Fresh osteochondral allograft for knee Osteochondritis Dissecans

Subjects: Orthopedics

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Osteochondritis dissecans (OCD) is an incompletely understood joint disorder affecting a broad spectrum of patients, but is most prevalent in adolescents and young adults. It is the end result of the aseptic separation of an osteochondral fragment with the gradual fragmentation of the articular surface and results in an osteochondral defect. The incidence of OCD is estimated to be approximately 15 to 30 per 100,000 patient-years. OCD lesions are most frequently seen in the knee. Reconstructive techniques for OCD of the knee are typically necessary when either non-operative or reparative/regenerative operative treatments fail, or when the OCD is irreversible. Although a limited number of low-level evidence studies concening the use of fresh osteochondral allograft in the treatment of the OCD as reconstructive technique are available in previous research, satisfactory clinical results and survival rates of the reconstruction are reported.

Keywords: osteochondral allograft transplantation ; osteochondritis dissecans ; knee ; lesion ; healing

1. Introduction

Osteochondritis dissecans (OCD) is an incompletely understood joint disorder affecting a broad spectrum of patients, but is most prevalent in adolescents and young adults [1]. The incidence of OCD is estimated to be approximately 15 to 30 per 100,000 patient-years [2][3]. OCD lesions are most frequently seen in the knee, occurring most often in the medial femoral condyle (70%, especially in the lateral aspect of the medial femoral condyle), followed by the lateral femoral condyle (15–20%), patella (5–10%), and trochlea (<1%) [4][5]. Although OCD was first described over 100 years ago, there is no consensus on its etiology. The original nomenclature suggested a major role for inflammation in OCD; however, histological evidence has failed to support this theory [6]. Current hypotheses on the origin of OCD include repetitive microtrauma, vascular insufficiency, or anomalous endochondral ossification [7]. This pathologic process involves the fragmentation of subchondral bone, which becomes avascular and detaches from the surrounding cartilage, often forming an intra-articular loose body [8]. The lesion can manifest as pain or through other symptoms, including catching and locking [2]. Age and skeletal maturity are important variables influencing clinical decision making because older, skeletally mature individuals (in the setting of lower healing potential) are less likely to succeed with non-operative treatment and more likely to progress to surgery [9][10].

The non-operative treatment of OCD with activity modification and bracing has been reported to be successful in 50% to 94% of patients with open physes and stable lesions [11][12]; therefore, most authors suggest initial non-operative treatment for juvenile OCD [9][13][14][15][16][17][18][19]. In the cases in which the physes are closed or the lesion is advanced—particularly in stage 3 (unstable but not dislocated fragment) or stage 4 (presence of loose body) according to the classification system proposed by Clanton and DeLee [20]—the success of non-operative treatment decreases [21]. Both reparative techniques, such as internal fixation [16][17][22], bone grafting [23], or debridement/fragment excision [24][25], and restoration techniques, such as anterograde/retrograde drilling [16][26][27] and autologous chondrocyte implantation (ACI) [28], have demonstrated variable healing outcomes. Large OCD de novo lesions, or those that progress after unsuccessful initial treatment and present with significant bone and cartilage defects, lead to long-term disability and are precursors to osteoarthritis at a young age [13][14]. These defects in children or adults should be considered for reconstructive treatment options, including various techniques using the bone of synthetic grafts associated with ACI [29][30], autologous osteochondral transplantation (OAT) or mosaicplasty (when multiple plugs are harvested to fill the defect in a mosaic-like pattern) [31][32][33][34] and osteochondral allograft (OCA).

Hypothetically, OCA is an attractive option because it can restore in a single-stage procedure both the bone and chondral components, potentially with neither the pitfalls of mosaicplasty (principally the morbidity of the donor zone of the knee, which limits the dimensions of the reconstruction), nor the high costs of the ACI-related procedures. The major indications for OCA transplantation include substantive joint surface compromise (>2 cm 2) with bone loss and/or failed prior cartilage repair. Pathologic OCD tissue can be removed by cylindrical drills and replaced by press-fit “dowel grafts” (if necessary, fixation can be augmented with bioabsorbable screws or chondral darts) or resected to create a flat surface for the

application of “shell grafts” [35]. The latter usually requires fixation to maintain compression (typically achieved by bioabsorbable or cannulated screws), although mixed methods have been described [36]. OCA can be fresh, frozen, cryo-preserved or freeze-dried tissue bank products. Stored allografts have shown reduced antigenicity and risk of disease transmission, but the preservation process also affects the biomechanical competency of the transplant [37][38]. Since it is relatively accepted that cartilage viability positively correlates with the integration of the graft, and consequently with the clinical outcome, fresh osteochondral allografts (FOCA) are preferred. FOCA transplantation procedures offer the primary advantage of containing viable hyaline cartilage and structurally competent bone. The term “fresh” refers to a graft harvested within 24 h of the donors’ death, stored (usually at 4 °C into an appropriate culture) until microbiological and viral tests are performed and then transplanted into a recipient host, usually within 28 days to avoid viability decrease [39].

2. Methods

An in-depth search of the scientific research was performed according to PRISMA. A search regarding the existing evidence for clinical healing out-comes and failure rates of FOCA transplantation of the knee joint in OCD population with no restriction on date of publication, up to the end of September 2021, was performed on the PubMed, Scopus, and Web of Science databases. The inclusion criteria were as follows: original research reporting clinical outcomes and failure rates of FOCA for the treatment of osteochondritis dissecans in the knee joint, English language, minimum of five patients, minimum follow-up of 12 months, and human studies. Only studies reporting data on homogeneous populations of patients with OCD, or from which data regarding patients with OCD were extractable, were included.

3. Patients’ Characteristics

As shown in **Table 1**, a total of 280 patients and 303 OCD lesions treated with FOCA was included. In the studies analyzed, the medium follow-up ranged from 2 years (range, 1–3.4) [40] to 7.7 years (range, 2–22) [41], with an approximated weighted mean of 6.3 years. The medium age at surgery ranged from 15.2 years (range, 13–20.4) [40] to 34 years (range, 20–49) [42], with an approximated weighted mean of 23.9 years. The location of the OCD lesions reported in the analyzed studies was predominantly at the level of the medial and lateral condyles of the distal femur, in a similar ratio. Lyon et al. and Sadr et al. also included a substantial proportion of OCD lesions at the level of the patella (7.5% and 1%, respectively) and trochlea (7.5% and 6%, respectively) [2][40]. The mean size of the OCD defects (reported in 5 studies [2][43][40][42][41]) was high, ranging from 4.5 cm^2 [42] (range, 0.9–15) to 7 cm^2 [41], with an approximated weighted mean of 6.7 cm^2. Only the study of Lyon et al. [40], on 11 patients, focused on juvenile OCD; however, no studies specified the exact number of patients with open physes, who were intended to be a very restricted minority of the total number of patients included in this entry. Four studies [2][43][41][44] described series in which all or most of the included patients had undergone previous surgery (included previous grafts), before FOCA transplantation. Concomitant surgeries were described in three studies [43][42][41].

Table 1. Fresh osteochondral allograft transplantation in the treatment of osteochondritis dissecans.

Year	Authors [Reference]	Patient, n° (OCA, n°)	Study Design (Level of Evidence)	Knee Site (%)	Age, y: Mean ± SD (Range)	FU, y: Mean ± SD (Range)	Lesion Size, cm^2: Mean ± SD (Range)	Failure at Last FU, n° (%)	Estimated Graft Survival Rate	Re-Operation Rate *	Mean Time t Failure y Mean ± SD
2018	Cotter et al. [43]	37 (43)	Case series (IV)	LFC 44% MFC 51% Both condyles 4%	26 ± 9.96 (15–49)	7.29 ± 3.3	4.6 ± 1.7	2 (5.1%)	97% at 5 years	35.9%	6.2 ± 3.8
2016	Sadr et al. [2]	135 (149)	Case series (IV)	MFC 62% LFC 29% Trochlea 6% Patella 1% Others 2%	Median. 21 (12–55)	Median: 6.3 (1.9–16.8)	7.3 (2.2–25)	12 (8%): 7 OCA revision, 3 UKA, 2 TKA	95% at 5 years 93% at 10 years	23%	6.1 ± 4.5
2012	Lyon et al. [40]	11 (12)	Case series (IV)	MFC 31% LFC 54% Patella 7.5% Trochlea 7.5%	15.2 (13–20.4)	2 (1–3.4)	5.1 (1.8–8)	0%	100% at last FU	0%	NA

Year	Authors [Reference]	Patient, n° (OCA, n°)	Study Design (Level of Evidence)	Knee Site (%)	Age, y: Mean ± SD (Range)	FU, y: Mean ± SD (Range)	Lesion Size, cm^2: Mean ± SD (Range)	Failure at Last FU, n° (%)	Estimated Graft Survival Rate	Re-Operation Rate *	Mean Time t Failure y Mean ± SD
2009	Pasqual-Garrido et al. [42]	46 (16)	Case series (IV)	NA	34 ± 9.5 (20–49) **	4.0 ± 1.8 (2.0–10.6) **	4.5 ± 2.7 (0.9–15) **	1/16 OCA (6%): TKA	94% at last FU **	NA	14 month
2007	Emmerson et al. [41]	64 (66)	Case series (IV)	MFC 62% LFC 38%	28.6 (15–54)	7.7 (2–22)	7.5	9 (13%): 6 OCA revision, 1 OCA removal, 1TKA, 1 UKA	91% at 5 years 76% at 10 and 15 years	10 (15%)	4.9 ± 2.4
1994	Garrett et al. [44]	17 (17)	Case series (IV)	LFC 100%	20 (16–46)	3.5 (2–9)	NA	1 (6%): not specified reconstructive surgery	94% at last FU	17 (100%): 1 failure + 16 hardware removal	15 month

Abbreviations: OCD, osteochondritis dissecans; OCA, osteochondral allograft transplantation; MFC, medial femoral condyle; LFC, lateral femoral condyle; TKA, total knee arthroplasty; UKA, unilateral knee arthroplasty; FU, follow-up; NA, not available. * Re-operation rate = failures + operations not related to the graft; ** On total study cohort.

4. Graft Survival

The definition of reconstruction failure varied across studies. In general, studies with shorter follow-up used clinical failure or radiological non-integration of the graft as criteria. By contrast, studies with a longer follow-up defined failure as the revision of the reconstruction or conversion to unicompartmental or total knee arthroplasty. The failure rate at last follow-up ranged from 0% (reported by Lyon et al. [40] with a mean follow-up of 2 years) to 13% (reported by Emmerson et al. [41] with a mean follow-up of 7.7 years). Cotter et al. [43] reported a 97% estimated reconstruction survival rate (RSR) at 5 years on 43 FOCA transplantations; Sadr et al. [2] reported 95% RSR at 5 years and 93% at 10 years on 149 FOCA; Emmerson et al. [41] reported 91% RSR at 5 years and 76% RSR at 10 and 15 years on 66 FOCA; while Lyon et al. [40], Pascual-Garrido et al. [42] and Garrett et al. [44] reported graft survival rates at last follow-up of 100%, 94%, and 94%, respectively. In the studies of Sadr et al. [2] and Emmerson et al. [41], the age at surgery were reported to be higher and the OCD lesion size was larger in the subgroups who received revision surgery due to graft failure. In the study by Sadr et al. [2], the median age and the mean lesion size were 31 years and 7.6 ± 2.8 cm^2 in the revised patients versus 21 years and 7.3 ± 3.3 cm^2 in the total cohort, while in the study of Emmerson et al. [41], the mean age and the mean lesion size were 32.9 ± 10.6 years and 11.3 ± 4.7 cm^2 in the revised patients versus 28.6 years and 7.5 cm^2 in the total cohort. The mean time to failure was reported in five studies [2][43][42]: Cotter et al. [43] reported a mean time to failure of 6.2 ± 3.8 years (mean follow-up 7.29 ± 3.3 years), Sadr et al. [2] reported 6.1 ± 4.5 years (mean follow-up 6.3 years, ranging from 1.9 to 16.8), Emmerson et al. [41] reported 4.9 ± 2.4 years (mean follow-up 7.7 years, ranging from 2 to 22), while both Pascual-Garrido et al. [42] and Garrett et al. [44] reported a single failure at 14 months and 15 months after surgery, respectively.

5. Functional Outcomes

Five studies reported the results of at least two clinical scores administered to patients pre- and post-operatively [2][43][40][42][41]. In all cases, better scores were observed after surgery, with the majority of differences being statistically significant. Four studies reported the percentage of patients who were satisfied overall, which ranged from 63% to 95% [2][43][42][41]. A more comprehensive overview of the results of the most frequently used clinical scores in the analyzed studies is provided in **Table 2.**

Table 2. Clinical scores reported in at least two of the studies included.

	Cotter et al., 2018	Sadr et al., 2016	Lyon et al., 2012	Pasqual-Garrido et al., 2009	Emmerson et al., 2007
18-point	NA	Pr: 13.6 (±2.0) F: 16.8 (±1.5) *p*: <0.001 *	Pr: 12.7 (10–14) F: 16.3 (10–18)	NA	Pr: 13.0 ± 1.7 F: 16.4 ± 2.0 *p*: <0.01 *

		Cotter et al., 2018	Sadr et al., 2016	Lyon et al., 2012	Pasqual-Garrido et al., 2009	Emmerson et al., 2007
IKDC total score		Pr: 31 F: 59 *p*: <0.001 *	Pr: 44.2 (± =17.5) F: 82.3 (± =15.8) *p*: <0.001 *	NA	Pr: 31 F: 45 *p*: 0.15	NA
KOOS	Symptoms	Pr: ≈52 F: ≈69 *p*: <0.001 *	NA	NA	Pr: 52 F: 74 *p*: 0.002 *	NA
	Pain	Pr: ≈50 F: ≈70 *p*: <0.001 *			Pr: 59 F: 67 *p*: 0.270	
	ADL	Pr: ≈61 F: ≈82 *p*: <0.001 *			Pr: 57 F: 67 *p*: 0.200	
	Sport	Pr: ≈23 F: ≈51 *p*: <0.001 *			Pr: 32 F: 46 *p*: 0.037 *	
	QOL	Pr: ≈21 F: ≈51 *p*: <0.001 *			Pr: 29 F: 39 *p*: 0.062	
SF-12	Physical	Pr: ≈33 F: ≈41 *p*: <0.001	NA	NA	Pr: 42 F: 52 *p*: 0.112	NA
	Mental	Pr: ≈53 F: ≈53 *p*: 0.910			Pr: 40 F: 43 *p*: 0.370	
VAS		NA	NA	Pr: 5.6 F: 1.2	NA	Pr: 6.7 ± 2 F: 0.9 ± 1.3
Satisfaction at Final FU, % (details)		81% (Es: 50%; S: 31.6%)	95% (Es: 78%; S: 17%; Ss: 3%; Sd: 1%; D: 1%)	NA	63%	92%

Abbreviations: Pr, preop. value; F, final FU value; *p*, *p*-value; 18 point, modified Merle d'Aubigné-Postel scale; IKDC, International Knee Documentation Committee; KOOS, knee injury and osteoarthritis outcome score; QOL, quality of life; ADL, activities of daily living; SF-12, 12 Item Short Form Survey; VAS, visual activity score; Es, extremely satisfied; S, satisfied; Ss, somewhat satisfied; Sd, somewhat dissatisfied; D, dissatisfied; NA, not available. * Statistically significant.

6. Conclusions

Fresh osteochondral allograft transplantation for irreversible osteochondritis dissecans lesions of the knee resulted, among the majority of patients, in significant improvements in pain and function with surviving grafts in the studies analyzed. Allografts also demonstrated good long-term durability, with high survivorship. The failure of previous treatments or allografts did not preclude revision allografting. Despite the very significant limitations imposed by the paucity and low quality of the available evidence, it can be concluded that this technique appears to be a safe and effective in the treatment of medium and large osteochondritis dissecans, representing a valid option to promote healing. Nevertheless, age at surgery and the size of the OCD lesion could affect graft survival, although there is insufficient data to state this definitively. The available research seems to suggest that the choice of FOCA can also be guided by the size of the lesion in the setting of OCD. However, only high-quality comparative studies with other techniques could define the possible and real advantages of FOCA.

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