Systematic Review

Large Fresh Osteochondral Allografts of the Knee: A Systematic Clinical and Basic Science Review of the Literature

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Purpose: The aim of this study was to conduct an updated review of the literature regarding the clinical and basic science knowledge on osteochondral allograft transplantation in the knee for the treatment of large defects. **Methods:** According to specific criteria, 2 investigators systematically reviewed the literature for clinical and basic science reports regarding osteochondral allograft transplantation; data were independently extracted, pooled, and analyzed. Clinical and functional outcomes, International Knee Documentation Committee and Western Ontario and McMaster Universities Osteoarthritis Index scores, return to sport, quality of life, and survivorship of the grafts were assessed from the clinical articles. Regarding the basic science articles, the effects of allograft storage time, temperature, and different storage media were assessed. **Results:** Eleven articles reporting on clinical data and 14 articles reporting on basic science data (animal, cell, and biomechanical studies) were selected. The articles included in the review were not homogeneous, and different outcome measures were adopted. Overall excellent results were achieved, with improvement in all objective and subjective clinical scores, a high rate of return to sport, and a survivorship rate of 89% at 5 years. When multiple plugs were implanted, posterior grafts seemed to fail. Only 1 article compared fresh versus frozen grafts, with a greater improvement in scores in the frozen group. Cellular viability and number were reduced during storage, even at low temperatures; polyphenol from green tea and arbutin and higher temperatures favorably influenced cell viability of the cartilage during storage. On the other hand, the structural properties of the extracellular matrix were not influenced by the storage at low temperatures. Integration of the graft to the host was also important, and bony integration was usually achieved; however, on the cartilage side, integration was scant or did not occur, especially in the frozen grafts. **Conclusions:** Fresh osteochondral allografts of the knee showed good clinical and functional outcomes even at longer-term follow-up. No other effective treatment exists, at the moment, for large osteochondral lesions. This surgical procedure is burdened by cost and difficulty in finding matching fresh donors. A new method to establish chondrocyte viability before the implantation of a new allograft would be a useful decision-making instrument. **Level of Evidence:** Level IV, systematic review of Level IV studies.

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Treatment of cartilage lesions in the young and active population can be challenging, and different options are currently available. Osteochondral allograft transplantation has been performed for approximately 3 decades, and encouraging clinical results have been reported.[1] The procedure is generally indicated for revision articular resurfacing after a previous failed cartilaginous procedure or in cases of large chondral lesions with significant bone loss (Figs 1A and 2A). Many techniques in terms of implantation, from smaller press-fit circular plugs to large bulk grafts, depending on the size of the graft necessary, have been described (Figs 1B and 2B).

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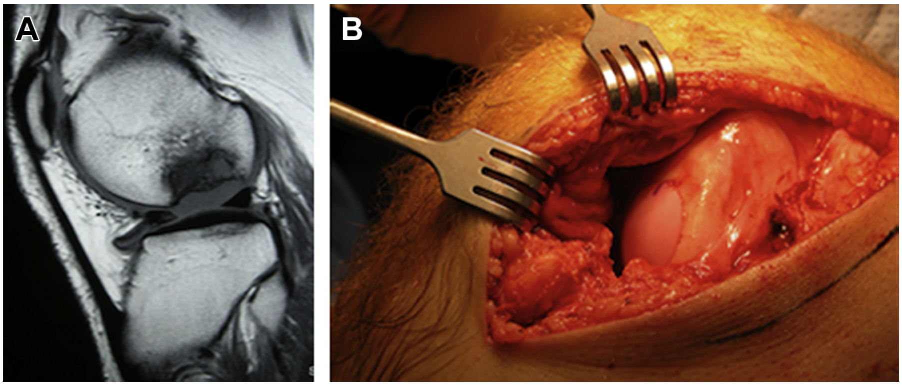

Fig 1. (A) Sagittal T1-weighted magnetic resonance image of a large osteochondral lesion of the lateral femoral condyle. (B) With the patient positioned supine and the knee flexed, through a medial parapatellar incision, a press-fit circular osteochondral plug is implanted in the medial femoral condyle.

Osteochondral allografts are most commonly implanted for femoral condyle defects, but they also can be implanted in the tibial plateau, the femoral trochlea, and the patella; moreover, case series have reported their use in more than 1 area of the knee in the same setting. To improve clinical results, osteochondral allograft transplantation can be performed in combination with other procedures such as osteotomy, meniscal allograft transplantation, and ligament reconstruction.[2]

Many factors influence the outcome after osteochondral allograft transplantation, which can be related to the patient, to the allograft itself, or to the surgical technique; most of the basic research has been focused on chondrocyte viability and the biomechanical properties of the extracellular matrix of the cartilage and how to preserve their features during the time required for the graft procurement, storage, and testing before release by the tissue bank. In fact, a period of 2 or 3 weeks is usually needed for testing for aerobic, anaerobic, and spore-forming bacteria, as well as viral testing, before release, according the American Association of Tissue Banks/Food and Drug Administration regulatory legislation.[3]

The aim of this study was to conduct an updated review of the literature regarding the clinical and basic science knowledge on osteochondral allograft transplantation in the knee for the treatment of large defects. This review attempts to answer the following questions: (1) What are the clinical outcomes of osteochondral allografts? (2) What is our basic understanding of osteochondral allografts?

Methods

At the end of December 2013, a systematic search of the PubMed, Google Scholar, and Scopus databases was performed by 2 independent authors (F.D.C., S.B.) using the following key words: "((osteochondral allografts) OR (osteoarticular fresh frozen allograft) OR (osteochondral fresh allograft) OR (osteoarticular fresh allograft)) AND ((knee) OR (femoral condyle) OR (tibial plateau) OR (patella) OR (patellofemoral))." The search led to a total of 328 titles, which were reviewed independently by the same 2 authors. Disagreements were resolved with discussion by the 2 reviewers or by the opinion of the senior author (A.A.). Duplicate titles were removed, leaving a total of 290 articles for this systematic review. Of these 290 articles, 11 articles reporting on clinical data and 14 articles reporting on basic science data (animal, cell, and biomechanical studies) were obtained according to the inclusion and exclusion criteria listed in Table 1. Data were extracted independently by the 2 reviewers and pooled in an Excel file (Microsoft Office, Redmond, WA) for analysis.

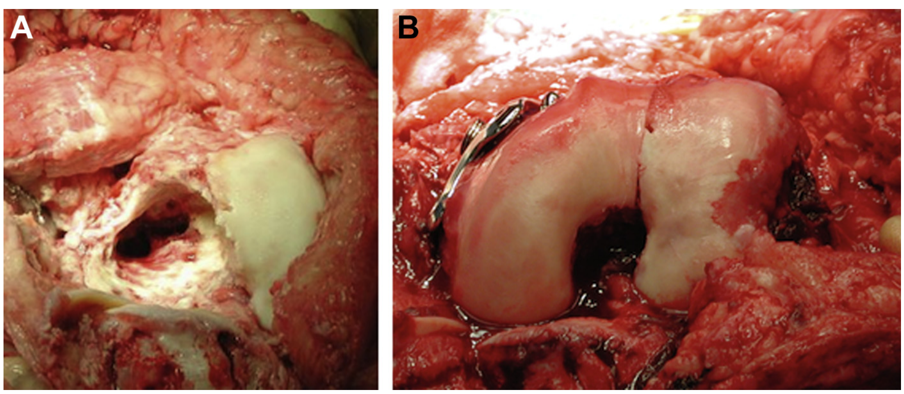

Fig 2. (A) Knee arthrotomy with a view of a large osteochondral defect involving the whole medial femoral condyle. (B) Knee arthrotomy with the whole medial femoral condyle replaced by a large bulk osteochondral allograft fixed with a medial plate and screws.

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Level I-IV clinical studies	Books chapters, power point presentations, citations, conferences papers
Basic science articles	Reviews
Articles published in past 5 yr	Case reports
English language	Expert opinion
≥10 patients/specimens	
≥1 yr of follow-up	

Results

Clinical Review

A total of 11 articles reporting on clinical data/ outcomes were included in this review.[4-14] There were 374 knees in 358 patients. Demographic data are reported in Table 2. One or more plugs were transplanted in the femoral condyles in 369 cases, in the tibial plateau in 7 cases, and in the patella in 1 case. A fresh osteochondral allograft was transplanted in 338 patients and a frozen allograft in 20 patients. Surgical data are reported in Table 3. Postoperatively, knees were kept in a brace for 4 to 6 weeks, and in 1 study, they were casted for 1 month.[4] Range of motion was started immediately after surgery, and the weight-bearing status was mainly related to associated procedures (i.e., osteotomy and meniscal allograft transplantation). Continuous passive motion devices were used postoperatively in only 1 study.[14] The results of the clinical studies are reported in Table 4.

Basic Science Review

A total of 14 articles (Table 5) reporting on basic science findings were included in this review.[15-28] Cellular viability has always been considered one of the most important factors for successful osteochondral allograft transplantation. The effects of different storage times and different media on cellular viability have been widely studied in the past.

Pallante et al.[15] studied, in a goat model, the effect of allograft storage on the macroscopic structure, cellular and matrix fixed cartilage composition, and biomechanical function of cartilage within osteochondral allografts at 12 months' follow-up in 15 recipient goats. The features of the osteochondral allografts stored at 4°C for either 14 days or 28 days were similar, but they were inferior to those of the fresh grafts and better than those of the frozen grafts. Cellularity was reduced at the articular surface and accompanied by reduced matrix content and structural properties, suggesting that decreased cellularity detrimentally affects repair outcomes.

Garrity et al.[16] used 45 canine femoral hemicondyles and hemitibial plateaus that were stored in either a standard or an anti-inflammatory medium at different temperatures (4°C or 37°C) for 28 or 56 days. They concluded that storage of osteochondral allografts at 37°C in the standard medium was associated with the most optimal maintenance of chondrocyte viability, extracellular matrix biomechanical composition, and biomechanical properties.

Bae et al.[17,18] used a polyphenol from green tea (epigallocatechin gallate [EGCG]) added to storage medium to improve cartilage viability. In the first study they used osteoarticular plugs harvested from rabbit knees and stored at 4°C with or without EGCG at different concentrations for different times.[17] They reported that EGCG maintained high cell density and normal properties for the extracellular matrix. In the second study they used articular cartilage from patients undergoing total hip arthroplasty stored at 4°C with or without EGCG for different times.[18] They reported that EGCG reduced the time-dependent loss in cellular viability but this protective action was less effective after

Table 2. Demographic Data From Clinical Studies

	Type of Study	Type of Graft	Storage Time, d	Patients	Knees	Age, yr
Bianchi et al.[4]	Retrospective cohort study	Frozen	NS	12 (4 M and 8 F)	12	33 (range, 16-63)
LaPrade et al.[5]	Prospective cohort study	Fresh	20.3 d (range, 15-25)	23 (13 M and 10 F)	23	20.3
Görtz et al.[6]	Retrospective cohort study	Fresh	5-21	22 (6 M and 16 F)	28	24.3 (range, 16-44)
Brown et al.[7]	Prospective cohort study	Fresh	21.1 (range, 16-26)	34 (9 M and 25 F)	34	34.5 (range, 15-61)
Pearsall et al.[8]	Prospective cohort study	18 fresh, 9 frozen	NS	27 (18 M and 9 F)	25	Refrigerated, 44 (range, 17-69); frozen, 57 (range, 35-66)
Scully et al.[9]	Retrospective cohort study	Fresh	NS	18 (1 M and 17 F)	18	26.7 (range, 20-35)
Krych et al.[10]	Retrospective cohort study	Fresh	7-30	43 (30 M and 13 F)	43	33 ± 10 (range, 18-49)
Giorgini et al.[11]	Retrospective cohort study	Fresh	14-21	11 (8 M and 3 F)	11	34 (range, 18-66)
Lyon et al.[12]	Retrospective cohort study	Fresh	14-21	11 (6 M and 5 F)	13	15.2 (range, 13-20.4)
Levy et al.[13]	Retrospective cohort study	Fresh	<7	122 (65 M and 57 F)	129	32.8 (range, 15-68)
Shaha et al.[14]	Retrospective cohort study	Fresh	<21	38 (34 M and 4 F)	38	29.83 ± 5.3

F, female; M, male.

Table 3. Surgical Data From Clinical Studies

	Lesion Size	Femur	Tibia	Patella	Follow-up	Associated Procedures
Bianchi et al.[4]	NA	3 LFC, 6 MFC	1 LTP, 2 MTP	0	10 yr (range, 4-18 yr)	NS
LaPrade et al.[5]	4.8 cm^2 (range, 3.1 to 9.6 cm^2)	3 LFC, 19 MFC, 1 both	0	0	3 yr (range, 1.9-4 yr)	7 HTO, 3 meniscal transplant (1 with ACL revision), 1 meniscectomy 1 hardware removal
Görtz et al.[6]	10.8 cm^2 (range, 5-19 cm^2)	12 LFC, 9 MFC, 7 both	0	0	67 mo (range, 25-235 mo)	NS
Brown et al.[7]	5.7 cm^2 (range, 1.5-15 cm^2)	34	0	0	24 mo	1 ACL, 3 HTO, 1 MPFL, 4 meniscal transplant
Pearsall et al.[8]	Refrigerated, 4.2 cm^2; frozen, 5.3 cm^2	NS	0	NS	46 mo	NS
Scully et al.[9]	Single plugs, 21.5 mm; mosaicplasty, 8.7 mm for each plug	3 LFC, 15 MFC	0	0	3.4 yr (SD, 1.98 yr)	4 HTO, 2 meniscal debridement, 1 meniscal repair
Krych et al.[10]	7.25 ± 2.36 cm^2 (range, 2.5-13.94 cm^2)	17 LFC, 17 MFC, 1 trochlea, 8 both	0	0	2.5 yr (range, 1-11 yr)	NS
Giorgini et al.[11]	10.3 ± 5.3 cm^2 (range, 3-20 cm^2)	5 LFC, 2 MFC	3 LTP, 1 MTP	0	25.6 mo (range, 12-55 mo)	NS
Lyon et al.[12]	5.1 cm^2 (range, 1.8-8 cm^2)	7 LFC, 4 MFC, 1 trochlea	0	1	24 mo (range, 12-41 mo)	NS
Levy et al.[13]	8.1 cm^2 (range, 1-27 cm^2)	45 LFC, 77 MFC, 7 both	0	0	13.5 yr (range, 2.4-27.5 yr)	NS
Shaha et al.[14]	5.02 ± 132 cm^2	13 LFC, 25 MFC	0	0	4.1 yr (range, 1-9 yr)	1 HTO, 1 tibial tubercle osteotomy, 3 meniscal transplantation (1 with ACL)

ACL, anterior cruciate ligament; HTO, high tibial osteotomy; LFC, lateral femoral condyle; LTP, lateral tibial plateau; MFC, medial femoral condyle; MPFL, medial patellofemoral ligament; MTP, medial tibial plateau; NA, not applicable; NS, not specified.

Table 4. Results From Clinical Studies

	Results	Failures	Complications
Bianchi et al.[4]	The functional outcome was “excellent” in 2 patients, “good” in 5, and “fair” in 3.	1 revision allograft	NS
LaPrade et al.[5]	Significant improvement in symptoms, function, and overall scores	0	1 superficial cellulitis
Görtz et al.[6]	Osteochondral allografting is a reasonable salvage option for osteonecrosis. TKA was avoided in 27 of the 28 knees.	5	NS
Brown et al.[7]	At CT scan, posterior grafts were more likely to fail in the patients with multiple grafts.	3	NS
Pearsall et al.[8]	Greater improvement in WOMAC score and KSS in frozen graft group	6 in refrigerated group (TKA)	NS
Scully et al.[9]	Osteochondral allograft transplantation does not appear to be conducive to retention on active duty.		NS
Krych et al.[10]	The overall rate of return to sport was 88%, but the rate of return to previous sport was 79%.	0	1 manipulation under anesthesia
Giorgini et al.[11]	Improvement in both objective and subjective IKDC scores	1 UKA	2 (1 pain for 3 mo, 1 removal of loosen screw)
Lyon et al.[12]	Return to sports at 9-12 mo, incorporation of graft on radiographs at 12 mo	0	1 persistent pain
Levy et al.[13]	The survivorship rate was 89% at 5 yr, 82% at 10 yr, 74% at 15 yr, and 66% at 20 yr.	31 (revision allograft or arthroplasty)	33 (29 debridement, 3 meniscectomy, 5 meniscus repair)
Shaha et al.[14]	29% return to full duty, 29% to limited duty	0	1 revision ACL

ACL, anterior cruciate ligament; CT, computed tomography; IKDC, International Knee Documentation Committee; KSS, Knee Society Score; NS, not specified; TKA, total knee arthroplasty; UKA, unicompartmental knee arthroplasty; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 5. Results From Basic Science Articles

Authors	Year	Specimens	Aim of Study	Results
Pallante et al.[15]	2012	Goats (15)	Effect of allograft storage on macroscopic structure, cellular and matrix fixed cartilage composition, and biomechanical function of cartilage	At 12 mo of follow-up, features of osteochondral allografts stored at 4°C for 14 d or 28 d were similar but were inferior to those of fresh grafts and better than those of frozen grafts. Cellularity, matrix content, and structural properties were reduced.
Garrity et al.[16]	2012	Canine femoral hemicondyles and hemitibial plateaus (45)	Effect of graft storage in either a standard or anti-inflammatory medium at different temperatures (4°C or 37°C) for 28 or 56 d	Storage at 37°C in standard medium provided the most optimal maintenance of chondrocyte viability, extracellular matrix biomechanical composition, and biomechanical properties.
Bae et al.[17]	2009	Rabbit knees (18)	Effect of a polyphenol from green tea (EGCG) added to storage medium at 4°C	EGCG maintained high cell density and normal properties of the extracellular matrix.
Bae et al.[18]	2010	Articular cartilage from patients undergoing total hip arthroplasty	Effects of EGCG added to storage medium at 4°C	EGCG reduced the time-dependent loss in cellular viability up to 4 wk. Chondrocyte metabolism was also preserved (higher collagen and GAG content in extracellular matrix). On biomechanical testing, there were no differences in the elastic modulus.
Rosa et al.[19]	2009	Human tibial plateaus (18)	Effects of arbutin on chondrocyte viability	Viability in tibial plateaus treated with arbutin, 50 mmol/L, was approximately 23%, whereas in those treated with 10% DMSO or 10% glycerol, it did not exceed 4%.
Stoker et al.[20]	2012	Adult canine cadavers (14 medial and lateral femoral condyles)	Effects of room-temperature storage in different media (nutritive, antidegradative, and anti-inflammatory) without CO_2 supplementation	Chondrocyte viability was maintained at 90% of harvest levels up to 63 d. However, no microbial testing to determine risk of contamination was performed.
Squillace et al.[21]	2014	Human specimens (25)	Efficacy of methylene blue light on viral inactivation	Methylene blue light reduced enveloped DNA and RNA viruses to nondetectable levels and non-enveloped DNA and RNA viruses by 3.1 to 5.6 logs while maintaining the biomechanical functionality of osteochondral allografts.
Jomha et al.[22]	2009	Porcine osteochondral dowels (396 plugs)	Permeation comparison of 4 different cryoprotective agents	A combination of different cryoprotective agents can be helpful because they can be used at nontoxic concentrations.
Forriol et al.[23]	2011	Sheep (36)	Comparison of osteochondral allograft integration stored at different temperatures and DMSO concentrations	There was little or no incorporation to the host cartilage at 6 mo after surgery, with no differences when comparing the gross cartilage morphology between the different groups.
Szarko et al.[24]	2010	Bovine medial tibial plateaus (17)	Analysis of mechanical properties of osteoarticular bovine allograft stored at 4°C, −20°C, or −80°C or frozen in liquid nitrogen (−196°C) for 2 min and then stored at −80°C	When combined with rapid thawing, subchondral allograft may be successfully stored at subzero temperatures.
Lane et al.[25]	2009	Caprine knees (23)	Evaluation of condylar coefficient of friction after graft transplantation and its modulation with hyaluronan	The coefficient of friction increases even when the plug is placed in a flat or recessed position. Application of hyaluronan diminishes this rise.
Bardos et al.[26]	2009	Porcine knee joints (20)	Comparison of 3 techniques: bone marrow stimulation, ACI, and processed chondrograft	Good osteochondral integration of the processed chondrograft was found; the resulting tissue appeared to be hyaline cartilage. No immune-surveillance reactions were shown. The chondrograft could also be freshly frozen and used as a natural scaffold.
To et al.[27]	2011	Rabbit knees (14)	Comparison between autograft and allograft, storage culture media, and time	There was a high degree of graft-host healing despite strain, age, and size mismatch between the rabbits.
Pallante-Kichura et al.[28]	2013	Adult goats (15)	Evaluation of structure and location of bone cysts of subchondral bone after osteochondral grafting and assessment of relation between cartilage and bone after allograft transplantation	Frozen allograft exhibited eroded subchondral bone, all allografts contained basal cysts, and subchondral bone pathology was related to overlying articular cartilage integrity.

ACI, autologous chondrocyte implantation; CO_2, carbon dioxide; DMSO, dimethyl sulfoxide; EGCG, epigallocatechin gallate; GAG, glycosaminoglycan.

4 weeks. Chondrocyte metabolism was also preserved as shown by the higher collagen and glycosaminoglycan content in the extracellular matrix. On biomechanical tests, there were no differences in the elastic modulus in the specimens treated with and without EGCG.

Rosa et al.[19] determined that arbutin, a glycosylated hydroquinone, is not cytotoxic and its cryoprotective effects are almost twice those elicited by other cryoprotective agents such as dimethyl sulfoxide (DMSO) and glycerol. In their study 18 human tibial plateaus were procured from multi-organ donors and were treated with or without arbutin (50 or 100 mmol/L), alone or in combination with various concentrations of DMSO and glycerol; were then frozen at −20°C; and were transferred 24 hours later to a biofreezer at −80°C. Two to 3 months later, thawing was achieved by immersion in cell culture medium at 37°C. Chondrocyte viability was assessed before and after freezing/thawing using a colorimetric assay based on the cell's metabolic activity and fluorescent dyes to evaluate cell membrane integrity. In tibial plateaus treated with arbutin, 50 mmol/L, viability was approximately 23%, whereas in those treated with 10% DMSO or 10% glycerol, it did not exceed 4%.

Stoker et al.[20] hypothesized that osteochondral tissue can be preserved at room temperature for at least 56 days with viable chondrocyte density maintained at 70% of harvest level and that tissue viability could be assessed nondestructively using media biomarkers. The medial and lateral femoral condyles of 14 adult canine cadavers were harvested and stored in 1 of 3 proprietary media compositions (nutritive, antidegradative, and anti-inflammatory media) in 3 different container conditions at 25°C without carbon dioxide supplementation. After 63 days, chondrocyte viability was assessed directly using fluorescent live tissue stain and indirectly by a metabolic essay of the media. The results were good, with chondrocyte viability maintained at 90% of harvest levels up to 63 days. However, no microbial testing to determine the risk of contamination was performed.

An interesting work on viral inactivation of human osteochondral allograft has been published by Squillace et al.[21] Human cadaveric osteochondral allografts were inoculated with one of the following viruses: bovine viral diarrhea virus, hepatitis A virus, human immunodeficiency virus type 1, porcine parvovirus, or pseudorabies virus. The samples were processed through a methylene blue light treatment that was effective in reducing enveloped DNA and RNA viruses to nondetectable levels and non-enveloped DNA and RNA viruses by 3.1 to 5.6 logs while maintaining the biomechanical functionality of the osteochondral allografts.

Jomha et al.[22] compared the permeation of 4 cryoprotective agents in osteochondral porcine dowels at different temperatures and different incubation times. They concluded that a combination of different cryoprotective agents could be helpful because they can be used at nontoxic concentrations.

Forriol et al.[23] in their animal study compared the integration of osteochondral allograft cryopreserved at different temperatures (either −80°C or −186°C) and different concentrations of DMSO for a total of 6 groups. They found no differences when comparing the gross cartilage morphology of each group; in most of the cases, the graft was recessed and there was little or no incorporation to the host cartilage at 6 months after surgery. Using 4 histopathologic classification scores for cartilage, they found no differences between groups and concluded that all the cryopreservation protocols adopted provided scanty integration in an in vivo sheep model of osteochondral allograft transplantation.

Szarko et al.[24] analyzed the mechanical properties of osteoarticular bovine allograft stored at 4°C, −20°C, or −80°C or frozen in liquid nitrogen (−196°C) for 2 minutes and then stored at −80°C. They concluded that when combined with rapid thawing, subchondral allograft may be successfully stored at subzero temperatures.

The condylar coefficient of friction after graft transplantation and its modulation with hyaluronan have been evaluated by Lane et al.[25] in 23 caprine knees. The grafting procedure increased the coefficient of friction even when the plug was placed in a flat or recessed position and, moreover, when the hole was left unfilled. The application of hyaluronan diminished the rise observed in the coefficient of friction after transfer surgery.

Bardos et al.,[26] using porcine knee joints, compared the efficacy of 3 techniques for the treatment of cartilage lesions: bone marrow stimulation, autologous chondrocyte implantation, and processed chondrograft. The processed chondrograft was obtained by intensively incising the bony side of the graft (deep and intermediate zone) without compromising the superficial layer of the tissue, hence increasing the integrational surface and providing easier access to the deeper zones for chondrocytes and bone marrow−derived mesenchymal stem cells. The processed chondrograft showed good osteochondral integration, and the resulting tissue appeared to be hyaline cartilage. No immune-surveillance reactions were shown with this technique. The chondrograft could also be freshly frozen and used as a natural scaffold.

A rabbit trochlear model of osteochondral allograft transplantation has been studied by To et al.[27] They evaluated different variables: autograft compared with allograft, storage culture media, and culture time. The main finding of the study was the high degree of graft-host healing despite strain, age, and size mismatch between the rabbits.

The importance of subchondral bone has been investigated by Pallante-Kichura et al.,[28] determining the effect of osteochondral storage on subchondral bone, characterizing the structure and location of bone cysts found in subchondral bone after osteochondral grafting, and assessing the relation between cartilage and bone after an allograft transplantation. Frozen allograft exhibited eroded subchondral bone, all allografts contained basal cysts, and subchondral bone pathology was related to overlying articular cartilage integrity.

Discussion

A variety of methods have been developed in an attempt to repair articular cartilage defects. These include bone marrow stimulation techniques (subchondral drilling, abrasion, microfracture), osteochondral grafting (mosaicplasty), autologous chondrocyte implantation, and matrix-assisted autologous chondrocyte implantation. The treatment becomes more challenging when the size of the lesion is larger and when subchondral bone is involved. In these cases fresh osteochondral allograft in an ideal option in restoring the cartilage surface and bone and normalizing biomechanics.

On the basis of our review of the current literature, we came to the following conclusions (Table 6): Osteochondral allografts do work when evaluating the long-term clinical results along with improved patient satisfaction and function. Most of the authors used fresh allograft, and cellular viability was considered the most important factor for successful osteochondral transplantation. Fresh osteochondral allografts of the knee seem to have promising clinical results for the treatment of large osteochondral defects. In the articles that we reviewed, large lesions, with a mean area of 6.4 cm^2, were treated and a survivorship rate of up to 60% at 20 years was found.[13]

Görtz et al.[6] and Giorgini et al.[11] treated lesions with a mean area of 10 cm^2 of the lateral and medial femoral condyles with mean follow-up periods of 5.5 years and 2 years, respectively. The storage time for the graft in both articles was a maximum of 21 days. The patients' mean age was 29 years. Görtz et al. reported that total knee arthroplasty was avoided in 27 of the 28 knees, being a very reasonable salvage option for the treatment of osteonecrosis. Giorgini et al. reported improvement in both the International Knee Documentation Committee objective scores (at least 1 class for each patient except the one in whom failure occurred) and subjective scores (27.3 to 58.7). Only 1 patient required a new surgical procedure and underwent unicompartmental knee arthroplasty.

The treatment of osteochondritis dissecans in the young population is highly debated. Lyon et al.[12] treated 11 patients (13 knees) with a fresh allograft with a mean age of 15.2 years. In 7 cases the lateral femoral condyle was involved; in 4 cases the medial femoral condyle was involved; in 1 case the lesion involved the trochlea; and in 1 case it involved the patella. Only 1 patient presented with persistent pain; all other patients returned to sporting activity at 9 to 12 months, and at 1 year of follow-up, all presented with incorporation of the graft on radiographs. In our review this is the only case in which a lesion of the patella was treated, but no specific results were reported.

It is also very rare to treat lesions of the trochlea with fresh osteochondral allografts. Only Lyon et al.[12] and Krych et al.[10] treated, in 1 case each, an osteochondral lesion of the trochlea, but no specific results concerning trochlear lesions were reported. Furthermore, Krych et al. evaluated the return to sporting activity after a fresh allograft surgical procedure. The overall rate of return to sport was 88%, but the rate of return to the previous level of sport was 79%. Patients who were aged younger than 25 years and had preoperative symptoms for less than 12 months were more likely to return to full athletic activity.

Return to an athletic lifestyle or active duty after osteochondral allograft transplantation of the knee has been evaluated by both Scully et al.[9] and Shaha et al.[14] in a military population. Scully et al. reported the results of 18 patients with a mean age of 26.7 years. One of the patients was still in the acute recovery phase and 1 patient was already undergoing the medical evaluation board process at the time of surgery. At a follow-up of 23.2 months, 9 of the 16 remaining patients had either entered or completed the medical evaluation board process whereas 6 of the 7 patients who had stayed on active duty remained on activity-restricting profiles. Unfortunately, these data seemed not to correlate to all data found in the literature, and in our opinion, in the setting of the unique demands of active-duty soldiers, fresh osteochondral allograft transplantation does relieve pain in military patients but does not permit a return to full active duty. Shaha et al. reported that 42.1% of patients (16 of 38) were unable to return to military activity because of the operative knee. When analyzed for return to sport, only 5.3% of patients (2 of 38) were able to return to their preinjury level. Eleven patients underwent concomitant procedures. Statistical power

Table 6. Summary: Main Findings

The level of evidence of the articles included in this review was low (Level IV).
Fresh osteochondral allografts were used in most of the studies.
Storage times ranged from 1 to 4 wk.
Single or multiple plugs were used.
Associated procedures were common.
The results after surgery were generally good, with improvement in all clinical and functional scores.
Complication and failure rates were generally low.
Basic science articles focused on storage time, medium, and temperature to improve cellular viability and graft integration.

was maintained by analyzing data in aggregate for cases with versus without concomitant procedures. When the 11 patients undergoing concomitant procedures were removed from the dataset, the rate of return to full activity was 33.3% (9 of 27), with 22.3% (6 of 27) returning to limited activity and 44.4% (12 of 27) unable to return to activity. In this subset, 7.4% of patients (2 of 27) were able to return to their preinjury level of sport.

It is still debated whether fresh allografts give better results than frozen grafts. Moreover, one of the most debated issues is chondrocyte viability after a prolonged storage time or at low temperature. One factor to keep in mind is that in many of these studies, chondrocyte viability was overestimated based on the techniques used to measure chondrocyte function and viability.[29]

The clinical results of Bianchi et al.[4] and Pearsall et al.[8] showed that frozen grafts yielded good results also at long-term follow-up, with greater improvement in the Western Ontario and McMaster Universities Osteoarthritis Index score and Knee Society Score in the frozen graft group.[8]

Chondrocyte viability seems to be the main concern and interest regarding basic science research on this topic. The time to implantation and various storage conditions have been studied in recent years. It is well known that chondrocyte viability diminishes when grafts are stored at 4°C after 28 days.[28] More recent studies have reported better results storing grafts at 37°C or room temperature.[20-26] These findings would lead to the potential of the allografts tolerating a longer storage time, but other factors need to be taken into consideration such as the risk of infection.[21]

Changes in subchondral bone and the formation of bone cysts around implanted allografts have been studied by Pallante et al.[15] The main concern in their study was the effect of the overlying cartilage layer on the subchondral bone and the incorporation/healing of the adjacent host bone and cartilage, and further investigation is needed to optimize healing and minimize the transitional area between allograft and recipient.

Each surgical procedure provokes a rise in the condylar coefficient of friction. The use of hyaluronic acid infiltration after surgery is recommended for reducing this coefficient of friction that may cause chondrocyte damage.[25]

Limitations

The limitations of this systematic review are mainly related to the quality of the articles included for review. No meta-analysis was performed because the included articles were not homogeneous and different outcome measures were used. In many of the studies, associated procedures were common, adding another confounding variable. Finally, the level of evidence is low; in fact, most of the included articles were retrospective case series.

Conclusions

Despite the limitations of this review, fresh osteochondral allografts of the knee showed good clinical and functional outcomes even at longer-term follow-up. No other effective treatment exists, at the moment, for large osteochondral lesions. This surgical procedure is burdened by cost and difficulty in finding matching fresh donors. A new method to establish chondrocyte viability before the implantation of a new allograft would be a useful decision-making instrument.

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