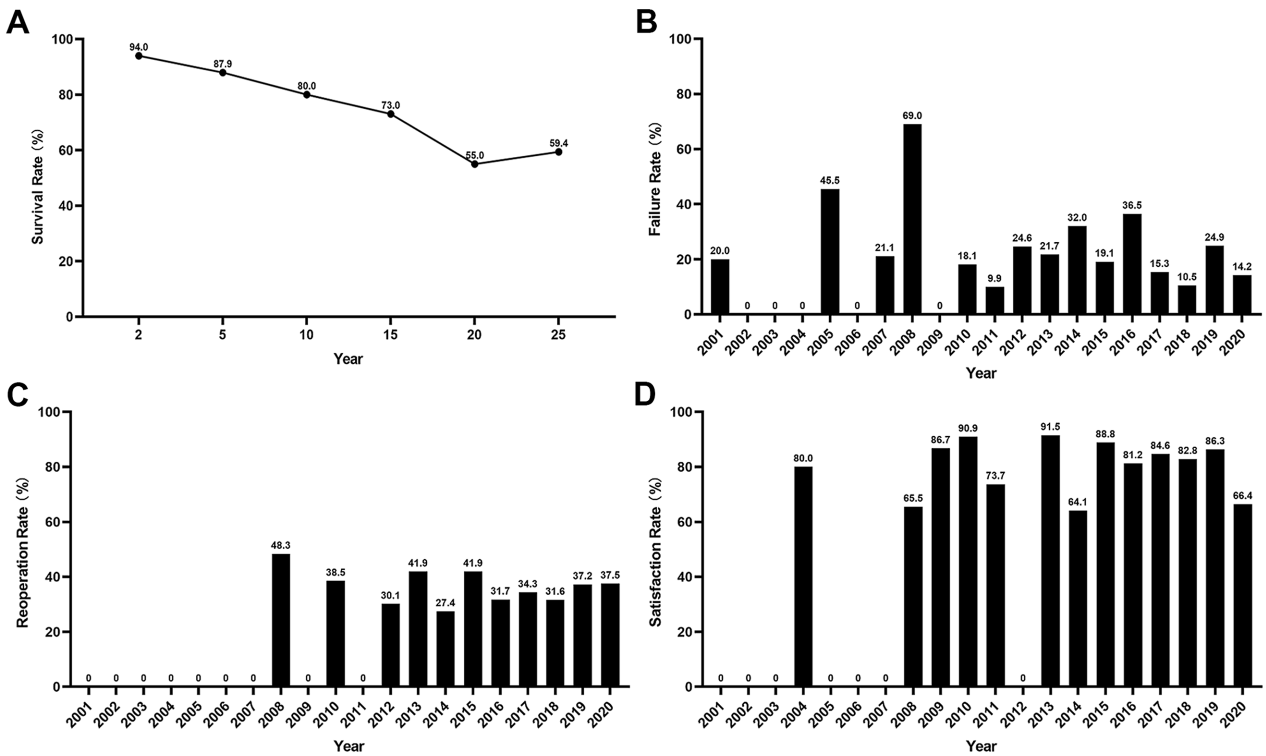

Figure 3. Annual clinical outcomes and variation trends of osteochondral allograft transplantation. (A) Trends in graft survival at 2, 5, 10, 15, 20, and 25 years after transplantation. (B) Annual failure rate and its trends after transplantation. (C) Annual reoperation rate and its trends after transplantation. (D) Annual satisfaction rate and its trends after transplantation. The value of 0 only represents that no relevant study reported the result in that year.

TABLE 3
Patient Characteristics and Allograft Details of Knee OCA[a]

Characteristic	Patients, n	Mean or Proportion (95% CI)	*P*	I^2, %
Age, y	5276	33.7 (31.6-35.8)	<.001	98.8
Sex, %				
Male	5210	60.6 (57.7-63.5)	<.001	77.5
Female	5210	39.4 (36.7-42.3)	<.001	77.5
Body mass index, kg/m^2	4240	26.7 (26.3-27.1)	<.001	85.6
Smoker, %	1093	18.5 (10.1-26.9)	<.001	94.1
Side affected, %				
Left	886	47.0 (43.8-50.3)	.641	0
Right	886	53.0 (49.7-56.2)	.641	0
Defect size, cm^2	1732	4.81 (4.42-5.19)	<.001	95.3
Graft size, cm^2	2213	7.07 (6.34-7.81)	<.001	97.1
No. of grafts	2630	1.51 (1.4-1.6)	<.001	92.5
Symptom duration, mo	353	28.2 (18.7-37.7)	<.001	96.4
Time to follow-up, mo	3658	58.4 (53.3-63.5)	<.001	99.7
Previous procedure on affected joint, %	2685	77.3 (72.9-81.6)	<.001	91.0
No. of previous surgeries	2690	1.96 (1.78-2.15)	<.001	92.3
Concomitant procedure, %	3194	39.6 (33.5-45.7)	<.001	93.8

[a]OCA, osteochondral allograft transplantation.

unicompartmental knee arthroplasty (Table 7). In total, 35.2% of 2843 patients returned to the operating room at least once. The Kaplan-Meier survival analysis demonstrated an allograft survivorship of 94% (95% CI, 90.4%-97.5%) of 259 patients at 2 years after transplantation, 89% of 1923 patients at 5 years (95% CI,

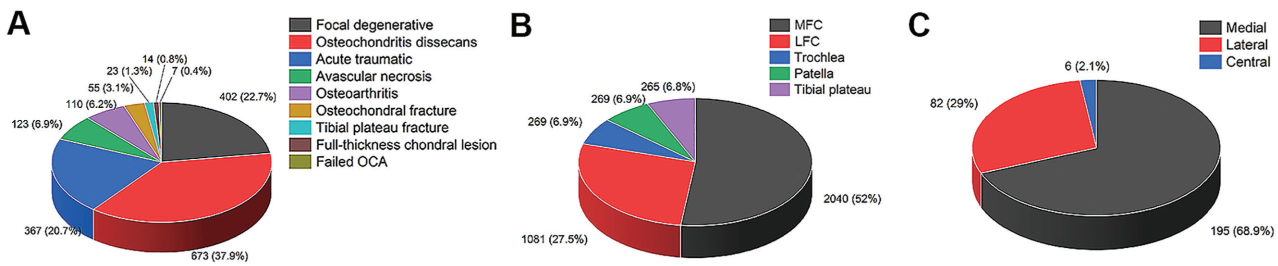

Figure 4. Classifications of knee surgery and specific defect sites in the knee and ankle. (A) The proportion and number of cases reported in studies for etiology of osteochondral allograft transplantation (OCA) performed on the knee. (B) The distribution and number of cases reported in studies for defect location in the knee. (C) The distribution and number of cases reported in studies for defect location in the ankle. LFC, lateral femoral condyle; MFC, medial femoral condyle.

TABLE 4
Types of Operations Performed Before Knee OCA (n = 1784)[a]

Previous Procedure	Patients, n
MST	481
Chondral debridement	305
ORIF	218
Removal of loose bodies	169
Meniscectomy	139
Ligament reconstruction	74
Osteotomy	69
Meniscal repair	52
Chondroplasty	43
ACI	39
OAT	30
OCA	30
Removal of hardware	31
Other[b]	104

[a]ACI, autologous chondrocyte implantation; MST, marrow stimulation technique; OAT, osteochondral autograft transfer; OCA, osteochondral allograft transplantation; ORIF, open reduction and internal fixation.

[b]Irrigation and debridement, n = 2; cartilage biopsy, 3; trochleoplasty, 1; arthroplasty, 1; bone allograft, 5; mosaicplasty, 2; synthetic scaffold, 12; meniscal allograft transplantation, 26; ligament repair, 6; lateral release, 9; lysis of adhesions, 7; bone grafting, 10; extensor mechanism surgery, 15; external fixation, 1; external fixation and fasciotomy, 1; incision and drainage, 1; incision and drainage of abscess, 1; partial patellectomy, 1.

86.6%-91.5%), 83.4% of 1621 patients at 10 years (95% CI, 79.6%-87.2%), 73% of 639 patients at 15 years (95% CI, 68.1%-77.9%), 55% of 387 patients at 20 years (95% CI, 41.3%-68.7%), and 59.4% of 118 patients at 25 years (95% CI, 50.5%-68.3%). A total of 23 studies (n = 1990) had patient satisfaction data regarding the results of the knee OCA procedure; 84.7% of patients reported being at least somewhat satisfied with the results of knee OCA (Table 6).

TABLE 5
Procedures Concomitant to Knee OCA (n = 1048)[a]

Concomitant Procedure	Patients, n
HTO	308
MAT	268
DFO	83
TTO	73
Ligament reconstruction	70
Meniscectomy	65
Removal of hardware	36
Lateral release	31
Removal of loose bodies	27
Arthroscopy	27
Other[b]	60

[a]DFO, distal femoral osteotomy; HTO, high tibial osteotomy; MAT, meniscal allograft transplantation; OCA, osteochondral allograft transplantation; TTO, tibial tubercle osteotomy.

[b]microfracture, n = 19; realignment osteotomy, 11; anteromedialization, 6; meniscal repair, 5; trochleoplasty, 5; marrow stimulation technique, 3; proximal patellofemoral realignment, 3; anterior release, 2; epiphysiodesis, 2; debridement, 1; posterolateral corner reconstruction, 1; synovectomy, 1; lateral imbrication, 1.

OCA of the Ankle

Patient Characteristics and Allograft Details of Ankle OCA. A total of 25 studies[##] reported 579 patients who underwent ankle OCA. The mean age of the patients at the time of surgery was 38.6 years. Most patients were men (61.4%). The mean BMI was 26.9 kg/m^2, and the mean lesion area was 1.48 mm^2. The mean symptom duration was 57.8 months, and the mean follow-up duration was 47.6 months. Graft size was reported in 2 studies[40,49] (n = 31), with a mean graft size of 3.64 cm^2. The most

[##]References 6, 7, 9, 13, 14, 19, 22, 34, 39, 40, 42, 43, 45, 49, 55, 57, 58, 66-68, 88, 103, 107, 118, 144.

TABLE 6
Clinical Outcomes of Knee OCA[a]

Characteristic	Patients, n	Mean or Proportion (95% CI)	*P*	I^2, %
Failure rate, %	3849	16.8 (14.3-19.4)	<.001	81.6
Time to failure, y	2598	4.53 (3.87-5.18)	<.001	99.6
Reoperation rate, %	2843	35.2 (32.2-38.3)	<.001	64.2
Patient satisfaction, %	1990	84.7 (81.1-88.3)	<.001	85.3

[a]OCA, osteochondral allograft transplantation.

TABLE 7
Reoperations in Knee After OCA Failure (n = 472)[a]

Procedure	Patients, n
TKA	258
Revision OCA	133
UKA	39
Chondroplasty	12
Graft removal	9
Patellofemoral arthroplasty	7
Repeat OCA	5
Patellectomy	5
PKA	3
Arthrodesis	1

[a]OCA, osteochondral allograft transplantation; PKA, partial knee arthroplasty; TKA, total knee arthroplasty; UKA, unicompartmental knee arthroplasty.

common defect location was the medial talus (68.9%), followed by the lateral (29%) and central talus (2.1%) (Figure 4C). Most patients (78.9%) underwent ≥1 operation on the same ankle. The affected joints underwent a mean of 1.59 procedures before OCA surgery. OCA was performed alone in most patients (71.3%), and other concomitant procedures were performed in 28.7% of patients (Table 8).

Clinical Outcomes of Ankle OCA. According to this analysis, 26.2% of patients had failed after ankle OCA in the 16 included studies[a] (n = 470). The mean time to failure was 3.41 years. In total, 36.5% of 251 patients returned to the operating room at least once for further treatment. The Kaplan-Meier survival analysis demonstrated an allograft survivorship rate of 78.1% (95% CI, 71%-85.2%) in 191 patients at 5 years after transplantation and 62% (95% CI, 46.9%-77%) in 239 patients at 10 years post-transplantation. Eight studies[b] (n = 328) had available data regarding patient satisfaction with ankle OCA, with 76.7% of patients being at least somewhat satisfied with the results (Table 8).

OCA of the Shoulder, Hip, and Elbow

For the shoulder, 2 studies[112,145] reported 39 patients who underwent shoulder OCA. Patients with OCA for reverse Hill-Sachs lesions after acute locked posterior shoulder joint dislocation have significantly improved function, a low degree of osteoarthritis, and excellent clinical outcomes compared with preoperative results.[84,145] Riff et al[112] concluded that OCA was a feasible treatment option for humeral head osteochondral defects. Regarding OCA of the hip, Oladeji et al[100] (n = 10), Khanna et al[72] (n = 17), and Kosashvili et al[73] (n = 8) analyzed the clinical and radiological results of OCA in patients with sizable femoral head osteochondral defects and considered fresh OCA (OCA using a freshly preserved graft) a reasonable choice for young patients with hip cartilage defects. For OCA of the elbow, Mirzayan[96] (n = 9) first reported fresh OCA to treat osteochondritis dissecans of the capitellum in 2016 in 9 male baseball players, showing that OCA significantly improved throwing function, reduced pain, and allowed all patients to resume sports.

DISCUSSION

OCA has become increasingly established and used clinically for >40 years as a cartilage restoration technique for treating focal articular cartilage defects.[20,82,123] The past 2 decades have shown an increase in research related to damaged articular cartilage repair with OCA.[35] This review demonstrated an increasing trend in the number of English-published articles on OCA from 2001 to 2020. The number of published articles in 2018 was 8 times greater than in 2000. The number of included cases was approximately 21.8 times greater, reflecting the growing interest of cartilage repair researchers in OCA. This analysis presented the cases studied in the United States, the dominant location among clinical studies of OCA, with 90.1% of global cases over the past 20 years. The widespread use of OCA programs in the United States may be due to the adequate development of OCA technology, the commercial availability of freshly stored osteochondral allografts, and reported clinical success.[20,35,82,122] In contrast, the availability of OCA in other countries is lower, which is most likely due to the meager donor rates resulting from cultural and educational differences among the populations, making OCA grafts scarce and expensive.[54,116,119,120]

OCA is a restorative cartilage technique that can restore joint function in the knee, hip, ankle, and shoulder joints in patients with symptomatic articular cartilage defects and is currently used in treating knee cartilage injury.[35,82,122] Our study showed that the number of cases studied in the knee accounted for 88.9% of all cases over

[a]References 6, 9, 13, 19, 34, 39, 40, 42, 43, 45, 49, 57, 68, 88, 103, 118.
[b]References 19, 34, 39, 40, 45, 49, 68, 107.

TABLE 8
Characteristics and Clinical Outcomes of Ankle OCA[a]

Characteristic	Patients, n	Mean or Proportion (95% CI)	*P*	I^2, %
Age, y	579	38.6 (37.0-40.1)	<.001	85.6
Sex, %				
Male	570	61.4 (54.3-68.5)	<.001	68.1
Female	570	38.6 (31.5-45.7)	<.001	68.1
Body mass index, kg/m^2	70	26.9 (24.5-29.4)	<.001	89.6
Smoker, %	27	22.0 (6.4-37.6)	.758	0
Side affected, %				
Left	178	49.7 (39.5-60.0)	.033	50.4
Right	178	50.3 (40.0-60.5)	.033	50.4
Defect size, cm^2	121	1.48 (1.31-1.65)	.055	53.7
Graft size, cm^2	31	3.64 (3.41-3.87)	.494	0
Symptom duration, mo	38	57.8 (20.5-95.1)	<.001	96.6
Time to follow-up, mo	547	47.6 (38.9-56.3)	<.001	99.3
Previous procedure on affected joint, %	32	78.9 (45.7-12.2)	.014	83.5
No. of previous surgeries	78	1.59 (1.08-2.09)	.004	77.7
Concomitant procedure, %	105	28.7 (19.0-38.3)	.29	20.0
Failure rate, %	470	26.2 (18.6-33.8)	<.001	73.1
Time to failure, y	217	3.41 (1.86-4.97)	<.001	98.6
Reoperation rate, %	251	36.5 (23.9-49.2)	.001	75.7
Patient satisfaction, %	328	76.7 (67.2-86.3)	<.001	77.3

[a]OCA, osteochondral allograft transplantation.

the past 20 years. OCA is primarily used to repair knee and ankle cartilage damage; however, there are fewer data on OCA for cartilage repair in the shoulder, hip, and elbow than in the knee or ankle. Therefore, future clinical research with long-term follow-up is needed to evaluate this technique's indications and clinical efficacy in shoulder, hip, and elbow cartilage injuries.

Since OCA is mainly used for knee cartilage defects, the overall clinical characteristics and results of OCA are similar to the knee. For OCA of the knee, our analysis showed the mean age of the patients was 34 years, and 61% were male. Therefore, OCA is suitable for young, athletic male patients, because they want to restore high activity levels. Studies have shown less effective outcomes in patients with OCA >30 years of age.[24,124] OCA grafts are likely to fail in older adults due to other combined confounders, such as concurrent disease and prior surgeries; therefore, surgeons tend to perform total knee arthroplasty to achieve generally good results for these patients.[38,85,123] The studies we reviewed showed that patients treated with knee OCA had a mean BMI of 26.7 kg/m^2. For some obese patients, OCA can also provide a successful option for the medium-term treatment of knee cartilage defects.[140] Our analysis showed that knee cartilage defects mainly occurred in the medial femoral condyle.

Articular cartilage defects in the knee can be caused by various factors such as trauma, degeneration, avascular necrosis, osteochondritis dissecans, or osteoarthritis. The principal diagnosis in patients treated with OCA is osteochondritis dissecans. Therefore, osteochondritis dissecans is the best indication for OCA, followed by degenerative lesions and acute trauma.[86] Furthermore, we found that common surgical procedures included chondral debridement and MSTs before knee OCA surgery. Traditionally, because of the expensive and complicated nature of OCA, it is often considered a second-line treatment after debridement or MST failures, and some authors believe that previous debridement and MST affects the outcome of OCA and suggest considering OCA as the preferred first-line treatment.[111] Studies analyzing the impact of various previous cartilage repair surgeries on the outcomes of OCA concluded that OCA can be a salvage surgical treatment after the failure of previous cartilage repair surgery.[51,141]

We found that the most common concomitant procedures were HTO and MAT. As knee joints with varus deformity accelerate the degeneration of the surrounding cartilage and joints by increasing their mechanical load, HTO is increasingly used as an auxiliary surgery for cartilage repair by optimizing the biomechanical microenvironment in the medial compartment. Several studies have shown that combining HTO and OCA is safe and effective for treating knee cartilage injury and has achieved satisfactory clinical results.[3,8,65,81] Meniscal loss leads to the development of cartilage lesions, and MAT and OCA are considered symbiotic surgeries due to their complementary indications and contraindications.[41] Most patients who had failed knee OCA underwent total knee arthroplasty. This suggests that total knee arthroplasty is the preferred treatment after cartilage repair failure.[69] Our data analysis showed a mean failure rate after knee OCA of 16.8%. Mathews et al[86] described 5- and 10-year survival rates of 95% and 85%, respectively, after knee OCA, consistent with the results of this review. Studies have reported overall satisfaction with 88.1% of knee OCA, and the satisfaction of patients who underwent OCA for osteochondritis dissecans could be as high as 95.6%.[132]

For OCA of the ankle, our analysis showed the mean age of the patients was 39 years, and 61% were male.

Ankle cartilage defects mainly occurred in the medial talus, followed by the lateral, with the fewest cases concerning the central region. The distribution pattern of talar osteochondral lesions described by Dahmen et al[27] and van Diepen et al[133] agrees with the analysis in this review. Our data analysis showed that the mean failure rate after ankle OCA reached 26.2%.

And analysis demonstrated allograft survivorship of 78.1% at 5 years and 62% at 10 years, with an overall patient satisfaction rate of 76.7%. Higher failure rates and lower allograft survival rates were observed in the ankle than in the knee at 5 and 10 years after OCA. Further extensive studies are needed to analyze the causes of ankle osteochondral allograft postoperative failure compared with the knee.[118]

Many studies have described graft storage methods, but there is a lack of consensus regarding the optimal storage conditions for osteochondral allografts. Regarding the graft preservation temperature, frozen allografts are thought to lack chondrocyte activity and decrease cartilage viability, leading to inferior clinical outcomes compared with fresh allografts. Therefore, freshly stored grafts are the preferred surgical choice.[20,61,119,126] We found that the most commonly used preservation protocol for clinical grafts is the standard hypothermic protocol (4°C). It has been shown that the grafts were significantly improved when stored at 22°C to 25°C or 37°C compared with a storage temperature of 4°C, yet some studies have also shown opposing results[60,125]; thus, these temperatures cannot be used to determine the optimal preservation temperature.[126] Regarding allograft storage and methodology, different countries have different conservation programs. The optimal approach for allograft preservation before OCA remains controversial; studies have shown that chondrocyte viability is greatly reduced when the allograft is stored beyond 15 days, and chondrocytes survive up to 28 days before implantation.[20,91] The short allograft preservation period causes logistical problems, such as donor tissue acquisition, transportation, processing, and time constraints. These logistical problems before the donor graft transplant and the high cost of the graft have seriously limited the use of OCA.[48,86,126] Therefore, more intensive scientific research on safe and effective storage processes and methods of allografts can improve current practices, thus improving the clinical availability of OCA surgery.

Limitations

This study has some limitations. The primary limitation was the high heterogeneity of included studies. Due to limited available data, clinical control studies comparing OCA and other surgical procedures, follow-up studies on clinical outcomes solely on OCA, and all other clinical studies related to OCA were included in the analysis. Therefore, the overall quality of the included studies was relatively low. Second, due to the different focuses of clinical outcomes of OCA in different studies, the evaluation protocol for clinical outcomes could not be precisely quantified. Finally, data on failure details and complications were lacking, and the causes of failure could not be analyzed separately. Therefore, more high-quality, high-sample, multicenter randomized controlled trials for the clinical application of OCA could provide a more accurate evaluation of OCA's clinical efficacy.

CONCLUSION

OCA has attracted significant research interest over the past 20 years, and the overall annual number of patients undergoing the procedure showed a significant upward trend, especially from 2016 to 2020. A majority of studies have been conducted in the United States. Patients receiving OCA were predominantly overweight, young adults, with most having had previous surgery at the same surgical site. The use of OCA is more established for cartilage injury in the knee than in other sites, and its best indication based on outcomes is osteochondritis dissecans. The results of our analysis demonstrated satisfactory long-term postoperative outcomes of OCA at all locations. More basic and clinical scientific research can improve the availability of OCA surgery in clinics and articular cartilage at other sites.

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