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Systematic Review: Osteochondral Allograft in Treatment of Knee Articular Cartilage Injuries

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ABSTRACT

Purpose: The objectives of this study were designed to conduct a systematic review of clinical outcomes after osteochondral allograft transplantation in the knee and to identify patients, defects, 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 patients after osteochondral allograft transplantation for chondral defects in the knee were included.

Results: There were 11 eligible studies resulting in 550 knees with a mean follow-up of 150 months (range, 30 to 261 months). The overall follow-up rate was 93%. The mean age was 31 years (range, 15 to 52 years), and 478 patients (63%) were men. With regard to etiology, the most common indications for transplantation included post-traumatic (38%), osteochondritis dissecans (31%), osteonecrosis from all causes (12%), AVN (1%) and idiopathic (9%). 63% of patients had concomitant procedures, and the mean defect size across studies was 6.3 cm2. The overall satisfaction rate was 93%.

Conclusions: Osteochondral allograft transplantation for focal and diffuse chondral defects results in predictably favorable outcomes and high satisfaction rates. Patients with osteochondritis dissecans, traumatic and idiopathic etiologies have more favorable outcomes as 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.

The level of Evidence: Level IV, a systematic review of Level IV studies.

Keywords: Osteochondral allograft, Knee, treatment, osteochondral lesion

INTRODUCTION

Managing 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[2]. Unfortunately, it is known that chondrocyte viability decreases in allografts stored for more than 14 days, and allografts generally should be implanted within 24 days[3,4]. Notably, frozen allografts have inferior biological and biomechanical properties compared with fresh allografts[5].

Fresh osteochondral allograft transplantation was initially used to treat 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]. 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 is clearly a large number of patient- and defect-specific variables that impact the outcomes after fresh osteochondral allograft

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transplantation. Despite multiple case series published over the course of three decades, there has been no attempt to conduct a systematic review of outcomes after osteochondral allograft transplantation in the current literature.

METHODS

Literature Search

With the aid of an experienced librarian, we searched PubMed (2007 to week 2 of March 2017), Medline (2006 to week 1 of July 2017), EMBASE (2005 to week 3 of2017), and the Cochrane Central Register of Controlled Trials (to week 2 of July 2016). This was performed using the following key words: (knee) AND (cartilage ORchondral 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) Series of using osteochondral allograft in treatment of articular cartilage injuries at knee joint are included relevant raw data must be available to calculate pure results; (2) English literature only; (3) Human studies only; (4) Minimal clinical follow-up of 12 months; and (5) Minimum of 5 patients in the study. We **excluded** (1) animal studies, (2) case reports, (3) narrative reviews, (4) Studies that did not report exact procedure where osteochondral allograft was used, and (5) Series not reporting osteochondral allograft transplantation outcomes.

Data Abstraction

Each study that met the inclusion criteria was reviewed independently by 2 reviewers. The 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, length of 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. ThemodifiedColemanscorewas used to assess the quality of each of the included studies[6,7]. 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 Form12 [SF-12], Short Form36 [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.

The study was approved by the Ethics Board of Ain Shams University.

Statistical Analysis

General and demographic characteristics including age, etiology, graft type 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 187 articles from 2005 to 2016, for a total of 704 articles.After titles were reviewed and excluded for the following, 55 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. 11 articles met the inclusion criteria for this study. All included studies were (5) retrospective study (Level IV) and of (6) prospective study (Level IV). Articles investigated fresh (9 studies), refrigerated (1 study), fresh-frozen (1 study).

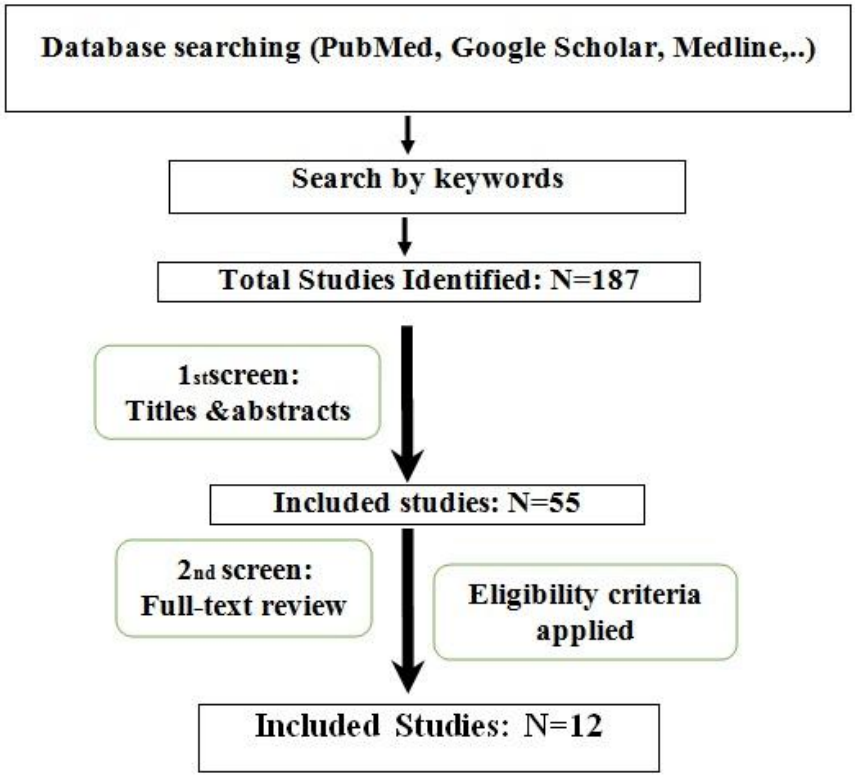

Fig.(1) Search Strategy

General Characteristics

The general characteristics of included studies are summarized in Table 1. All studies were Level IV retrospective (5 studies) or prospective (6 studies). Overall, 466 of 505 knees (92.4%) were available at a mean follow-up of 58 months (range, 19 to 120 months).

The study quality improved with later dates of publication.

Processing: The methods of procurement and storage time included fresh (n = 469), refrigerated (n=23), and fresh frozen (n =9).

Defect Location and Etiology. The location of the allograft included all or a portion of the medial femoral condyle (n =227), lateral femoral condyle (n =113), patella (n=43), trochlea (n=20), tibial plateau (n=40), and bipolar locations (n =16). Overall, the indications for transplantation in the included studies were post-traumatic (n =205),OCD (n =158), osteonecrosis from all causes (n = 64), idiopathic (n =59), osteoarthritis (n =24), and chondromalacia patella (n =17). The distribution of etiologies according to graft processing is described in detail in Table 2.

Demographics

The general demographics of the included age, lesion size, and concomitant procedure are outlined in table 2. There was 478 patient in the studies the reported [17-27], the mean age across all studies was range 16.4 to 51.6 years.Some studies reported on prior operative procedures past surgical treatment included arthroscopic debridement of osteochondral's defect, arthroscopic loose body removal, microfracture, and OCD lesion fixation. These studies did not discuss the types of conservative treatment measures they were under taken before the prior surgical procedures.

Functional Outcome scores

Functional outcomes are listed in Table 3. There are 12 different outcome measures recorded for the 12 articles.

The IkDC score was adopted in most studies to assess preoperative and postoperative patients' status[17,19,20,23,24,25,26,27].

Table (1): Study Characteristics

Author	Year of study	Method of processing	Type of study	Level of evidence	Location of Allograft	Etiology	Follow-up length (mean)	N.of patient
Davidson PA. et al. (17)	2007	Fresh stored osteochondral grafts	Retro-spective	IV	Distal femur MFC =6 FT=2 MFC+FT=2	OA dissecans=5 Trauma=5	40.4	8 patients (10 knees)
Williams RI et al.(18)	2007	Fresh osteochondral grafts	Prospective	IV	NA	NA	48	90 patients
Laprade RF et al. (19)	2009	Refrigerated osteochondral grafts	Prospective	IV	Femoral condyle	NA	36	23 patients (23 knees)
Krych AJ et al. (20)	2012	Fresh stored osteochondral grafts	Prospective	IV	MFC (40%) LCF (40%) Trochlear (2%) Multi- location (18%)	OCD=12% Trauma=5% Non-traumatic =37%	30	43 patients
Shaha JS et al (21)	2013	Fresh stored osteochondral grafts	Retrospective	IV	LCF=13 MFC=25	NA	36	38 patients
Lyon R. et al. (22)	2013	Fresh stored osteochondral grafts	Retrospective	IV	Patella=1 LCF=7 Trochlea=1 MFC=3	Juvenile OCD	12	11 Patients
Murphy RT. et al. (23)	2014	Fresh osteochondral grafts	Prospective	IV	MFC=18 LFC=15 Patella=3 Trochlea=2 Tibial plateau=1 Multi-site=4	OCD AVN Traumatic Osteochondral fracture Degenerative Lesion	16.4	39 patients (43 knees)
Briggs DT. et al (24)	2015	Fresh stored osteochondral grafts	Prospective	IV	MFC = 47.5 LFC = 24.6 Patella = 8.2 Trochlear = 4.9	OCD = 44.3% AVN = 31.1% OA = 8.2% Degenerative chondral lesion = 6.6%	32.9	55 patients (61 knees)
Graciteli GC. et al. (25)	2015	Fresh osteochondral grafts	Prospective	IV	Patella	OCD=1 Degenerative=15 Traumatic=4 Osteochondral fracture =5 OA=2 AVN=1	116.4	27 patients (28 knees)
Sadr KN. et al. (25)	2016	Fresh osteochondral grafts	Retro-spective	IV	MFC=62% LFC=29% Trochlea=6% Patella=1%	OCD	75.6	135 patients (149knees)
Hohmann E. et al.(26)	2016	Fresh frozen graft	Retrospective	IV	MFC LFC	Trauma OCD Microfracture	24	9 patients

Table (2): Study demographics

Auther	Age	Concomitant Procedure	Lesion Size (cm2)
Davidson PA. et al. (17)	32.6	ACL allograft reconstruction=1 PCL allograft reconstruction=1 Distal patellar realignment with tibial tubercle osteotomy=2 Meniscal repair=1 Partial meniscectomy=1 Isolated resurfacing =4	6.2
Williams RI et al.(18)	34	Knee osteotomy	60.2
Laprade RF et al. (19)	30.9	NA	4.8
Krych AJ et al. (20)	32.9	Meniscal transplant ACL reconstruction	7.25
Shaha JS et al (21)	29.83	Meniscal allograft Osteotomy ACL reconstruction	5
Lyon R. et al. (22)	15.2	NA	5.1
Murphy RT. et al. (23)	16.4	Lateral meniscal repair=1 Patellofemoral realignment=3 Loose body removal=3 Micro fracture=3 Osteotomy=2	8.4
Briggs DT. et al (24)	32.9	NA	9.6
Graciteli GC. et al. (25)	33.7	Osteotomy	10.1
Sadr KN. et al. (25)	21	NA	7.2
Hohmann E. et al.(26)	32.1	NA	2.8

Table (3): Functional outcomes

Author	Outcome Measure 1			Outcome Measure 2		
	Measure	Pre-operative	Post-operative	Measure	Pre-operative	Postoperative
Davidson PA. et al. (17)	IKDC	26.7	79.4	Tegner	4.3	5.3
Williams RI et al.(18)	Active daily living scale	56	70	SF-36 physical score	32	40
Laprade RF et al. (19)	IKDC	52	68.2	Cincinnati Knee rating	27.3	36.5
Krych AJ et al. (20)	IKDC	46.27	79.29	Active daily living scale	62	82.82
Shaha JS et al (21)	KOOS	249.51	340.88	Active daily living scale	71.64	89.75
Lyon R. et al. (22)	Active daily living scale	1	11	Pain	5.6	1.2
Murphy RT. et al. (23)	IKDC	42	75.2	KS-F score	69.3	89.4
Briggs DT. et al (24)	IKDC	36.9	80.4	KOOS (pain)	57.9	88.2
Graciteli GC. et al. (25)	IKDC	36.5	66.5	KS-f	64.6	80.5
Sadr KN. et al. (25)	IKDC	44.2	28.3	Knee Society Score (function)	72.3	95.7
Hohmann E. et al.(26)	IKDC	40.9	90	NA	NA	NA

Davidson *et al.*[17] evaluated the outcome of fresh osteochondral allografts which were stored for 4 to 6 weeks to treat full thickness cartilage and osteochondral defects of the distal femur for 8 patients with 10 knees. These patients have OA dissecans and post-traumatic lesions. All patients had sequential MRI scanning and clinical evaluation. Surgical technique involved arthroscopy and medial arthrotomy. Postoperatively, patients were maintained on the rehabilitation program for 6 weeks. The 8 patients had second look arthroscopy and cartilage biopsy at the mean of 40 m after the initial procedure. Histological analysis was sampled from the most normal appearing. MRI analysis the allograft cartilage appearance. In all knees evaluated at the time of biopsy documented improvement in cartilage appearance of at least one grade of Outerbridge classification, that means an improvement of three Outerbridge grade. The outcome measurement improved is listed in table 3. Histological analysis was performed by measuring cell viability and cellular density, comparing graft to native cartilage.

Williams *et al.*[18] evaluated the effect of fresh osteochondral allograft to treat 90 patients with symptomatic chondral and osteochondral lesion of the knee. The patients had mean follow-up 48m from 1999 to 2002. All donor allografts tested for the transmitted disease. Surgeons do an arthroscopic examination to match the lesion size to the donor allograft. A limited knee arthrotomy was done. A press-fit technique was used that did not require internal fixation. Postoperatively, the patients were managed with the rehabilitation program. The outcome scores were increased compared with baseline scores. On MRI, the thickness of implant allograft was maintained with no graft displacement observed and no overgrowth of the subchondral plate was apparent on any planes.

Laprade *et al.*[19] used results of 23 patients who underwent treatment of focal articular cartilage defects of the femoral condyles with refrigerated osteochondral grafts. A small parapatellar arthrotomy was performed at the time of surgery, the surgeon used press-fit technique into the socket to match the exact height of the surrounding articular cartilage. The patient remained in the rehabilitation program for 8 weeks. Refrigerated osteochondral allografts with the mean time between donor procurement and implantation were 20.3 days. The baseline score of patients preoperatively improved postoperatively as mention in results before.

Krych *et al.* [20] used the results of 43 patients to evaluate the outcome of fresh stored-osteochondral grafts from 2000 to 2010 that stores 1 to 4 weeks to resurface large chondral and osteochondral defects of the knee. All grafts were screened for the transmitted disease. Patients were treated with an initial diagnostic arthroscopy for assessment of osteochondral lesion, osteochondral allograft transplantation was performed via the technique described by **Williams** *et al* [18]. The lesion was exposed via a small parapatellar arthrotomy. Grafts were gently impacted into place for a press-fit technique. Postoperatively, patients were in the rehabilitation program. For outcome scores, it was improved as mentioned in table3. There was no intraoperative complication of graft failure over the period of follow-up that had mean 30 months.

Shaha *et al.*[21] reported the results of 38 patients who used osteochondral allografts as a treatment option from 2002 to 2011 to restore large areas of hyaline cartilage anatomy and structure for returning to activity in a population. A diagnostic arthroscopy examination was performed to assess the lesion and identify any other inter-articular injuries. A parapatellar arthrotomy was made. A guide pin wire placed in the center, perpendicular to the lesion. A counter bone was used to ream the lesion to a depth of 5 to 10 mm, ensuring a bed of normal bone at the base. The press-fit technique was used to seat the graft.

All grafts were screened as guidelines of the American Association of Tissue Banks. All grafts were placed within 3 weeks of harvest. Postoperatively, patients were in the rehabilitation program. At an average of 4.1 years (range, 0.6-8.9 years), 29% were able to return to full activity, and 42% were unable to return. There was no significant difference found with respect to years of service, operating surgeon, the location of the lesion, concomitant procedures, number of osteochondral plugs, or prior cartilage procedures.

Lyon *et al.*[22] used a retrospective study to the result of 11 patients who used fresh stored

osteochondral grafts between 2004 to 2009. All were harvested fresh and stored until transplantation. All fresh stored allografts were transplanted between 14 to 21 days. All knees had an open arthrotomy. The grafts either were round plugs or custom keyhole shell grafts. Supplementary fixation (either metal or bio-absorbable screws) was used in four cases to improve graft stability. Postoperatively, patients underwent the rehabilitation program. All patients had returned to activities of daily living without difficulties at 6 months.

Murphy *et al.*[23] used studies in adults that have shown that osteochondral allograft transplantation is an option for large chondral and osteochondral lesion of the knee. **Murphy** [23] used the fresh type of grafts that were implanted between 5 and 28 days after recovery to allow time for testing and processing. All procedure was performed through a medial or lateral parapatellar arthrotomy. A dowel technique and a shell technique were used. Postoperatively patients underwent rehabilitation program protocol. Five knees (12%) failure of the allograft at a median of 2.7 years (range 1.0 – 14.7 years) after the index surgery. Failed allografts were salvage with a revision osteochondral allograft transplant and 4 of 5 (80%) of these grafts were still in situ at latest follow-up. Extreme satisfaction was reported subjectively by 26 (74%) and 5 (14%) patient.

Briggs *et al.*[24] used prospective study to assess the outcome of osteochondral allograft transplantation as the primary treatment for cartilage injury in the patient with no previous surgical treatment. **Briggs** [24] used his study for 55 patients with 61 knees. Fresh stored osteochondral grafts that processed in accordance with standards of the American Association of Tissue Banks. Following the initial OCA transplantation, 18 knees (29.5%) had further surgery. Of these additional surgeries, 11 knees (10 patients) had a surgical procedure to address on OCA failure or progression of arthritis and 7 knees (9 surgical total) had a surgical procedure performed in conjunction with a functional graft. The median time to failure was 3.5 years, and the mean age of patients with failed OCAs was 42.2 years.

Graciteli *et al.*[25] used OCA transplantation in the treatment of patellofemoral cartilage injuries to evaluate functional outcomes and survivorship of the grafts between 1983 to 2010 in 27 patients with 28 knees. Donor tissue was recovered within 24 of donor death and stored within 5 and 21 days of donor death. Dowel technique and shell technique were used. Postoperatively, all patient had a rehab program from 6 to 12 months. Twenty of 28 knees (71.4%) had the allograft in situ at the latest follow-up. Seventy-seven percent of knees showed excellent or good results according to modified Merle d'Aubigne-Postel score categories. Eighty-nine percent of patients were extremely satisfied or satisfied with the results of the OCA transplantation.

Sadr *et al.*[26] had135 patients with 149 knees who had OCD that was treated with fresh osteochondral grafts that recovered within 24 hours of death until the time of implantation, between 7 and 28 days. Surgery was performed through a midline skin incision with a small arthrotomy. Dowel technique and shell technique were used. Postoperatively care included rehabilitation program protocol. The patient had allowed returning to recreational and athletic activities between 4 and 6 weeks after surgery. Of 149 knees, 34 (23%) underwent reoperation after the OCA transplantation. Of these, 22 knees (15%) had a procedure not requiring allograft. Twelve knees (8%) were classified as OCA failures with revision or removal of the allograft (7 revision OCA transplantation, 3 UKAs, and 2 TKAs). The mean time to failure was 6.1+-1.3 years. OCA survivorship was 95% at 5 years and 93% at 10 years.Of the 149 knees, 137 (92%) had the OCA in situ at the latest follow-up, when comparing OCA failure (n =12) with non-failures (n=137), no statistically significant difference was found between groups with regard to age, sex, previous surgery, total graft area, anatomic location. The majority of patients were satisfied with the outcome of the OCA transplantation (78% extremely satisfied, 17% satisfied, 3% somewhat satisfied, 1% somewhat dissatisfied and 1% dissatisfies).

Hommann *et al.*[27] used irradiated fresh frozen osteochondral allografts for large osteochondral defects of 9 patients using the mega-OATs technique. Between 2010 to 2012 a 9 patients that underwent diagnostic arthroscopy. The osteochondral defect was approached via a midline skin incision and a median parapatellar

approach. The mega-OATs system was performed as described by **Brucker** [28]. The graft was inserted by press-fit technique and fixation was achieved using screws. All patients were inserted in the rehabilitation program for 6 weeks. The results of this case series suggested that irradiated osteochondral allograft provide significant clinical improvement in patients treated for large articular surface lesions within 2 years follow-up period.

DISCUSSION

Since **Gross** *et al.*[11]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 osteochondral defects in the knee[12]. Our systematic review involved a qualitative synthesis of 11 Level IV case series. 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 from 12 to 261.4, good clinical outcomes have been reported with a high satisfaction rate (93%).

Our review included patients who were managed with osteochondral allografts for osteochondral defects secondary to a variety of etiologies. The mean age of

patients across studies was 30.1, and the majority of them were men. Furthermore, 63% of patients had concomitant procedures at the time of osteochondral allograft transplantation. The size of the osteochondral lesions was also quite varied.

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].

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[14,13].

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 micro-fracture 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, most of the 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) [15,16].

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.

CONCLUSION

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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