Systematic Review

Outcomes of Osteochondral Allograft Transplantation in the Knee

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Purpose: The objectives of this study were (1) to conduct a systematic review of clinical outcomes after osteochondral allograft transplantation in the knee and (2) to identify patient-, defect-, and graft-specific prognostic factors. **Methods:** We searched PubMed, Medline, EMBASE, and the Cochrane Central Register of Controlled Trials. Studies that evaluated clinical outcomes in adult patients after osteochondral allograft transplantation for chondral defects in the knee were included. Pooled analyses for pertinent continuous and dichotomous variables were performed where appropriate. **Results:** There were 19 eligible studies resulting in a total of 644 knees with a mean follow-up of 58 months (range, 19 to 120 months). The overall follow-up rate was 93% (595 of 644). The mean age was 37 years (range, 20 to 62 years), and 303 patients (63%) were men. The methods of procurement and storage time included fresh (61%), prolonged fresh (24%), and fresh frozen (15%). With regard to etiology, the most common indications for transplantation included post-traumatic (38%), osteochondritis dissecans (30%), osteonecrosis from all causes (12%), and idiopathic (11%). Forty-six percent of patients had concomitant procedures, and the mean defect size across studies was 6.3 cm^2. The overall satisfaction rate was 86%. Sixty-five percent of patients (72 of 110) showed little to no arthritis at final follow-up. The reported short-term complication rate was 2.4%, and the overall failure rate was 18%. Heterogeneity in functional outcome measures precluded a meta-analysis; a qualitative synthesis allowed for the identification of several positive and negative prognostic factors. **Conclusions:** Osteochondral allograft transplantation for focal and diffuse (single-compartment) chondral defects results in predictably favorable outcomes and high satisfaction rates at intermediate follow-up. Patients with osteochondritis dissecans and traumatic and idiopathic etiologies have more favorable outcomes, as do younger patients with unipolar lesions and short symptom duration. Future studies should include comparative control groups and use established outcome instruments that will allow for pooling of data across studies. **Level of Evidence:** Level IV, systematic review of Level IV studies.

Managing large osteochondral defects of the knee in young to middle-aged patients poses a difficult problem for orthopedic surgeons. In the setting of bony defects, as well as for larger chondral lesions, treatments such as microfracture, autologous chondrocyte implantation (ACI), and osteochondral autograft transfer may be inadequate, leaving osteochondral allograft transplantation as the main treatment option.[1] Osteochondral allografts are also indicated in patients after failure of other cartilage repair technologies for chondral defects.

The main advantage of using allograft is the presence of both viable hyaline cartilage and structural bone.[2] Historically, grafts were implanted within 24 hours of procurement, but concerns about disease transmission have led to a minimum of 14 days required for aerobic, anaerobic, and spore forming bacteria, as well as, viral testing before release. In addition, aseptically processed prolonged fresh grafts are most commonly used and maintained at 4°C as opposed to frozen or cryopreserved grafts.[3] Unfortunately, it is known that chondrocyte viability decreases in allografts stored for more than 14 days, and allografts

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The authors report that they have no conflicts of interest in the authorship and publication of this article.

Received November 2, 2012; accepted December 4, 2012.

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0749-8063/12716/$36.00
http://dx.doi.org/10.1016/j.arthro.2012.12.002

generally should be implanted by 24 days.[4,5] Notably, frozen allografts have inferior biological and biomechanical properties compared with fresh allografts.[6]

Fresh osteochondral allograft transplantation was initially used to treated osteochondral defects after trauma or tumor; however, its indications have expanded to include acute and degenerative chondral defects of the knee (osteoarthritis, spontaneous osteonecrosis of the knee [SONK], avascular necrosis, inflammatory conditions).[1,7,8] Most commonly implanted in the femoral condyle, allograft can also be implanted in the tibial plateau, the femoral trochlea, and the patella; case series also report its use in more than one area of the knee at a time.[7,8] Other variables in the allograft literature include the size of the lesion treated, the use of concomitant procedures (high tibial osteotomy, distal femoral osteotomy, meniscal allograft), patient age, and the number of previous procedures. As such, there are clearly a large number of patient- and defect-specific variables that impact the outcomes after fresh osteochondral allograft transplantation. Despite multiple case series published over the course of 3 decades, there has been no attempt to conduct a systematic review of outcomes after osteochondral allograft transplantation in the current literature.

The objectives of this study were (1) to conduct a systematic review of clinical outcomes after osteochondral allograft transplantation in the knee and (2) to identify patient-, defect-, and graft-specific prognostic factors. We hypothesized that the use of fresh osteochondral allograft in the knee would result in good functional outcomes but would be less reliable in the setting of degenerative or multifocal disease, osteonecrosis, and with the use of delayed-fresh and fresh-frozen allograft.

Methods

Literature Search

With the aid of an experienced librarian, we searched PubMed (1948 to week 2 of July 2012), Medline (1946 to week 1 of July 2102), EMBASE (1947 to week 27 of 2012), and the Cochrane Central Register of Controlled Trials (to week 2 of July 2012). This was performed using the following key words: (knee) AND (cartilage OR chondral OR osteochondral) AND (transplant*) AND (allograft). General search terms were used to prevent the possibility of missing relevant studies. The references of all applicable studies and review articles were also manually cross-referenced to ensure completeness.

Inclusion criteria were (1) studies that reported clinical outcomes after allograft transplantation in the knee, either in isolation or in combination with meniscal allograft transplantation or osteotomy; (2) adult patients aged 18 years or older; (3) osteochondral allograft transplants performed for pain due to osteochondritis dissecans (OCD), post-traumatic defects, idiopathic causes, or failed prior cartilage repair procedures (microfracture, ACI, and so on); (4) minimal clinical follow-up of 12 months; and (5) minimum of 10 patients in the study. We excluded (1) technique articles, (2) case reports, (3) narrative reviews, (4) studies in which procedures were performed in association with ligamentous reconstruction, and (5) studies in which the primary indication was for treatment of tuberculosis or tumor of the knee.

Data Abstraction

Each study that met the inclusion criteria was reviewed independently by 2 reviewers. Disagreement was resolved by discussion. Data were abstracted by one reviewer and verified by a physician with advanced training in clinical epidemiology. Study data that were determined to be of interest a priori included year of publication, type of study, level of evidence, study period, inclusion/exclusion criteria, number of patients, age, gender, length of follow-up, loss to follow-up, number of preceding surgeries, preservation method of the allograft (fresh, prolonged fresh, fresh frozen), location of the lesion in the knee, single or multiple lesions, etiology (OCD, post-traumatic, failed prior surgery, avascular necrosis), lesion size, number of lesions, plug size, concomitant procedures, and prior surgical treatments. The modified Coleman score was used to assess the quality of each of the included studies.[9,10]

Preoperative and postoperative data that were available were collected, including functional outcome scores (International Knee Documentation Committee [IKDC], Lysholm, Tegner, Merle D'Aubigné-Postel, Marx Activity Rating Scale, Cincinnati Sports Activity Scale, Short Form 12 [SF-12], Short Form 36 [SF-36], Knee Injury and Osteoarthritis Outcome Score [KOOS], Noyes), return to sport, patient satisfaction, histology, radiographic outcomes (union, arthritis), Kaplan-Meier survival curves, complications, failure rates, and prognostic factors.

Statistical Analysis

General and demographic characteristics including age, gender, etiology, graft type and processing, and follow-up were pooled across eligible studies. Although weighted means were used when applicable, a comparison of weighted means could not be performed with statistical integrity. A majority of the studies reported their results as mean values without standard deviations. In addition, whereas some studies used validated outcome scores, others used subjective personal assessments based on the clinicians' own functional and pain scores. Given the heterogeneity of functional outcomes used across studies, a meta-analysis was unable to be performed.

Results

The search results are summarized in Fig 1. Approximately 144 articles from Medline, 168 articles from

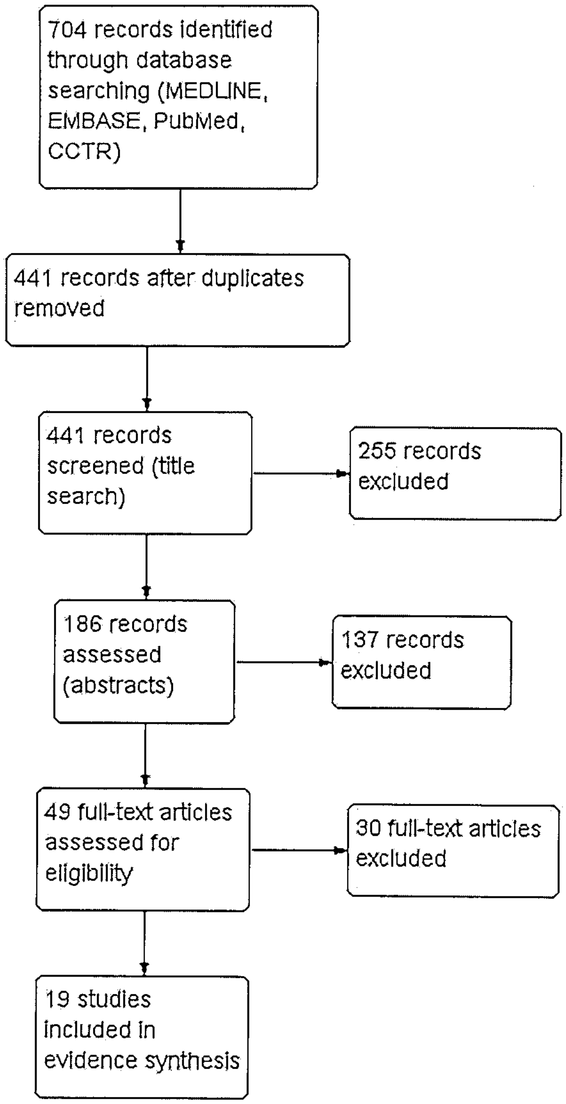

Fig 1. Search strategy results. (CCTR, Cochrane Central Register of Controlled Trials.)

EMBASE, 3 articles from the Cochrane Central Register of Controlled Trials, and 389 articles from PubMed were cited over a 64-year period (1948 to 2012), for a total of 704 articles. After duplicates were removed, 441 articles remained. After titles were reviewed and excluded for the following, 186 articles remained: sites unrelated to the knee (e.g., shoulder, talus, or hip), isolated meniscus allograft transplantation, anterior cruciate ligament reconstruction, posterior cruciate ligament reconstruction, and osteoarticular transplantation for tuberculosis or tumor cases. After an abstract review in which case reports, technique articles, and review articles were excluded, 49 eligible studies remained for full review. In the case in which a single center reported outcomes on a procedure over several time points, the study with the longest follow-up was included. Two authors independently reviewed 19 articles that met the inclusion criteria for this study. All included studies were retrospective cases series (Level IV) with the exception of 2 prospective trials (Level IV).[11,12] Articles investigated fresh (8 studies),[7,8,11-16] delayed-fresh (5 studies),[2,17-20] fresh-frozen (5 studies),[21-25] and mixed allografts (1 study).[26]

General Characteristics

The general characteristics of included studies are summarized in Table 1. All studies were Level IV retrospective (17 studies) or prospective (2 studies) case series. Overall, 595 of 644 knees (92.4%) were available at a mean follow-up of 58 months (range, 19 to 120 months).

Modified Coleman methodology scores ranged from 19 to 45, with a mean of 34 and mode of 41. These scores are considered poor,[27] likely related to their Level IV study design. The study quality improved with later dates of publication (moderate correlation, $r^2 = 0.52$).

Processing. The methods of procurement and storage time included fresh (n = 362), prolonged fresh (n = 142), and fresh frozen (n = 91). One study had 3 processing methods: autograft (n = 24), prolonged fresh (n = 12), and fresh frozen (n = 12).[26] The knees treated with autograft transplants were not factored into any statistical analysis presented in this report.

Defect Location and Etiology. The location of the allograft included all or a portion of the medial femoral condyle (n = 261), lateral femoral condyle (n = 142), patella (n = 45), trochlea (n = 20), tibial plateau (n = 77), and bipolar locations (n = 16).

Overall, the indications for transplantation in the included studies were post-traumatic (n = 205, 38%), OCD (n = 158, 30%), osteonecrosis from all causes (n = 64, 12%), idiopathic (n = 59, 11%), osteoarthritis (n = 24, 5%), and chondromalacia patella (n = 17, 3%). The distribution of etiologies according to graft processing is described in detail in Table 2.

Demographics

The general demographics of the included studies and details regarding lesion size, plug size, concomitant procedure, and prior surgical treatment are outlined in Table 3. There were 303 men in the studies that reported gender,[2,7,8,11,12,14-20,22-25] representing 63% of the total study population. The mean age across all studies was 37 years (range, 20 to 62 years).

Thirteen studies reported on prior operative procedures.[2,11,12,14-20,23,24] Past surgical treatment included arthroscopic debridement of osteochondral defects, arthroscopic loose body removal, microfracture, and OCD lesion fixation. These studies did not discuss the types of conservative treatment measures that were

Table 1. Study Characteristics

Author	Method of Processing	Type of Study	Level of Evidence	Location of Allograft	Etiology	No. at Follow-up	Effective Follow-up (%)	Follow-up Length [Mean (Range)] (mo)
Bakay et al.[21]	Frozen	Retro	IV	MFC, LFC, TC, patella, BP	OA, OCD, post-traumatic	33	100	19 (10-38)
Davidson et al.[22]	Frozen	Retro	IV	MFC, trochlea, MFC + trochlea	OCD, trauma	10	100	40 (20-60)
Flynn et al.[23]	Frozen	Retro	IV	LFC, MFC	Trauma, SLE, post-txp, IBD, SONK	15	100	51 (24-109)
Karataglis and Learmonth[24]	Frozen	Retro	IV	MFC, LFC, trochlea	OCD, AVN	5	100	33 (30-36)
Scully et al.[25]	Frozen	Retro	IV	MFC, LFC	NA	16	100	41
Gortz et al.[17]	Delayed fresh	Retro	IV	LFC, MFC, BP, multiple	Steroids	22	96	67 (25-235)
Krych et al.[2]	Delayed fresh	Retro	IV	MFC, LFC, trochlea	Trauma, OCD, idiopathic	43	100	30 (12-132)
LaPrade et al.[18]	Delayed fresh	Retro	IV	MFC, LFC, multiple	OCD, idiopathic	23	100	36 (23-48)
McCulloch et al.[19]	Delayed fresh	Retro	IV	MFC, LFC, multiple	Trauma, OA, OCD, AVN	23	100	35 (24-67)
Williams et al.[20]	Delayed fresh	Retro	IV	MFC, LFC	OCD, OA, AVN	19	100	48 (21-68)
Bayne et al.[7]	Fresh	Retro	IV	MFC, LFC, PF, BP	Trauma, SONK, steroids, OCD	28	100	58 (24-120)
Chu et al.[13]	Fresh	Retro	IV	MFC, LFC, TC, patella, BP, multiple sites	Trauma, OCD, AVN, OA	55	100	BP, 79 (39-129); UP, 74 (11-14)
Convery et al.[8]	Fresh	Retro	IV	MFC, LFC, PF, BP	Trauma, OCD, AVN, OA	38	42	MFC, 45 (24-84); LFC, 57 (25-96); PF, 60 (25-96)
Emmerson et al.[14]	Fresh	Retro	IV	MFC, LFC	OCD	65	98	92 (24-264)
Garrett[15]	Fresh	Retro	IV	LFC	OCD	17	100	42 (24-108)
Gross et al.[11]	Fresh	Prosp	II	MFC, LFC, TP	Trauma, OCD, AVN, OA	MFC/LFC, 60; TP, 65	MFC/LFC, 83; TP, 97	MFC/LFC, 120 (58-259); TP, 142 (24-288)
Jamali et al.[16]	Fresh	Retro	IV	Patella, trochlea	Trauma	20	100	94 (24-214)
Rue et al.[12]	Fresh	Prosp	IV	MFC, LFC	NA	14	93	35 (23-60)
Pearsall et al.[26]	Fresh/frozen	Retro	IV	MFC, LFC, PF	Trauma, OCD	24	83	37 (24-63)

AVN, avascular necrosis; BP, bipolar; IBD, inflammatory bowel disease; LFC, lateral femoral condyle; MFC, medial femoral condyle; NA, not available; OA, osteoarthritis; PF, patellofemoral; post-txp, after renal transplant; Prosp, prospective; Retro, retrospective; SLE, systemic lupus erythematosus; TC, tibial condyle; TP, tibial plateau; UP, unipolar.

Table 2. Distribution of Clinical Indications for Osteochondral Allograft Transplantation According to Graft Processing

	Idiopathic	OA	OCD	Post-traumatic	Chondromalacia Patella	Avascular Necrosis	SONK	Steroid-Induced Osteonecrosis	Other*
Fresh frozen (n = 63)	0%	22% (14)	19% (12)	38% (24%)	8% (5)	2% (1)	2% (1)	0%	9% (6)
Delayed fresh (n = 138)	32% (44)	7% (9)	17% (24)	22% (30)	0%	1% (3)	0%	20% (28)	0%
Fresh (n = 326)	5% (15)	0.3% (1)	37% (122)	45% (151)	4% (12)	5% (16)	2% (6)	1% (3)	0%

OA, osteoarthritis.
*Inflammatory bowel disease, after transplant, and systemic lupus erythematosus.

undertaken before the prior surgical procedures. The mean weighted number of prior surgeries for these studies was 1.7 per person (range, 1.2 to 2.6).

Many studies also included additional concomitant surgical procedures that may have confounded results (co-intervention bias).[11,12,14,16,18-22,24-26] These studies included high tibial osteotomies, distal femoral osteotomies, meniscal transplants, and lateral retinacular release. Of the studies that included the number of concomitant procedures, the aggregate percentage was 46% of patients who underwent simultaneous procedures.

Eight studies reported the mean lesion size of the articular surface.[2,12,17-20,22,26] The aggregate mean size of the defect that was filled with an allograft transplant was 6.3 cm^2 (range, 4.2 to 10.8 cm^2). However, only 6 studies reported the mean allograft plug size.[13,14,16,19,25,26] The aggregate mean size of the plug size was 7.1 cm^2 (range, 2.2 to 9.3 cm^2).

Functional Outcome Scores

Functional outcomes are listed in Table 4. There are 18 different outcome measures recorded for the 19 articles. The IKDC score was measured by 6 studies (4 of these used prolonged-fresh allograft).[2,12,14,17-19] The aggregate mean preoperative IKDC score was 37.1, and the postoperative value was 64.3. All studies showed a significant increase in the postoperative value. When the prolonged-fresh data were aggregated (4 studies), the mean preoperative IKDC value was 43.3 and the postoperative value was 71.0.

Of the 19 studies, 5 included their own subjective scores of excellent, good, fair, or poor.[7,8,13,14,21] When using fresh-frozen allografts, Bakay et al.[21] and Flynn et al.[23] reported 13 excellent (37%), 12 good (34%), 4 fair (11%), and 6 poor (17%) results for allografts for either the medial or lateral femoral condyle. Bakay et al. also rated the outcomes of patellar and tibial plateau allografts. The patellar allografts had 2 excellent (25%), 4 good (50%), 2 fair (25%), and no poor results. The tibial plateau allografts had one excellent (20%), 2 good (40%), one fair (20%), and one poor (20%) result. All bipolar grafts had poor outcomes.

Four of the 19 studies used the Lysholm score,[12,19,22,24] and 3 used the Tegner scale.[12,22,24] The aggregate preoperative Lysholm score was 39.3, and the postoperative score was 70.1. The aggregate preoperative Tegner score was 3.9, and the postoperative score was 5.5. Both postoperative results were significantly different compared with baseline scores.

Fresh-Frozen Allografts. Davidson et al.[22] investigated the histology and compared the allograft and patient's own chondrocytes and matrix. There was no significant difference between allograft and host thickness of articular cartilage, chondrocyte cellular viability, and chondrocyte cell density. Karataglis and Learmonth[24] saw

Table 3. Study Demographics

Author	Age [Mean (Range)] (yr)	Male Gender [n (%)]	Concomitant Procedure [n (%)]; Most Common Procedure	Lesion Size [Mean (Range)] (cm^2)	Plug Size (cm^2)	Prior Surgery (%); Mean No. of Procedures per Patient
Frozen						
Bakay et al.[21]	48 (21-64)	NA	6 (18); lateral release	NA	NA	NA
Davidson et al.[22]	33 (21-48)	4 (50)	10 (100); resurfacing	6.2 (2.5-17.2)	NA	NA
Flynn et al.[23]	30 (15-50)	8 (53)	NA	Smallest, 5; largest, entire MFC or LFC		60; 1.2
Karataglis and Learmonth[24]	30 (22-41)	3 (60)	0	NA	NA	100; 1.6
Scully et al.[25]	27 (20-35)	17 (94)	7 (44); HTO	NA	Single plug, 2.2; mosaic, 1.9	33; NA
Delayed fresh						
Gortz et al.[17]	24 (16-44)	6 (27)	NA	10.8 (5-19)	NA	50; 1.5
Krych et al.[2]	33 (18-49)	30 (70)	NA	7.3 (2.5-14)	NA	58; NA
LaPrade et al.[18]	31 (18-47)	13 (57)	11 (48); HTO	4.8 (3.1-9.6)	NA	87; 1.7
McCulloch et al.[19]	35 (17-49)	18 (72)	15 (63); meniscal txp	Primary, 5.2 (2.3-10.5); secondary, 2.3 (0.8-4)	Primary, 4 (1.8-7); secondary, 2.3 (0.8-4)	96; NA
Williams et al.[20]	34 (19-49)	13 (68)	9 (47); meniscal txp	6 (1.2-15)	NA	90; 2
Fresh						
Bayne et al.[7]	62 (10-82)	26 (67)	NA	NA	NA	NA
Chu et al.[13]	BP, 39 (19-62); UP, 35 (15-68)	NA	NA	NA	9.3 (1-30); UP, 7.7; BP, 15	NA
Convery et al.[8]	35 (15-68)	11 (31)	NA	NA	NA	NA
Emmerson et al.[14]	29 (15-54)	45 (70)	1 (2); ACL	NA	7.5	100; 1.7
Garrett[15]	20 (16-46)	12 (71)	NA	NA	NA	100; 1
Gross et al.[11]	FC, 27 (15-47); TP, 43 (26-69)	FC, 48 (58-259); TP, 29 (45)	FC, 10 (17); meniscal txp 41 (68); realignment TP, 39 (60); meniscal txp 38 (58); realignment	NA	NA	FC, NA; TP, 83
Jamali et al.[16]	42 (19-64)	7 (39)	9 (45); lateral release	NA	Trochlea, 13.2 (2.5-22.5); plugs, 7.1 (1.8-7.8)	90; 2.6
Rue et al.[12]	37 (20-48)	3 (20)	14 (100); meniscal txp	5.5 (2.3-9.5)	NA	100; 2.3
Mixed						
Pearsall et al.[26]	46 (16-71)	NA	42; HTO	4.8 (0.2-22)	Refrigerated, 7; frozen, 8.2	NA

ACL, anterior cruciate ligament; BP, bipolar; FC, femoral condyle; HTO, high tibial osteotomy; LFC, lateral femoral condyle; MFC, medial femoral condyle; NA, not available; TP, tibial plateau; txp, transplant; UP, unipolar.

Table 4. Outcome Measures

	Outcome Measure I			Outcome Measure II				
Author	Measure	Preoperative Value [Mean (Range)]	Postoperative Value [Mean (Range)]	Measure	Preoperative Value [Mean (Range)]	Postoperative Value [Mean (Range)]	Complications	Failures [n (%)]
Frozen								
Bakay et al.[21]	Bentley score	NA	FC, 6 E/7 G/3 F/2 P; patella, 2 E/4 G/2 F/0 P; TP, 1 E/2 G/1 F/1 P; BP, 2 P	NA	NA	NA	1 hyperergic reaction	FC, 4 (22); TP, 1 (20); patella, 1 (13); BP, 2 (100)†
Davidson et al.[22]	IKDC	27	79*	Histology: thickness articular cartilage/ chondrocyte cellular viability, chondrocyte cell density	NA	3.2 ± 0.9 (1-4); 78% ± 14.4% (53%-92%); 429 ± 279 cell/mm^2 (69-896 cell/mm^2)	NA	NA
Flynn et al.[23]	Subjective rating scale	NA	7 E/5 G/1 F/4 P	NA	NA	NA	2 arthroscopy, LOA, ROH; 1 patient with 3 re-allograft before TKA; 1 with 2 allograft before TKA; 1 TKA; 1 allograft revision and distal femoral osteotomy	3 TKA (20)
Karataglis and Learmonth[24]	Lysholm score	37.8 (31-47)	73.8 (34-99)*	Tegner	2	4	0	0
Scully et al.[25]	Return to duty, MEB	NA	9 of 16 completed MEB process; 1 of 12 soldiers returned to combat duty; the other 6 soldiers who returned to active duty remain on profiles prohibiting running and athletics; 1 retired; 1 became noncombatant	NA	NA	NA	0	0

(continued)

Table 4. Continued

Author	Outcome Measure I			Outcome Measure II			Complications	Failures [n (%)]
	Measure	Preoperative Value [Mean (Range)]	Postoperative Value [Mean (Range)]	Measure	Preoperative Value [Mean (Range)]	Postoperative Value [Mean (Range)]		
Delayed fresh								
Gortz et al.[17]	IKDC	Pain, 7.1; function, 3.5	Pain, 2*; function, 8.3*	Merle D'Aubigné-Postel	11.3	15.8*	0	5 (18%) failures: 1 TKA, 2 repeat allografting, 1 distal femoral osteotomy, and 3 partial meniscectomy (2 in same patient)
Krych et al.[2]	Return to sport, time to return to sport	NA	Return to sport, 88%; return to previous level of sport, 79%; time to return to sport, 9.6 ± 3.0mo (7-13mo)	IKDC	46.3 ± 14.9	79.3 ± 15.5*	0	0; 1 patient had MUA
LaPrade et al.[18]	Cincinnati score	Symptoms, 21.9; function, 27.3	69*; symptoms, 32.5*; function, 36.5*	IKDC	52	68.5*	1 superficial infection; 5 surgical procedures: 3 ROH and 1 repeat arthroscopy, 1 lateral patellotibial ligament reconstruction	0
McCulloch et al.[19]	KOOS	Pain, 43; symptoms, 46; ADL, 56; sports, 18; QOL, 22	Pain, 73; symptoms, 64; ADL, 83; sports, 46; QOL, 50*	IKDC	29	58	0	2 (8): 1 patient with allograft fragmentation and 1 patient with pain
Williams et al.[20]	ADLS	56 ± 24 (20-100)	70 ± 22 (30-98)*	SF-36	51 ± 23; mental, 51 ± 23; physical, 32 ± 10	49 ± 11*; mental, 66 ± 24; physical, 40 ± 12*	0	4 (7.2); 2 revision: 1 TKA and 1 OATS
Fresh								
Bayne et al.[7]	Subjective score	NA	Traumatic: UP, 5 E/2 G/1 F/6; BP, 1 E/2 G/1 F/2 P; patella—failed and then did well SONK: BP, 1 G/5 P Steroid, 2 F/1 P OCD: FC, 2 E/1 P	Satisfaction	NA	Traumatic: 76.4%; SONK, 46%; steroid, 57%; OCD, 71.3	1 superficial wound, 1 deep that needed I + D	Trauma, 5 (33); SONK, 5 (83); steroid, 3 (100); and OCD, 1 (25)

Table 4. Continued

	Outcome Measure I			Outcome Measure II				
Author	Measure	Preoperative Value [Mean (Range)]	Postoperative Value [Mean (Range)]	Measure	Preoperative Value [Mean (Range)]	Postoperative Value [Mean (Range)]	Complications	Failures [n (%)]
Chu et al.[13]	Subjective score		UP: MFC, 10 E/8 G/1 F/1 P/1 failure; LFC, 6 E/2 G/1 F/1 failure; patella: 1 E/4 G; TP: 1 E; multiple: 1 E/3 G/1 P/1 failure; BP: 5 E/1 G; 6 failure	Subjective scale of success	NA	UP, success rate of 82%; BP, 50%	NA	9; 6 BP (50%); 3 UP (7%); 4 TKA; and 1 AKA
Convery et al.[8]	Subjective rating scale	NA	MFC: UP, 13/16 E/G LFC: UP, 7/8 E/G; BP, 0/3 E/G PF: UP, 3/4 E/G; BP, 5/8 E/G	Success rate	NA	UP, 82%; BP, 56% suc	NA	MFC: UP, 3 (19); BP, 3 (100) LFC: UP, 1 (9) PF: 4 (33)
Emmerson et al.[14]	Merle D'Aubigné-Postel	3.0 ± 1.7	16.4 ± 2.0*	Subjective score; satisfaction	NA	47 E/G, 7 F, 1 P; 92%	NA	10 reoperation (15); 5 revision: 1 second OCA at separate site, 1 TKA, 1 revision then TKA, 1 UKA, and 1 UKA and allograft removal
Garrett[15]	Success	NA	16/17	Radiographic healing	NA	100%	0	1 (6)
Gross et al.[11]	HSS score	NA	FC, 83; TP, 85.3 ± 11	Radiographic arthritis	NA	FC, 18 (48%) had no/mild arthritis, 10 (26%) had moderate arthritis, and 10 (26%) had severe arthritis TP, 61% of patients had no/mild arthritis and 39% had severe/deg changes	FC, 1 deep infection; TP, 1; DVT, 1 early loosening; 4 graft fracture	FC, 12 (20): 3 graft removal and 9 TKA; TP, 21 TKA (32)
Jamali et al.[16]	Merle D'Aubigné-Postel	11.7	16.3*	Satisfaction		8 extremely satisfied, 6 satisfied, and 2 dissatisfied	0	5 (25): 2 revision allograft, 2 TKA, and 1 arthrodesis

(continued)

Table 4. Continued

Author	Outcome Measure I: Measure	Outcome Measure I: Preoperative Value [Mean (Range)]	Outcome Measure I: Postoperative Value [Mean (Range)]	Outcome Measure II: Measure	Outcome Measure II: Preoperative Value [Mean (Range)]	Outcome Measure II: Postoperative Value [Mean (Range)]	Complications	Failures [n (%)]
Rue et al.[12]	KOOS	Pain, 47.3 ± 15.5; symptoms, 49.2 ± 17.9; ADL, 60.9 ± 23.3; sports, 20.8 ± 14.8; QOL, 13.9 ± 17.5	Pain, 73.1 ± 19.3; symptoms, 65.1 ± 21.1; ADL, 84.3 ± 13.7; sports, 42.7 ± 18.8; QOL, 41.3 ± 15.4*	IKDC	31.4 ± 12.8	57.1 ± 17.8*	0	2 (14): 1 patient with bucket-handle meniscal txp tear and 1 patient with repeat arthroscopy and OA
Mixed								
Pearsall et al.[26]	WOMAC	Pain, 30.9; stiffness, 4.1; function, 38.3	Pain, 14.5; stiffness, 5.6; function, 49.7*	KSS	112.8	154.2*	NA	9 (19%) needed TKA

ADL, activities of daily living; ADLS, activities-of-daily-living scale; AKA, above-knee amputation; BP, bipolar; deg, degenerative; DVT, deep venous thrombosis; E, excellent; F, fair; FC, femoral condyle; G, good; I + D, irrigation and debridement; KSS, Knee Society Score; LFC, lateral femoral condyle; LOA, lysis of adhesions; MEB, medical evaluation board; MFC, medial femoral condyle; MUA, manipulation under anesthesia; OA, osteoarthritis; OATS, osteochondral autografts; P, poor; PF, patellofemoral; QOL, quality of life; ROH, removal of hardware; suc, sucess; TKA, total knee arthroplasty; TP, tibial plateau; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
*Statistically significant.
†Failure defined radiographically with sclerosis, narrowing/no joint space, and osteophytes.

significant postoperative Lysholm and Tegner (74 and 4, respectively) differences as compared with the preoperative values (38 and 2, respectively). Scully et al.[25] investigated the use of osteochondral allografts in active military personnel. Only one of 16 soldiers (6%) returned to active combat, 6 (38%) returned to active duty but had work restrictions that prohibited running and athletics, one retired, one became noncombatant, and the rest underwent evaluation by the medical evaluation board.

Prolonged-Fresh Allografts. Gortz et al.[17] measured clinical outcomes by a modified IKDC scale as well as the Merle D'Aubigné-Postel score. This group saw significant postoperative decreases in IKDC pain and increases in IKDC function. The modified Merle D'Aubigné-Postel score also significantly increased from 11.3 preoperatively to 15.8 postoperatively. Krych et al.[2] looked at osteochondral allografts in athletes. They discovered that the rate of return to sport was 88%, with a return to previous level of sport of 79% (as defined by achieving the pre-injury level on the Cincinnati Sports Activity Scale). In their patients the time to return to sport was 9.6 months (range, 7 to 13 months). In the athletes who returned to their previous level of competition, the postoperative IKDC score, activities-of-daily-living score, and Marx Activity Rating Scale score were all significantly greater than in those athletes who did not return to sport. LaPrade et al.[18] reported that the mean modified Cincinnati knee ratings for both function and symptoms significantly improved from baseline to final follow-up. A significant improvement was also found for effusion and functional testing (single-leg hop). McCulloch et al.[19] reported significant improvements in the physical component of the SF-12 and all 5 components of the KOOS (pain, activities-of-daily-living function, other disease-specific symptoms, sport and recreation function, and quality of life). Similarly, Williams et al.[20] noted significant increases in the physical portion of the SF-36 and increased scores on the activities-of-daily-living scale.

Fresh Allografts. Bayne et al.[7] reported on the influence of etiology of the osteochondral lesion on outcome. They reported 5 excellent, 2 good, and one fair outcome for unipolar traumatic lesions. Bipolar traumatic lesions had one excellent, 2 good, one fair, and one poor result. Patients who had SONK and bipolar grafts had one good and 5 poor results. Similarly, steroid-induced lesions also had suboptimal outcomes: 2 fair and one poor. OCD lesions had 2 excellent and one poor outcome. Convery et al.[8] and Chu et al.[13] reported their own subjective scores. Unipolar lesions on the medial femoral condyle had excellent or good results in 86% (31 of 36) and fair or poor results in 14% (aggregate data). Unipolar lesions on the lateral femoral condyle had excellent or good results in 15 of 17 cases (88%). A unipolar patellar allograft had excellent or good results in 8 of 9 cases (89%). Bipolar patellofemoral lesions did not fare as well, with only 63% excellent or good results. Emmerson et al.[14] also used a similar rating system but based on the Merle D'Aubigné-Postel score. They noted that 85% of patients had excellent or good results (47 of 55), with a significant increase in the Merle D'Aubigné-Postel score to 16.4. Similarly, Jamali et al.[16] reported a significant improvement in the Merle D'Aubigné-Postel score postoperatively to 16.3. Rue et al.[12] compared autologous cartilage implantation with osteoarticular allografts. They found that there were no postoperative percentage differences in the KOOS, IKDC score, Tegner score, Noyes score (sports activity and symptom), Lysholm score, and SF-12 physical score. There was a statistical percentage difference in the SF-12 mental score for osteoarticular allograft versus ACI.

In a mixed analysis of delayed-fresh and fresh-frozen allografts, Pearsall et al.[26] recorded a significant improvement in pain, stiffness, and function in the Western Ontario and McMaster Universities Osteoarthritis Index score, as well as a significant increase in the Knee Society Score.

Satisfaction

There were 6 studies that included patient satisfaction as a measured outcome.[7,12,14,16,19,24] Bayne et al.[7] reported on the satisfaction rates of different etiologies: posttraumatic, 76.4%; SONK, 46%; steroid-induced, 57%; and OCD, 71.3%. The aggregate data of the remaining studies indicate that 86% of patients were either extremely or mostly satisfied with their outcome with the use of any osteochondral allograft. Because of the small number of patients in the studies reporting satisfaction for frozen[24] and delayed-fresh[21] grafts, a comparison of satisfaction rates according to graft procurement and processing could not be performed.

Radiographic Analysis

Of the 19 articles reviewed, 11 investigated radiographic outcomes.[11,14-23] Of the studies that looked at radiographic union at least 1 year postoperatively,[14,15,17-19,21,23] 86% (119 of 139) showed healing or good incorporation of the allograft to the host bone. Of the studies that qualified the degree of arthritis in the knee,[11,14,16,19,22] 65% (72 of 110) showed little to no arthritis. Emmerson et al.[14] showed that 41% of the medial compartments (12 of 29) and 83% of the lateral compartments (24 of 29) showed few to no arthritic changes. Davidson et al.[22] reported a significant decrease in the Outerbridge classification of the defects from 4.3 to 0.6. The study by Williams et al.[20] was the only study to investigate the findings of postoperative magnetic resonance imaging, discovering that the Outerbridge classification of the surrounding or opposing surface cartilage did not correlate with functional outcome. In terms of trabecular incorporation, the allograft bone healed completely in 3 grafts, partially in 11, and poorly in 4.

Kaplan-Meier Survival Curve

Two studies created Kaplan-Meier survival curves for fresh osteochondral allografts.[11,14] Emmerson et al.[14] showed 91% survivorship at 5 years and 76% survivorship at both 10 and 15 years for osteochondral allografts of the medial and lateral femoral condyles. Gross et al.,[11] analyzing the results of fresh allografts of the femoral condyles, showed a 95% survival rate at 5 years, 85% at 10 years, and 74% at 15 years. This latter study also reported poorer survivorship of tibial plateau allografts: 95% at 5 years, 80% at 10 years, 65% at 15 years, and 46% at 20 years.

Adverse Effects and Failure Rates

The reported short-term complication rate of fresh, prolonged-fresh, and fresh-frozen allografts was relatively low, at 2.3% (14 of 595). The most common complications included removal of hardware (n = 3), repeat arthroscopy (n = 3), superficial infection (n = 2), deep infection requiring incision and debridement (n = 2), deep vein thrombosis (n = 1), hyperemic reaction (n = 1), and early loosening of the graft (n = 1). No study indicated any intraoperative complication.

Failure rates were reported widely; however, many studies used different definitions of failure. For example, Bakay et al.[21] defined failure as radiographic fragmentation, whereas Emmerson et al.[14] defined failure as a repeat operation for any reason. Gross et al.[11] defined failure as allograft revision or conversion to total knee arthroplasty. On the basis of the individual authors' definitions of failure, there were 108 reported failures (18.1%). By far, the most common treatment for failure was conversion to total knee arthroplasty (n = 52, 48%). Fifteen allografts (14%) had to be revised or removed because of a poor clinical outcome. Allograft fragmentation was also a common consequence (n = 10, 9%). There were reports of 2 serious failures, with 2 patients undergoing an arthrodesis,[13,16] whereas another patient required an above-the-knee amputation for deep infection after multiple revision total knee arthroplasties.[13] In the studies that reported bipolar allograft failure rates,[7,8,13,21] there was a 65% failure rate (17 of 26).

Prognostic Factors

Of the 19 studies, 8 reported prognostic indicators that may affect allograft survival and functional outcomes.[2,7,8,11,16,17,20,22,26] Bayne et al.[7] noted that patients with an osteochondral allograft due to SONK are likely to have lower satisfaction rates (46%) and poorer outcomes (83%). Convery et al.[8] reported a success rate of unipolar allografts of 82% compared with a 56% success rate for bipolar lesions. Gross et al.[11] discussed the prognostic factors of allografts of the femoral condyle and the tibial plateau separately. On the femoral side, the researchers noted that there was no correlation between outcome and the need for *meniscal* transplant or limb realignment or late etiology. On the tibial side, Gross et al. showed that patients undergoing concomitant osteotomy with grafting fared better than patients with prior or delayed osteotomy. Furthermore, concomitant meniscus transplantation was associated with improved long-term survivorship of bulk tibial osteochondral allografts; patients with late osteoarthritic degeneration also had poorer outcomes.[11] Using data from the same group of patients, Ghazavi et al.[28] stated that factors related to failure included age older than 50 years, bipolar defects, Workers' Compensation status, and any varus or valgus malalignment of knee. With regard to radiographic findings, any graft collapse of more than 3 mm or joint space narrowing of 50% or more was likely to be associated with graft failure. Gortz et al.[17] similarly noted that if there is radiographic healing of the allograft-host interface, patients are likely to have better outcomes. In a cohort with patellofemoral arthritis, Jamali et al.[16] reported failure in 5 of 20 cases, indicating that osteochondral allograft transplantation may have diminished outcomes for the patellofemoral joint, especially in the context of diffuse degenerative lesions.

Krych et al.[2] looked at athletes' return to sport after osteochondral allograft transplantation. Using a multiple logistic regression model for risk factors for failure, they reported that patients aged older than 25 years and with preoperative symptoms for more than 12 months were less likely to return to full athletic activity. Pearsall et al.[26] showed that age younger than 35 years, male gender, and graft size less than 2 cm^2 were associated with better outcomes.

Williams et al.[20] and Davidson et al.[22] discussed graft storage time in relation to outcome. Davidson et al. noted that storage time had no influence on chondrocyte cell density or viability. Williams et al. showed no correlation between graft storage time and scores on the SF-36 or activities-of-daily-living scale. A longer graft storage time did, however, correlate with less subchondral edema, better graft morphology, and increased trabecular incorporation.

Discussion

Since Gross et al.[29] popularized the concept of osteochondral allograft transplantation in the mid 1970s, there has been increasing attention on this cartilage restoration technique for managing patients with both focal and diffuse (single-compartment) osteochondral defects in the knee.[30] Our systematic review involved a qualitative synthesis of 19 Level IV case series over a period of approximately 30 years. Given the heterogeneity of clinical outcome measures used across studies and over time, a formal meta-analysis could not be performed. Nevertheless, our findings are meaningful and show that at a mean follow-up of 5 years, good clinical outcomes have been reported with a high satisfaction rate (86%) and a low short-term complication rate (2.4%). Furthermore, 2 studies also estimated that the survivorship of osteochondral allografts was 75% at 15 years' follow-up.[11,14]

Our review included patients who were managed with osteochondral allografts for osteochondral defects secondary to variety of etiologies. The aggregate age of patients across studies was 37 years, and the majority of them were men. Furthermore, the patients had undergone an average of 1.7 previous surgical procedures, whereas 46% had concomitant procedures at the time of osteochondral allograft transplantation. The size of the osteochondral lesions and plugs was also quite varied. Because of this heterogeneity in etiology, defect location, size, graft processing, and concomitant surgical procedures, between-group comparisons were precluded, given the small numbers in each of the relevant subgroups.

A qualitative assessment of the included studies showed less favorable clinical outcomes for patients with SONK or steroid-induced osteonecrosis, as well as individuals presenting with bipolar lesions. On the femoral side, Gross and colleagues[11,28] also showed that age older than 50 years, bipolar defects, and Workers' Compensation status, as well as varus or valgus malalignment of the knee, were negative clinical prognostic factors. Furthermore, Gross et al.[11] showed that among patients with osteotomies, improved results were seen when realignment preceded or coincided with the allograft surgery. Krych et al.[2] studied an athletic population with focal defects and showed that patients aged older than 25 years and with preoperative symptoms for more than 12 months were less likely to return to full athletic activity. Pearsall et al.[26] showed that age younger than 35 years, male gender, and graft size less than 2 cm^2 were associated with better outcomes. With regard to location, Gross et al.[11] showed that although both tibial- and femoral-sided grafts had good long-term survivorship, bulk osteochondral allografts on the femoral side fared slightly better. It is also evident that diffuse patellofemoral lesions treated with fresh osteochondral grafting show poorer results compared with lesions in the femoral condyle or tibial plateau.[16] The aforementioned information can be used during the informed-consent process and for patient selection during the perioperative decision-making process.

Given limitations in sample sizes and the heterogeneity in outcomes that were reported, our study could not determine the optimal procurement, processing, and storage procedures. Nonetheless, a plethora of basic science data have confirmed decreased chondrocyte viability, cell density, and tissue metabolism with prolonged osteochondral allograft storage.[31] By 3 weeks, chondrocyte viability falls to 70%, and by 7 weeks, it falls to 67%.[32] As such, current recommendations advise 42 days as the maximum storage period for a fresh allograft, and ideally, implantation should be performed by 24 to 28 days.[1,3,6] With regard to the optimal temperature, osteochondral allografts are usually stored at 4°C; however, Pallante et al.[32] found higher chondrocyte viability at 37°C compared with 4°C. Frozen allografts are also available, but cartilage may fissure and delaminate, with articular surface breakdown, because freezing of mature articular cartilage causes chondrocyte death and damage to the extracellular matrix.[1] Gross et al.[33] showed that the histologic features associated with long-term allograft survival included viable chondrocytes, functional preservation of matrix, and complete replacement of the graft bone with the host bone. They also showed that with a stable osseous graft base, the hyaline cartilage portion of the allograft can survive and function for 25 years or more. Although the precise association of cell viability and clinical outcomes remains unknown, this latter study serves as the rationale for our continued preference for using fresh osteochondral allografts for focal and degenerative chondral defects.

To our knowledge, this is the first systematic review of outcomes after osteochondral allograft transplantation in the knee. This review will allow readers to understand the scope of studies that have been published on this topic and identify subgroups of patients who are most likely to have good outcomes. To definitively establish the role of osteochondral allograft transplantation in the management of chondral defects in the knee, there needs to be further work in conducting prospective cohort studies in which a comparative cohort is included. Examples of pertinent comparisons would include patients undergoing microfracture or ACI. In addition, the use of uniform outcome measures across studies would allow for pooling of data in a meaningful manner. According to the International Cartilage Repair Society, all studies evaluating outcomes after cartilage repair procedures should use a joint-specific outcome measure (IKDC or KOOS), a health-related quality-of-life measure (e.g., SF-36) for concomitant economic analyses, and a validated activity scale (Tegner Activity Scale or Marx Activity Scale).[34]

Limitations

The limitations of this study result from the study design and quality of the included studies. All of the included studies are Level IV case series without comparative controls. The use of different clinical outcome tools across studies precluded a formal meta-analysis. Furthermore, the heterogeneity of patients and outcomes across studies did not allow determination of which graft processing and storage methods are associated with the most favorable outcomes.

Conclusions

Osteochondral allograft transplantation for focal and diffuse (single-compartment) chondral defects results in predictably favorable outcomes and high satisfaction rates at intermediate follow-up. Patients with OCD, traumatic and idiopathic etiologies have more favorable outcomes, as do younger patients with unipolar lesions and short symptom duration. Future studies should include comparative control groups and use established outcome instruments that will allow for pooling of data across studies.

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