European Journal of Trauma and Emergency Surgery
https://doi.org/10.1007/s00068-022-02155-y

REVIEW ARTICLE

Prognostic factors for the management of chondral defects of the knee and ankle joint: a systematic review

Filippo Migliorini[1,2] · Nicola Maffulli[3,4,5] · Jörg Eschweiler[1] · Christian Götze[6] · Frank Hildebrand[1] · Marcel Betsch[7]

Received: 25 August 2022 / Accepted: 21 October 2022
© The Author(s) 2022

Abstract

Purpose Different surgical techniques to manage cartilage defects are available, including microfracture (MFx), autologous chondrocyte implantation (ACI), osteoarticular auto- or allograft transplantation (OAT), autologous matrix-induced chondrogenesis (AMIC). This study investigated the patient-related prognostic factors on the clinical outcomes of surgically treated knee and ankle cartilage defects.

Methods This study followed the PRISMA statement. In May 2022, the following databases were accessed: PubMed, Google Scholar, Embase, and Scopus. All the studies investigating the outcomes of surgical management for knee and/or talus chondral defects were accessed. Only studies performing mesenchymal stem cells transplantation, OAT, MFx, ACI, and AMIC were considered. A multiple linear model regression analysis through the Pearson Product–Moment Correlation Coefficient was used.

Results Data from 184 articles (8905 procedures) were retrieved. Female sex showed a positive moderate association with visual analogue scale at last follow-up ($P = 0.02$). Patient age had a negative association with the American Orthopaedic Foot and Ankle Score ($P = 0.04$) and Lysholm Knee Scoring Scale ($P = 0.03$). BMI was strongly associated with graft hypertrophy ($P = 0.01$). Greater values of VAS at baseline negatively correlate with lower values of Tegner Activity Scale at last follow-up ($P < 0.0001$).

Conclusion The clinical outcomes were mostly related to the patients' performance status prior surgery. A greater BMI was associated with greater rate of hypertrophy. Female sex and older age evidenced fair influence, while symptom duration prior to the surgical intervention and cartilage defect size evidenced no association with the surgical outcome. Lesion size and symptom duration did not evidence any association with the surgical outcome.

Keywords Chondral defect · Knee · Talus · Prognostic factors

✉ Filippo Migliorini
migliorini.md@gmail.com

Nicola Maffulli
n.maffulli@qmul.ac.uk

Jörg Eschweiler
joeschweiler@ukaachen.de

Christian Götze
christian.goetze@muehlenkreiskliniken.de

Frank Hildebrand
fhildebrand@ukaachen.de

Marcel Betsch
marcel.betsch@gmx.de

[1] Department of Orthopaedic, Trauma and Reconstructive Surgery, RWTH University Hospital Aachen, 52074 Aachen, Germany

[2] Department of Orthopaedic and Trauma Surgery, Eifelklinik St. Brigida, 52152 Simmerath, Germany

[3] Department of Medicine, Surgery and Dentistry, University of Salerno, 84081 Baronissi, Italy

[4] School of Pharmacy and Bioengineering, Faculty of Medicine, Keele University, Thornburrow Drive, Stoke on Trent, England

[5] Barts and the London School of Medicine and Dentistry, Centre for Sports and Exercise Medicine, Queen Mary University of London, Mile End Hospital, London E1 4DG, England

[6] Department of Orthopaedics, Auguste-Viktoria-Klinik, 32545 Bad Oeynhausen, Germany

[7] Department of Orthopaedics and Trauma Surgery, University Hospital Erlangen, 91054 Erlangen, Germany

Published online: 07 November 2022

Abbreviations

MFx	Microfracture
ACI	Autologous chondrocyte implantation
OAT	Osteoarticular auto- or allograft transplantation
AMIC	Autologous matrix-induced chondrogenesis
PROMs	Patient-reported outcome reports
VAS	Visual analogic scale
AOFAS	American Orthopedic Foot and Ankle Score
BMI	Body mass index
IKDC	International Knee Documentation Committee
FU	Follow-up

Introduction

The treatment of articular cartilage defects of the lower extremities is challenging given the poor recruitment of regenerative cells into the defect, which results in a limited self-healing capacity of native cartilage tissue [1, 2]. Patients with full-thickness cartilage defects may experience significant pain, decrease in joint function and quality of life [3]. Cartilage defects result from trauma or repetitive shear and torsional forces applied to the cartilage surface [4]. If left untreated, cartilage lesions can progress to early osteoarthritis, joint pain, and mobility impairment [5, 6]. The previous studies estimated that the incidence of full-thickness cartilage lesions varies from 5% to 10% in knees of patients undergoing arthroscopy [7–9]. The prevalence of cartilage lesions in the ankle joint varies from 40% to 95% in patients with persistent pain after an ankle sprain with and without chronic ankle instability [10].

Microfracture (MFX) is considered the first-line treatment for cartilage defects, in both the knee and ankle joints, given the simplicity of the procedure, its low cost, minimal invasiveness, and satisfactory short-term clinical outcome [11, 12]. However, there have been concerns regarding the durability of MFX over time, since the clinical outcomes may worsen over time, in particular in larger lesions and more active patients [13–15]. To overcome limitations of the MFX technique, various forms of autologous chondrocyte implantation (ACI) and osteoarticular transfer system (OATS) have been introduced [16]. Although multiple techniques have been suggested to be effective in the management of articular cartilage defects, international recommendations and clear guidelines are missing. Moreover, it is also uncertain in which patient-dependent factors predict success after any of the above-mentioned cartilage treatment options.

Therefore, a systematic review was conducted to investigate whether patient characteristics at baseline exert an influence on surgical outcome in terms of patient-reported outcome reports (PROMs) and complications.

Materials and methods

Search strategy and data source

This systematic review is according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement [17]. The literature search was conducted independently by two authors (F.M. & J.E.). In May 2022, the following databases were accessed: PubMed, Google scholar, Embase, and Scopus. The following keywords were used in combination: *chondral*, *cartilage*, *articular*, *damage*, *defect*, *injury*, *chondropathy*, *knee*, *pain*, *matrix-induced*, *periosteal*, *periosteum*, *collagen*, *autologous*, *chondrocyte*, *transplantation*, *implantation*, *MFX*, *microfractures*, *mosaicplasty*, *mACI*, *cACI*, *pACI*, *AMIC*, *OAT*, *osteochondral transplantation*, *allograft*, *autograft*, *membrane*, *therapy*, *management*, *surgery*, *outcomes*, *revision*, *hypertrophy*, *failure.* Articles resulting from the literature search were screened by the same authors. The full text of the articles of interest was accessed. The bibliographies were also screened by hand for inclusion. Disagreements were solved by a third author (NM).

Eligibility criteria

All the studies investigating the outcomes of surgical management for knee and/or talus chondral defects were accessed. Only studies performing OAT, MFX, ACI or AMIC were considered. Given the authors language abilities, articles in English, German, Italian, French and Spanish were eligible. Studies with level I to IV of evidence, according to Oxford Centre of Evidence-Based Medicine [18], were considered. Abstracts, reviews, comments, editorial and opinion were not considered. Animals, biomechanics or in vitro studies were not considered. Studies enhancing the surgical procedures with stem cells were also eligible. Only studies that clearly stated the nature of the surgical intervention were included. Studies which included patients with large chondral and/or osteochondral lesions (>5 cm^2) and obese (BMI > 30 kg/m^2) were not included. Studies that reported data on patients with end-stage joint degeneration were not eligible. Only articles reporting quantitative data under the outcomes of interest were considered for inclusion. Missing data under the outcomes of interest warranted the exclusion from this study.

Outcomes of interest

Data extraction was performed separately by two authors (F.M. & J.E.). Data concerning author, year, journal, type of study and length of the follow-up were collected. The following

data at baseline were collected: the number of patients, age, sex, mean BMI (kg/m^2), size of the defect (cm^2), and duration of symptoms (months). Data concerning the following scores were extracted at baseline and at last follow-up: visual analogic scale (VAS), American Orthopedic Foot and Ankle Score (AOFAS) [19], Tegner Activity Scale [20], Lysholm Knee Scoring Scale [21], and International Knee Documentation Committee (IKDC) [22] scores. Furthermore, rate of hypertrophy, failures, and revisions were also retrieved. The primary outcome was to investigate the association of baseline patient-specific characteristics on surgical outcomes following restorative cartilage procedures for the knee and ankle.

Methodology quality assessment

The methodological quality assessment was performed by two authors independently (F.M. & J.E.). The risk of bias graph tool of the Review Manager Software (The Nordic Cochrane Collaboration, Copenhagen) was used. The following risk of bias was evaluated: selection, detection, attrition, and other source of bias.

Statistical analysis

All statistical analyses were performed by one author (F.M.) using the software STATA/MP 14.1 (StataCorp, College Station, TX). The Shapiro–Wilk test was performed to investigate data distribution. For normal data, mean and standard deviation were calculated. For nonparametric data, median and interquartile range were calculated. The Student's *T* test was used to assess significance for parametric data, while the Mann–Whitney *U*-test was used for nonparametric variables. Values of $P < 0.05$ considered statistically significant. A multivariate analysis was performed to assess associations between data of patients at baseline with the clinical scores at last follow-up and complications. A multiple linear model regression analysis through the Pearson Product–Moment Correlation Coefficient (r) was used. The Cauchy–Schwarz formula was used for inequality: + 1 is considered as positive linear association, while − 1 a negative one. Values of $0.1 < |r| < 0.3$, $0.3 < |r| < 0.5$, and $|r| > 0.5$ were considered to have weak, moderate, and strong association, respectively. The overall assessment of significance was performed using the χ^2 test, with values of $P < 0.05$ considered statistically significant.

Results

Search result

The literature search resulted in 795 articles. Of them, 309 were duplicates. A further 302 articles were not eligible: surgical technique ($N = 74$), not focusing on knee or ankle ($N = 41$) study design ($N = 140$), not reporting quantitative data under the outcomes of interest ($N = 19$), other ($N = 24$), language limitations ($N = 4$). This left 184 articles for the present study. The literature search results are shown in Fig. 1.

Methodological quality assessment

The risk of selection bias was judged as moderate. Indeed, 46.7% of studies (86 of 184) performed a retrospective analysis, while 38.0% (70 of 184) were prospective, and 15.2% (28 of 184) were randomized. Only few studies (35 of 184) performed assessor blinding; thus, the risk of detection bias was high. The risk of attrition and reporting bias were moderate, as was the risk of other bias. In conclusion, the overall review authors' judgements about each risk of bias item scored moderate, attesting to this study acceptable methodological assessment. The risk of bias graph is shown in Fig. 2.

Patient demographics

Data from 8905 procedures were retrieved. The median duration of symptoms before the index surgery was 36 (23.6–50.8) months. 41.7% (3713 of 8905) of patients were women. The mean age of the patients was 33.9 ± 6.9 years, while the mean BMI 25.6 ± 1.5 kg/m^2. The mean defect size was 3.3 ± 2.3 cm^2. The median follow-up time was 41.8 (24 to 60) months. Generalities and demographic data of the study are shown in Table 1.

Outcomes of interest

Female sex evidenced moderate association with greater VAS at last follow-up ($r = 0.3$; $P = 0.02$). Patient's age evidenced negative association with the AOFAS score ($r = -0.2$; $P = 0.04$) and Lysholm Knee Scoring Scale ($r = -0.4$; $P = 0.03$). Greater BMI was moderately associated with the rate of graft hypertrophy ($r = 0.6$; $P = 0.009$). VAS, IKDC, AOFAS, and Tegner Activity Scale at baseline were positively associated with themselves at last follow-up: VAS ($r = 0.9$; $P < 0.0001$), IKDC ($r = 0.5$; $P = 0.007$), AOFAS ($r = 0.6$; $P = 0.0002$), Tegner Activity Scale ($r = 0.4$; $P = 0.009$). The VAS score at baseline was inversely associated with the Tegner Activity Scale ($r = -0.8$; $P < 0.0001$) at last follow-up. No further statically significant associations were evidenced. The results of each of the pairwise correlation is shown in greater detail in Table 2.

Discussion

The management of articular cartilage defects still presents a major challenge. Therefore, identification of prognostic factors would allow to predict the outcome of various



Fig. 1 Flowchart of the literature search

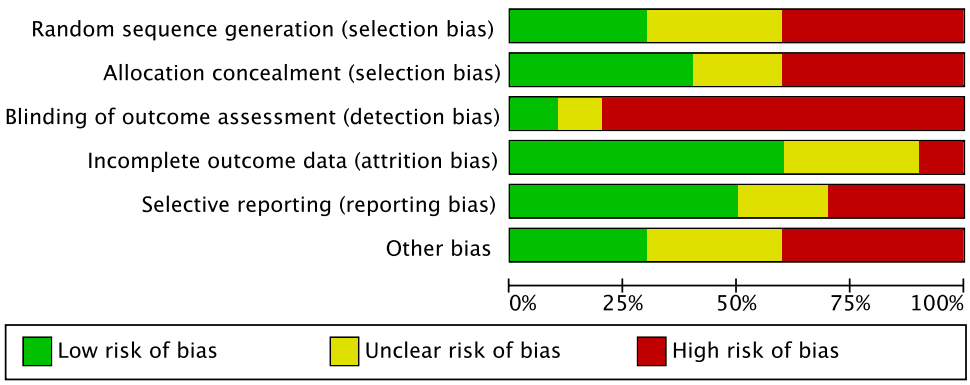


Fig. 2 Methodological quality assessment

surgical techniques in multiple joints, and it would help to educate patients on the success (or not) of their surgical intervention. Older age was associated with lower values of the AOFAS and Lysholm scores at last follow-up, while women evidenced a positive association with VAS. Given the weak associations between these endpoints, the role of sex and age still remain not fully defined. BMI evidenced a moderate positive association with the rate of graft hypertrophy. VAS, IKDC, AOFAS, and Tegner scores at baseline were associated among themselves at last follow-up,

Table 1 Generalities and patient baseline of the included studies

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Adams et al. 2011 [42]	*J Bone Joint Surg*	Retrospective	48.0	Talus	OAT	8	62.5%	31.4
Adams et al. 2018 [43]	*Foot Ankle Int*	Prospective	55.0	Talus	OAT	14	42.9%	40.0
Ahmad et al. 2015 [44]	*Foot Ankle Int*	Randomized	40.5	Talus	OAT	16	37.5%	39.7
			35.2	Talus	OAT	20	45.0%	41.3
Akgun et al. 2015 [45]	*Arch Orthop Trauma Surg*	Prospective, randomized	24.0	Knee	Syn-MSC	7	57.1%	32.3
				Knee	mACI	7	57.1%	32.7
Albano et al. 2017 [46]	*BMC Musculos Dis*	Retrospective	30.0	Talus	AMIC	16	50.0%	42.6
Anders et al. 2012 [47]	*Int Orthop*	Prospective	63.5	Talus	MACI	22	22.7%	23.9
Anders et al. 2013 [48]	*Open Orthop J*	Prospective, randomized	24.0	Knee	AMIC	8	12.0%	35.0
				Knee	AMIC	13	23.0%	39.0
				Knee	MFX	6	33.0%	41.0
Apprich et al. 2012 [49]	*Osteoarthritis Cartilage*	Retrospective	48.0	Talus	MACT	10	60.0%	31.0
			59.6	Talus	MFX	10	40.0%	32.4
Astur et al. 2018 [50]	*Rev Bras Orthop*	Prospective	12.0	Knee	AMIC	7	14.3%	37.2
Aurich et al. 2010 [51]	*Am J Sports Med*	Retrospective	24.5	Talus	MACI	19	27.8%	29.2
Bartlett et al. 2005 [52]	*J Bone Joint Surg*	Prospective, randomized	12.0	Knee	cACI	44	40.7%	33.7
				Knee	mACI	47		33.4
Basad et al. 2010 [53]	*Knee Surg Sports Traumatol Arthrosc*	Prospective, randomized	24.0	Knee	mACI	40	38.0%	33.0
				Knee	MFX	20	15.0%	37.5
Basad et al. 2015 [54]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	60.0	Knee	mACI	25	37.0%	32.0
Battaglia et al. 2011 [55]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	60.0	Talus	MACI	20	30.0%	35.0
Baumfeld et al. 2018 [56]	*Foot*	Retrospective	10.8	Talus	AMIC	17	47.1%	37.5
Baums et al. 2007 [57]	*J Bone Joint Surg*	Retrospective	63.0	Talus	PACI	12	58.3%	29.7
Becher et al. 2015 [58]	*Arch Orthop Trauma Surg*	Prospective	21.0	Knee	MFX	5	40.0%	27.0
Becher et al. 2017 [59]	*J Orthop Surg Res*	Prospective, randomized	36.0	Knee	mACI	25	32.0%	33.0
				Knee	mACI	25	16.0%	34.0
				Knee	mACI	25	40.0%	34.0
Becher et al. 2018 [60]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	67.2	Talus	MFX	16	56.3%	33.3
			68.4	Talus	AMIC	16	56.3%	32.4
Behrens et al. 2006 [61]	*Knee*	Prospective	34.5	Knee	mACI	38	50.0%	35.0
Bentley et al. 2012 [62]	*J Bone Joint Surg*	Prospective, randomized	120.0	Knee	pACI, cACI	58	43.1%	31.0
				Knee	Mosaicplasty	42	59.5%	32.0
Berruto et al. 2017 [63]	*Injury*	Prospective	162.0	Knee	pACI	9	31.3%	31.6
				Knee	cACI	24		
Bode et al. 2013 [64]	*Arch Orthop Trauma Surg*	Prospective	71.9	Knee	cACI	19		40.2
				Knee	cACI	24		38.3

Table 1 (continued)

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Brittberg et al. 2018 [65]	*Am J Sports Med*	Prospective, randomized	60.0	Knee	mACI	65	38.0%	35.0
				Knee	MFX	63	33.0%	34.0
Browne et al. 2006 [66]	*Clin Orthop Rel Res*	Prospective	60.0	Knee	pACI	100	35.0%	37.0
Buda et al. 2010 [67]	*J Bone Joint Surg*	Prospective	29.0	Knee	BM- MSC	20	40.0%	
Buda et al. 2015 [68]	*Int Orthop*	Retrospective	48.0	Talus	MACI	40	37.5%	31.4
				Talus	BMC	40	32.5%	30.2
Buda et al. 2019 [69]	*Europ J Orthop Trauma Surg*	Retrospective	48.0	Knee	BMAC	28	42.9%	38.0
Chan et al. 2018 [70]	*Cartilage*	Prospective	65.8	Talus	pACI	24	41.7%	34.1
Chung et al. 2014 [71]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	24.0	Knee	MFX	12	83.3%	44.3
				Knee	AMIC	24	41.7%	47.4
Cole et al. 2011 [72]	*Am J Sports Med*	Prospective, randomized	24.0	Knee	Control group			
				Knee	MFX	9	44.0%	33.0
Cole et al. 2012 [72]	*Am J Sports Med*	Prospective	48.0	Knee	pACI	32	25.0%	30.5
Cvetanovich et al. 2017 [73]	*Am J Sports Med*	Prospective	24.0	Knee	pACI, cACI	12	22.0%	17.0
			24.0	Knee	mACI	11	22.0%	17.0
			24.0	Knee	mACI	14	22.0%	17.0
D'Ambrosi et al. 2017 [74]	*Arthroscopy*	Retrospective	27.0	Talus	AMIC	17	52.9%	25.0
				Talus	AMIC	14	26.0%	47.0
D'Ambrosi et al. 2019 [75]	*Clin J Sport Med*	Retrospective	42.6	Talus	AMIC	26	34.6%	33.7
de l'Escalopier et al. 2015 [76]	*Orthop Traumatol Sur Res*	Retrospective	76.0	Talus	Mosaicplasty	37	33.0%	21.6
De Windt et al. 2017 [77]	*Stem Cells*	Prospective	12.0	Knee	Allo-MSC	10	20.0%	26.0
De Windt et al. 2017 [78]	*Stem Cells*	Prospective	18.0	Knee	Allo-MSC	35	31.0%	30.0
De Girolamo et al. 2019 [79]	*J Clin Med*	Prospective, randomized	100.0	Knee	AMIC	12	38.0%	30.0
				Knee	AMIC	12	50.0%	30.0
Desando et al. 2017 [80]	*Cartilage*	Prospective	36.0	Talus	MACI	7	42.9%	31.2
			36.0	Talus	MBMAC	15	33.3%	31.0
Dhollander et al. 2012 [81]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	36.0	Knee	cACI	32	31.0%	30.0
Dixon et al. 2011 [82]	*Foot Ankle Int*	Retrospective	44.4	Talus	MACI	28	22.2%	41.0
Domayer et al. 2012 [83]	*Osteoarthritis Cartilage*	Retrospective	113.8	Talus	MFX	10	55.6%	30.8
			65.4	Talus	MACT	10	77.8%	25.4
Duramaz et al. 2018 [84]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	28.9	Talus	MFX	14	62.5%	34.6
				Talus	Control group			
Ebert et al. 2011 [85]	*Am J Sports Med*	Prospective	60.0	Knee	mACI	44	48.0%	39.0
Ebert et al. 2012 [86]	*Arthroscopy*	Prospective	24.0	Knee	mACI	20	50.0%	34.0

Table 1 (continued)

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Ebert et al. 2015 [87]	*Am J Sports Med*	Prospective	24.0	Knee	mACI	10	20.0%	39.0
				Knee	mACI	13	7.0%	36.0
				Knee	mACI	9	66.0%	38.0
				Knee	mACI	15	53.0%	37.0
Ebert et al. 2017 [88]	*Am J Sports Med*	Prospective	60.0	Knee	mACI	31	51.0%	35.0
Efe et al. 2011 [89]	*Am J Sports Med*	Prospective	24.0	Knee	mACI	15	60.0%	26.0
El-Rashidy et al. 2011 [90]	*J Bone Joint Surg*	Retrospective	37.7	Talus	OAT	38	42.1%	44. 2
Emre et al. 2012 [91]	*J Foot Ankle Surg*	Retrospective	16.8	Talus	Mosaicplasty	32	9.4%	27.5
Enea et al. 2013 [92]	*Knee*	Retrospective	22.0	Knee	AMIC	9	45.0%	48.0
Enea et al. 2015 [93]	*Knee*	Retrospective	29.0	Knee	AMIC	9	44.0%	43.0
Espregueira-Mendes et al. 2012 [94]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	110.0	Knee	OAT	31	29.0%	30.0
Ferruzzi et al. 2008 [95]	*J Bone Joint Surg*	Prospective	60.0	Knee	pACI	48	38.0%	32.0
				Knee	mACI	50	28.0%	31.0
Filardo et al. 2011 [96]	*Am J Sports Med*	Prospective	84.0	Knee	mACT	62	23.0%	28.0
Filardo et al. 2014 [26]	*BMC Musculos Dis*	Prospective	84.0	Knee	mACT	131	35.0%	29.0
Fraser et al. 2016 [97]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	70.8	Talus	OAT	36	3.3%	31.0
Galla et al. 2019 [98]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	33.5	Talus	AMIC	23	34.8%	35.6
Gaul et al. 2018 [99]	*Foot Ankle Int*	Retrospective	116.4	Talus	OAT	20	47.0%	34.7
Gaul et al. 2018 [100]	*Foot Ankle Int*	Retrospective	123.6	Talus	OAT	20	55.0%	43.6
Gautier et al. 2002 [101]	*J Bone Joint Surg*	Retrospective	24.0	Talus	OAT	11	66.5%	32.0
Georgiannos et al. 2016 [102]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	66.0	Talus	OAT	48	19.5%	36.0
Giannini et al. 2008 [103]	*Am J Sports Med*	Retrospective	36.0	Talus	mACI	46	37.0%	31.4
Giannini et al. 2009 [104]	*Am J Sports Med*	Retrospective	119.0	Talus	PACI	10	50.0%	25.8
Giannini et al. 2014 [105]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	87.2	Talus	mACI	46	36.9%	31.4
Giannini et al. 2017 [106]	*Injury*	Retrospective	121.0	Talus	OAT	48	25.0%	36.0
Gille et al. 2013 [107]	*Arch Orthop Trauma Surg*	Prognostic study	24.0	Knee	AMIC	57	33.0%	37.0
Giza et al. 2010 [108]	*Foot Ankle Int*	Retrospective	24.0	Talus	MACI	10	50.0%	40.2

Table 1 (continued)

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Gobbi et al. 2006 [109]	*Arthroscopy*	Prospective	53.0	Talus	MFX	10	40.0%	24.0
				Talus	Control group			
				Talus	OAT	12	33.3%	27.8
Gobbi et al. 2009 [110]	*Am J Sports Med*	Prospective	60.0	Knee	mACI	34	32.0%	31.0
Gobbi et al. 2011 [111]	*Cartilage*	Prospective	24.0	Knee	cACI	15	33.0%	48.0
Gobbi et al. 2014 [112]	*Am J Sports Med*	Prospective	41.0	Knee	cACI	25	36.0%	47.0
Gobbi et al. 2017 [113]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	48.0	Knee	cACI	20		50.0
				Knee	mACI	20		37.0
Gomoll et al. 2014 [114]	*Am J Sports Med*	Prospective	48.0	Knee	pACI	110	64.0%	33.0
Gooding et al. 2006 [115]	*Knee*	Prospective, randomized	24.0	Knee	pACI	33	51.0%	31.0
				Knee	cACI	35		
Gottschalk et al. 2017 [116]	*J Foot Ankle Surg*	Retrospective	60.0	Talus	AMIC	21	38.1%	37.0
Gudas et al. 2006 [117]	*Knee Surg Sports Traumatol Arthrosc*	Prospective, randomized	37.1	Knee	MFX	28	42.9%	24.3
				Knee	OAT	29	34.5%	24.6
Gudas et al. 2009 [118]	*J Pediatr Orthop*	Prospective, randomized	24.0	Knee	OAT	25	40.0%	15.0
				Knee	MFX	22	40.0%	14.0
Gudas et al. 2012 [119]	*Am J Sports Med*	Prospective, randomized	120.0	Knee	OAT	28	32.0%	25.0
				Knee	MFX	29	41.0%	24.0
Gudas et al. 2018 [120]	*J Orthop Surg*	Retrospective	54.0	Knee	AMIC	15	33.0%	31.0
Gül et al. 2016 [121]	*Foot Ankle Surg*	Retrospective	30.5	Talus	OAT	15	33.3%	32.6
			28.9	Talus	OAT	13	830.0%	36.7
Guney et al. 2016 [122]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	47.3	Talus	MFX	19	37.4%	47.4
			40.4	Talus	MFX & PRP	22	43.9%	50.0
			30.1	Talus	Mosaicplasty	13	37.6%	15.4
Haleem et al. 2010 [123]	*Cartilage*	Retrospective	12.0	Knee	pACI	5	20.0%	25.0
Haleem et al. 2014 [124]	*Am J Sports Med*	Retrospective	93.0	Talus	OAT	14	50.0%	42.8
			85.3	Talus	OAT	28	39.3%	44.1
Haasper et al. 2007 [125]	*Arch Orthop Trauma Surg*	Retrospective	24.0	Talus	Mosaicplasty	14	57.1%	24.8
Hahn et al. 2010 [126]	*Foot Ankle Int*	Retrospective	47.9	Talus	OAT	13	61.5%	30.4
Hangody et al. 1997 [127]	*J Bone Joint Surg*	Retrospective	19.0	Talus	Mosaicplasty	11		25.1
Hangody et al. 2001 [128]	*Foot Ankle Int*	Retrospective	50.4	Talus	Mosaicplasty	36		27.0
Hoburg et al. 2019 [129]	*Orthop J Sports Med*	Prospective	63.0	Knee	mACI	29	48.0%	16.0
			48.0	Knee	mACI	42	29.0%	27.0
Horas et al. 2003 [130]	*J Bone Joint Surg*	Prospective	24.0	Knee	pACI	20	60.0%	31.4
				Knee	OAT	20	25.0%	35.4
Imhoff et al. 2011 [131]	*Am J Sports Med*	Retrospective	84.0	Talus	OAT	26	46.2%	33.0

Table 1 (continued)

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Jackson et al. 2019 [132]	*Foot Ankle Surg*	Retrospective	21.0	Talus	OAT	31	9.7%	33.6
Kim et al. 2019 [133]	*Foot Ankle Int*	Retrospective	47.3	Talus	MFX	64	26.6%	40.5
Knutsen et al. 2016 [134]	*J Bone Joint Surg*	Prospective, randomized	180.0	Knee	pACI	40		
				Knee	MFX	40		
Koh et al. 2016 [135]	*Arthroscopy*	Prospective, randomized	27.0	Knee	MFX	40	65.0%	38.0
				Knee	MFX	40	60.0%	39.0
Kon et al. 2009 [136]	*Am J Sports Med*	Prospective	60.0	Knee	mACT	40	17.0%	29.0
				Knee	MFX	40	32.0%	31.0
Kon el al. 2011 [137]	*Am J Sports Med*	Prospective	61.0	Knee	mACT	22	32.0%	46.0
			58.0	Knee	mACI	39	35.0%	45.0
Kretzschmarr et al. 2015 [138]	*Eur Radiol*	Prospective		Talus	AMIC	25	32.0%	38.0
Kreulen et al. 2018 [139]	*Foot Ankle Spec*	Prospective	84.0	Talus	MACI	9	55.6%	45.8
Kreuz et al. 2005 [140]	*Am J Sports Med*	Retrospective	48.9	Talus	Mosaicplasty	35	48.6%	30.9
Kubosch et al. 2016 [33]	*Int Orthop*	Retrospective	39.5	Talus	AMIC	17	47.1%	38.8
Kwak et al. 2014 [141]	*Am J Sports Med*	Retrospective	70.0	Talus	PACI	29	48.3%	34.0
Lahner et al. 2018 [142]	*Biomed Res Int*	Prospective	14.7	Knee	AMIC	9		48.0
Lee et al. 2003 [143]	*Foot Ankle Int*	Retrospective	36.0	Talus	Mosaicplasty	18	5.6%	22.7
Li et al. 2017 [144]	*BMC Musculos Dis*	Retrospective	21.2	Talus	OAT	11	63.6%	55.4
Lim et al. 2012 [12]	*Clin Orthop Rel Res*	Prospective, randomized	60.0	Knee	MFX	30	40.0%	33.0
				Knee	OAT	22	45.0%	30.0
				Knee	pACI	18	44.0%	25.0
Liu et al. 2011 [145]	*Foot Ankle Int*	Prospective	36.3	Talus	OAT	16	37.5%	33.9
Liu et al. 2019 [146]	*Foot Ankle Soc*	Retrospective	18.0	Talus	OAT	14	21.4%	29.6
Lopez-Alcorocho et al. 2018 [147]	*Cartilage*	Prospective	24.0	Knee	mACI	50	30.0%	35.0
López-Alcorocho et al. 2019 [148]	*Cartilage*	Prospective	24.0	Talus	HD-ACI	26	41.7%	31.0
Macmull et al. 2011 [149]	*Int Orthop*	Prospective	66.0	Knee	pACI, cACI	24	29.0%	16.0
				Knee	mACI	7		
Macmull et al. 2012 [150]	*Am J Sports Med*	Prospective	45.0	Knee	cACI	25	80.0%	35.0
			35.3	Knee	mACI	23	61.0%	35.0
Magnan et al. 2012 [151]	*Advance Orthop*	Retrospective	45.0	Talus	MACI	30	50.0%	28.9
Marlovits et al. 2012 [152]	*Am J Sports Med*	Prospective	60.0	Knee	mACI	24	12.0%	35.0
McNickle et al. 2009 [153]	*Am J Sports Med*	Prospective	52.0	Knee	pACI	140	42.0%	30.0
Mehl et al. 2019 [154]	*Knee*	Retrospective	78.0	Knee	pACI, cACI	78	59.0%	32.0

Table 1 (continued)

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Meyerkort et al. 2014 [155]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	60.0	Knee	mACI	23		42.0
Micheli et al. 2001 [156]	*Clin J Sport Med*	Prospective	36.0	Knee	pACI	50	26.0%	36.0
Minas et al. 2014 [157]	*Clin Orthop Rel Res*	Prospective	120.0	Knee	pACI	210	46.0%	36.0
Moseley et al. 2010 [158]	*Am J Sports Med*	Prospective	110.0	Knee	pACI	72	39.0%	37.0
Murphy et al. 2019 [159]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	36.7	Talus	MAST	38	31.2%	35.0
Nam et al. 2009 [160]	*American Journal Sports Med*	Retrospective	37.5	Talus	PACI	11	54.5%	33.5
Nawaz et al. 2014 [161]	*J Bone Joint Surg*	Retrospective	74.0	Knee	pACI, cACI	827	40.0%	34.0
				Knee	mACI			
Nehrer et al. 2011 [162]	*Cartilage*	Prospective	61.0	Talus	pACT, MACT	17	58.8%	28.0
Nejadnik et al. 2010 [163]	*Am J Sports Med*	Retrospective	24.0	Knee	mACI	36	50.0%	43.0
				Knee	MFX	36	44.0%	44.0
Nguyen et al. 2019 [164]	*Am J Sports Med*	Retrospective	44.7	Talus	OAT	38	0.0%	26.0
Niemeyer et al. 2008 [165]	*Arch Orthop Trauma Surg*	Retrospective	38.0	Knee	pACI	95		34.0
				Knee	mACI			
Niemeyer et al. 2010 [166]	*Arthroscopy*	Prospective	37.0	Knee	cACI	59		37.0
Niemeyer et al. 2014 [167]	*Am J Sports Med*	Prospective	131.0	Knee	pACI	70	64.0%	33.0
Niemeyer et al. 2016 [168]	*Am J Sports Med*	Prospective, randomized	12.0	Knee	mACI	25	33.0%	33.0
				Knee	mACI	25	16.0%	34.0
				Knee	mACI	25	40.0%	34.0
Niemeyer et al. 2019 [169]	*Orthop J Sports Med*	Prospective, randomized	24.0	Knee	mACI	52	36.0%	36.0
				Knee	MFX	50	44.0%	37.0
Ogura et al. 2017 [170]	*Am J Sports Med*	Prospective	240.0	Knee	pACI	24	30.0%	35.0
Ogura et al. 2019 [171]	*Orthop J Sports Med*	Prospective	24.0	Knee	pACI, cACI	15	20.0%	31.0
Orr et al. 2017 [172]	*Foot Ankle Spec*	Retrospective	28.5	Talus	OAT	8	0.0%	34.4
Pagliazzi et al. 2018 [173]	*Foot Ankle Surg*	Retrospective	87.2	Talus	MACI	20	30.0%	35.0
Park et al. 2018 [174]	*American Journal Sports Med*	Retrospective	71.4	Talus	OAT	18	41.6%	
				Talus	OAT	28		
Park et al. 2020 [175]	*Bone Joint Journal*	Retrospective	22.0	Talus	OAT	25	40.0%	19.6
Paul et al. 2012 [176]	*Am J Sports Med*	Retrospective	60.0	Talus	OAT	131	38.2%	31.0
Peterson et al. 2010 [177]	*Am J Sports Med*	Retrospective	154.0	Knee	pACI	224		33.0
Polat et al. 2016 [178]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	121.3	Talus	MFX	82	41.5%	35.9

Table 1 (continued)

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Quirbach et al. 2009 [179]	*Skeletal Radiol*	Retrospective	19.8	Talus	MACT	12	33.3%	32.8
Randsborg et al. 2016 [180]	*BMC Musculos Dis*	Prospective, randomized	24.0	Knee	cACI	82		
				Knee	Control group			
Richter et al. 2017 [181]	*Foot Ankle Surg*	Prospective	24.0	Talus	MAST	26	28.0%	33.0
Richter et al. 2020 [182]	*Foot Ankle Surg*	Prospective	24.4	Talus	MAST	129	41.0%	35.3
			23.8	Talus	AMIC	129	40.0%	35.6
Rosa et al. 2016 [183]	*J Orthop Traumatol*	Retrospective	148.0	Knee	pACI	15	40.0%	21.0
Ross et al. 2016 [184]	*Arthroscopy*	Retrospective	51.0	Talus	OAT	76	34.2%	35.8
Sabaghzadeh et al. 2019 [185]	*Chinese Journal of Traumatology*	Retrospective		Talus	Mosaicplasty	19	42.1%	43.0
Sadlik et al. 2016 [186]	*Foot Ankle Surg*	Retrospective	46.4	Talus	OAT	10	40.0%	37.0
Saris et al. 2009 [187]	*Am J Sports Med*	Prospective, randomized	36.0	Knee	pACI	57	39.0%	33.9
				Knee	MFX	61	33.0%	33.9
Saris et al. 2014 [188]	*Am J Sports Med*	Prospective, randomized	24.0	Knee	mACI	72	37.0%	35.0
				Knee	MFX	72		33.0
Schagemann et al. 2018 [189]	*Arch Orthop Trauma Surg*	Retrospective	24.0	Knee	AMIC	20	35.0%	38.0
				Knee	AMIC	30	43.0%	34.0
Schiavone Panni et al. 2018 [190]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	84.0	Knee	AMIC	21		
Schneider et al. 2009 [191]	*Foot Ankle Int*	Retrospective	21.1	Talus	MACI	20	65.0%	36.2
Schneider et al. 2011 [192]	*Am J Sports Med*	Prospective	30.2	Knee	mACI	116	42.0%	33.0
Schneider et al. 2016 [193]	*J Orthop Surg*	Prospective, Randomized	12.0	Knee	MFX	13	50.0%	47.0
				Knee	MFX	4		37.0
Schüttler et al. 2019 [194]	*Arch Orthop Trauma Surg*	Prospective	60.0	Knee	mACI	23	34.0%	
Siebold et al. 2018 [195]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	34.8	Knee	mACI	30	36.0%	36.0
Shimozono et al. 2018 [196]	*Am J Sports Med*	Retrospective	52.0	Talus	OAT	63	42.9%	36.0
			45.0	Talus	OAT	31	32.3%	34.0
Shimozono et al. 2018 [197]	*Bone Joint Surg*	Retrospective	26.3	Talus	OAT	25	64.0%	38.4
			22.3	Talus	OAT	16	37.5%	43.6
Skowronski et al. 2013 [198]	*Orthop traumatol Rehab*	Prospective	60.0	Knee	cACI	21	42.0%	26.0
				Knee	cACI	25	44.0%	26.0
Solheim et al. 2018 [199]	*Am J Sports Med*	Prospective, randomized	180.0	Knee	MFX	20	30.0%	35.0
				Knee	Mosaicplasty	20	30.0%	31.0
Steinwachs et al. 2019 [200]	*Knee*	Retrospective	6.0	Knee	AMIC	93	28.0%	42.0
Teo et al. 2013 [201]	*Clin Orthop Rel Res*	Retrospective	24.0	Knee	pACI	20	20.0%	17.0
				Knee	pACI	3		
Tohyama et al. 2009 [202]	*J Orthop Sci*	Prospective	24.0	Knee	pACI	27		

Table 1 (continued)

Author, year	Journal	Study Design	Follow-up (*months*)	Place	Type of treatment	Procedures (*n*)	Female (%)	Mean age
Usuelli et al. 2016 [203]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	24.0	Talus	AMIC	20	45.0%	36.1
Valderrabano et al. 2013 [204]	*Am J Sports Med*	Retrospective	30.9	Talus	AMIC	26	30.8%	34.6
Van Assche et al. 2010 [205]	*Knee Surg Sports Traumatol Arthrosc*	Prospective, randomised	24.0	Knee	pACI	33	33.0%	31.0
				Knee	MFX	34	10.0%	31.0
Vanlauwe et al. 2011 [206]	*Am J Sports Med*	Prospective, randomised	60.0	Knee	MFX	61	20.0%	34.0
				Knee	pACI	51	43.0%	34.0
Vanlauwe et al. 2012 [207]	*Am J Sports Med*	Prospective	48.0	Knee	pACI	38	68.0%	31.0
Volz et al. 2017 [208]	*Int Orthop*	Prospective, randomised	60.0	Knee	AMIC	17	29.0%	34.0
				Knee	AMIC	17	11.0%	39.0
				Knee	MFX	13	23.0%	40.0
Von Keudell et al. 2017	*Cartilage*	Prospective	88.0	Knee	pACI	30		32.0
Weigelt et al. 2019 [34]	*Am J Sports Med*	Retrospective	56.4	Talus	AMIC	33	4.2%	35.1
Whittaker et al. 2005 [209]	*J Bone Joint Surg*	Prospective	23.0	Talus	PACI	10	30.0%	41.8
Wiewiorski et al. 2013 [210]	*Clin Radiology*	Retrospective	23.3	Talus	AMIC	23	30.4%	34.2
Wiewiorski et al. 2016 [211]	*Am J Sports Med*	Retrospective	46.9	Talus	AMIC	60	40.0%	34.9
Wolf et al. 2018 [212]	*Cartilage*	Prospective	24.0	Knee	MFX	18	55.0%	38.0
				Knee	MFX	3		50.0
Woelfle et al. 2013 [213]	*Knee Surg Sports Traumatol Arthrosc*	Retrospective	29.0	Talus	OAT	32	24.5%	46.9
Yontar et al. 2018 [214]	*Acta Orthop Traumatol Turc*	Retrospective	20.3	Talus	AMIC	20	30.0%	32.9
Yoon et al. 2014 [215]	*Am J Sports Med*	Retrospective	45.0	Talus	OAT	22	31.8%	37.1
		Retrospective	50.0	Talus	MFX	22	18.2%	41.6
Zaslav et al. 2009 [216]	*Am J Sports Med*	Prospective	48.0	Knee	pACI	154	31.0%	35.0
Zeifang et al. 2010 [217]	*Am J Sports Med*	Prospective, randomised	24.0	Knee	mACI	11	45.0%	29.0
				Knee	pACI	10	0.0%	30.0
Zhu et al. 2016 [218]	*Foot Ankle Soc*	Retrospective	25.4	Talus	OAT	12	38.5%	40.5

Syn-MSC synovial mesenchymal stem cell; *BMAC* bone marrow aspirate concentrate; *BM-MSC* bone marrow-derived mesenchymal stem cells; *Allo-MSC* allogenic mesenchymal stem cell

demonstrating that the final outcome is influenced by the pre-operative performance status of the patients. Interestingly, symptom duration prior to the surgical intervention and cartilage defect size did not show any significant association with the surgical outcome.

Neri et al. analyzed 48 patients who underwent microfractures of knee cartilage defects at a mean follow-up of 5.7 years [23]. Patients' age, BMI, time from diagnosis to surgery, and size of the cartilage lesion were negatively associated with the functional outcome. Differences between these findings and our results may be explained by the fact that Neri et al. only included 48 patients treated for knee articular cartilage defects with a longer follow-up, while we included 8905 procedures including various treatment options with a variable follow-up. Similar findings were reported by Andriolo et al. in 113 patients with

Table 2 Overall results of the multivariate analyses

Demographic data at baseline																							
Endpoint at last FU	Sex		Age		BMI		Defect size		Symptoms Duration		VAS		Tegner		Lysholm		AOFAS		IKDC				
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*			
VAS	0.2	0.02	0.0	0.9	0.0	0.7	0.0	0.7	0.3	0.1	0.9	< 0.0001	0.3	0.2	−0.3	0.2	−0.3	0.2	0.1	0.7			
Tegner	−0.2	0.07	0.0	0.9	−0.2	0.3	0.2	0.1	−0.0	0.8	−0.8	< 0.0001	0.4	0.009	0.0	0.9	−0.0	0.9	−0.1	0.5			
AOFAS	0.1	0.4	−0.2	0.04	0.0	0.7	0.0	0.9	−0.1	0.7	−0.1	0.4	−0.1	0.9			0.6	0.0002					
Lysholm	−0.3	0.05	−0.3	0.03	0.3	0.2	0.0	0.7	0.2	0.6	−0.1	0.5	−0.4	0.05	0.2	0.1			0.3	0.3			
IKDC	−0.2	0.08	0.0	0.8	−0.2	0.4	0.3	0.05	−0.3	0.2	0.0	0.8	0.1	0.5	0.0	0.8			0.4	0.0007			
Hypertrophy	0.2	0.2	0.0	0.8	0.6	0.009	−0.1	0.4	0.1	0.5	−0	0.1	0.0	0.9	0.1	0.7	0.1	0.7	0.0	0.9			
Failure	0.0	0.5	0.0	1	0.2	0.2	0.0	0.5	0.0	0.6	−0.0	0.9	−0.2	0.3	−0.2	0.4	−0.2	0.4	−0.0	0.9			
Revision	0.0	0.5	0.0	0.8	0.2	0.2	0.1	0.1	0.3	0.1	0.2	0.2	0.0	0.9	−0.4	0.1	−0.4	0.1	−0.2	0.4			

Values of $0.1 < |r| < 0.3$, $0.3 < |r| < 0.5$, and $|r| > 0.5$ were considered to have weak, moderate, and strong association, respectively

FU follow-up

knee cartilage defects treated with matrix-assisted autologous chondrocyte implantation [24]. Older age, female sex, degenerative lesions, longer symptoms duration, and previous surgery were negatively associated with outcome.

Age has been identified as one of the most important factors for success in the treatment of cartilage defects [25, 26]. A study comparing microfracture to ACI or OATS showed better clinical outcomes for patients younger than 30 years compared to those older than 30 years, unrelated to treatment type [27, 28]. Robb et al. were able to identify age as a prognostic factor for lower clinical outcomes after treatment [29]. The structure and composition of the matrix molecules as well as the synthetic function of chondrocyte change with age, may explain the lower functional outcomes after cartilage defect management in older patients [30, 31]. These previous findings confirm our results of age being negatively associated with AOFAS and Lysholm scores.

Previously, it was also shown, in particular for the ankle joint, that patients' BMI is a negative prognostic factor [32], with worse clinical outcomes for patients with a BMI > 30 kg/m^2 [33, 34]. Jaiswal et al. found similar results showing an influence of BMI on the Modified Cincinnati Score after anterior cruciate ligament reconstruction and matrix-assisted autologous chondrocyte implantation [35]. The poorer results following cartilage repair in obese patients may be explained by an increase in mechanical forces across the joint leading to cartilage breakdown.

There was evidence of weak association between female sex and VAS. Females have lower femoral and retropatellar cartilage volumes than males, and this decreases with age [36]. These findings might explain the higher risk for knee osteoarthritis in women compared to men. Kreutz et al. studied 52 patients after ACI showing worse outcomes in women compared to men [37]. Furthermore, higher complication rates in cartilage repair surgery were found in women 24 months after surgery, which might be related to lower satisfaction levels in women, possibly resulting in more postoperative complaints [38–40].

Interestingly, cartilage defect size, in both the knee and ankle joints, is not associated with negative outcome. This was previously confirmed in studies highlighting that defect size does not predict the clinical outcome after treatment of cartilage defects, confirming that functional outcome seems to be independent of cartilage defect size [25, 41].

This study identified prognostic factors for successful cartilage repair management in the knee and ankle joints, regardless of the surgical procedure. However, there are also some limitations that need to be addressed. Although we followed established guidelines for the preparation of systematic reviews, the risk of bias of the included studies was only moderate, with acceptable methodological assessment. Given the lack of quantitative data, primary and revision settings could not be analyzed separately. To increase the

pooling data, the sex of the patients, mean age and BMI, defect size, and mean length of prior symptoms duration were not analyzed separately according to the body location (knee and ankle). Furthermore, we considered only the most common surgeries strategy for chondral repair, potentially increasing the risk of selection bias. Given their uncertain results, less common or more innovative procedures were not considered. Given the lack of data, surgical indications were not considered separately for analysis. Patients with larger chondral and/ or osteochondral lesions (>5 cm^2) and obese (BMI > 30 kg/m^2) were not considered, as the surgical outcomes are strongly negatively influenced by these variables [33–35]. Large lesions require challenging surgery, with transplants and unpredictable outcome. Similarly, in obese patients, the articular cartilage is subjected to high loads, and lesions may not heal properly. Further clinical investigations are required to establish the proper management of chondral defects. Results from the present study should be considered in the light of these limitations. Further high-quality investigations should validate the results of the present study in a clinical setting.

Conclusion

Our results suggest that the clinical outcomes were mostly related to the patients' performance status prior surgery and that greater BMI could be associated with greater rate of hypertrophy. Female sex and older age evidenced fair influence on outcome, while symptom duration prior to the surgical intervention and cartilage defect size evidenced no association with the surgical outcome. These results should be interpreted in the light of the limitations of the present study, and further investigations are needed to validate them in a clinical setting.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00068-022-02155-y.

Acknowledgements None

Author contributions FM contributed to literature search, data extraction, methodological quality assessment, statistical analyses, writing; NM contributed to supervision, revision, final approval; JE contributed to literature search, data extraction, methodological quality assessment; CG, FH contributed to supervision; MB contributed to writing.

Funding Open Access funding enabled and organized by Projekt DEAL. No external source of funding was used.

Availability of data and materials The data underlying this article are available in the article and in its online supplementary material.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

References

1. Buckwalter JA. Articular cartilage injuries. Clin Orthop Relat Res. 2002;402:21–37. https://doi.org/10.1097/00003086-200209000-00004.
2. Hinzpeter J, Zamorano A, Barahona M, Campos P. Treatment of osteochondritis dissecans of the knee with autologous iliac bone graft and hyaluronic acid scaffold. Knee Surg Relat Res. 2019;31(2):143–6. https://doi.org/10.5792/ksrr.18.053.
3. Zamborsky R, Danisovic L. Surgical techniques for knee cartilage repair: an updated large-scale systematic review and network meta-analysis of randomized controlled trials. Arthroscopy. 2020;36(3):845–58. https://doi.org/10.1016/j.arthro.2019.11.096.
4. Negrin LL, Vecsei V. Do meta-analyses reveal time-dependent differences between the clinical outcomes achieved by microfracture and autologous chondrocyte implantation in the treatment of cartilage defects of the knee? J Orthop Sci. 2013;18(6):940–8. https://doi.org/10.1007/s00776-013-0449-3.
5. Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, Klag MJ. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. Ann Intern Med. 2000;133(5):321–8. https://doi.org/10.7326/0003-4819-133-5-200009050-00007.
6. Buckwalter JA. Articular cartilage: injuries and potential for healing. J Orthop Sports Phys Ther. 1998;28(4):192–202. https://doi.org/10.2519/jospt.1998.28.4.192.
7. Hjelle K, Solheim E, Strand T, Muri R, Brittberg M. Articular cartilage defects in 1,000 knee arthroscopies. Arthroscopy. 2002;18(7):730–4. https://doi.org/10.1053/jars.2002.32839.
8. Aroen A, Loken S, Heir S, Alvik E, Ekeland A, Granlund OG, Engebretsen L. Articular cartilage lesions in 993 consecutive knee arthroscopies. Am J Sports Med. 2004;32(1):211–5. https://doi.org/10.1177/0363546503259345.
9. Widuchowski W, Widuchowski J, Trzaska T. Articular cartilage defects: study of 25,124 knee arthroscopies. Knee. 2007;14(3):177–82. https://doi.org/10.1016/j.knee.2007.02.001.
10. Schafer D, Boss A, Hintermann B. Accuracy of arthroscopic assessment of anterior ankle cartilage lesions. Foot Ankle Int. 2003;24(4):317–20. https://doi.org/10.1177/107110070302400402.

11. Bekkers JE, Inklaar M, Saris DB. Treatment selection in articular cartilage lesions of the knee: a systematic review. Am J Sports Med. 2009;37(Suppl 1):148S-155S. https://doi.org/10.1177/0363546509351143.
12. Lim HC, Bae JH, Song SH, Park YE, Kim SJ. Current treatments of isolated articular cartilage lesions of the knee achieve similar outcomes. Clin Orthop Relat Res. 2012;470(8):2261–7. https://doi.org/10.1007/s11999-012-2304-9.
13. Gobbi A, Karnatzikos G, Kumar A. Long-term results after microfracture treatment for full-thickness knee chondral lesions in athletes. Knee Surg Sports Traumatol Arthrosc. 2014;22(9):1986–96. https://doi.org/10.1007/s00167-013-2676-8.
14. Goyal D, Keyhani S, Lee EH, Hui JH. Evidence-based status of microfracture technique: a systematic review of level I and II studies. Arthroscopy. 2013;29(9):1579–88. https://doi.org/10.1016/j.arthro.2013.05.027.
15. Solheim E, Hegna J, Inderhaug E, Oyen J, Harlem T, Strand T. Results at 10–14 years after microfracture treatment of articular cartilage defects in the knee. Knee Surg Sports Traumatol Arthrosc. 2016;24(5):1587–93. https://doi.org/10.1007/s00167-014-3443-1.
16. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. N Engl J Med. 1994;331(14):889–95. https://doi.org/10.1056/NEJM199410063311401.
17. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535. https://doi.org/10.1136/bmj.b2535.
18. Howick J CI, Glasziou P, Greenhalgh T, Carl Heneghan, Liberati A, Moschetti I, Phillips B, Thornton H, Goddard O, Hodgkinson M. The 2011 Oxford CEBM levels of evidence. Oxford Centre for Evidence-Based Medicine. https://www.cebmnet/indexaspx?o=5653. 2011.
19. Kitaoka HB, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. Foot Ankle Int. 1994;15(7):349–53. https://doi.org/10.1177/107110079401500701.
20. Briggs KK, Lysholm J, Tegner Y, Rodkey WG, Kocher MS, Steadman JR. The reliability, validity, and responsiveness of the Lysholm score and Tegner activity scale for anterior cruciate ligament injuries of the knee: 25 years later. Am J Sports Med. 2009;37(5):890–7. https://doi.org/10.1177/0363546508330143.
21. Lysholm J, Gillquist J. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. Am J Sports Med. 1982;10(3):150–4. https://doi.org/10.1177/036354658201000306.
22. Higgins LD, Taylor MK, Park D, Ghodadra N, Marchant M, Pietrobon R, Cook C, International Knee Documentation C. Reliability and validity of the International Knee Documentation Committee (IKDC) Subjective Knee Form. Joint Bone Spine. 2007;74(6):594–9. https://doi.org/10.1016/j.jbspin.2007.01.036.
23. Neri T, Dehon M, Klasan A, Putnis SE, Farizon F, Philippot R. Predictors of functional outcome after microfracture treatment of cartilage defects of the knee. Surg Technol Int. 2020;37:341–7.
24. Andriolo L, Reale D, Di Martino A, De Filippis R, Sessa A, Zaffagnini S, Filardo G. Long-term results of arthroscopic matrix-assisted autologous chondrocyte transplantation: a prospective follow-up at 15 years. Am J Sports Med. 2020;48(12):2994–3001. https://doi.org/10.1177/0363546520949849.
25. de Windt TS, Bekkers JE, Creemers LB, Dhert WJ, Saris DB. Patient profiling in cartilage regeneration: prognostic factors determining success of treatment for cartilage defects. Am J Sports Med. 2009;37(Suppl 1):58S-62S. https://doi.org/10.1177/0363546509349765.
26. Filardo G, Kon E, Andriolo L, Di Matteo B, Balboni F, Marcacci M. Clinical profiling in cartilage regeneration: prognostic factors for midterm results of matrix-assisted autologous chondrocyte transplantation. Am J Sports Med. 2014;42(4):898–905. https://doi.org/10.1177/0363546513518552.
27. Knutsen G, Drogset JO, Engebretsen L, Grontvedt T, Isaksen V, Ludvigsen TC, Roberts S, Solheim E, Strand T, Johansen O. A randomized trial comparing autologous chondrocyte implantation with microfracture. Findings at five years. J Bone Joint Surg Am 2007;89(10):2105–12. https://doi.org/10.2106/JBJS.G.00003.
28. Gudas R, Kalesinskas RJ, Kimtys V, Stankevicius E, Toliusis V, Bernotavicius G, Smailys A. A prospective randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint in young athletes. Arthroscopy. 2005;21(9):1066–75. https://doi.org/10.1016/j.arthro.2005.06.018.
29. Robb CA, El-Sayed C, Matharu GS, Baloch K, Pynsent P. Survival of autologous osteochondral grafts in the knee and factors influencing outcome. Acta Orthop Belg. 2012;78(5):643–51.
30. Buckwalter JA, Roughley PJ, Rosenberg LC. Age-related changes in cartilage proteoglycans: quantitative electron microscopic studies. Microsc Res Tech. 1994;28(5):398–408. https://doi.org/10.1002/jemt.1070280506.
31. Plaas AH, Sandy JD. Age-related decrease in the link-stability of proteoglycan aggregates formed by articular chondrocytes. Biochem J. 1984;220(1):337–40. https://doi.org/10.1042/bj2200337.
32. Chuckpaiwong B, Berkson EM, Theodore GH. Microfracture for osteochondral lesions of the ankle: outcome analysis and outcome predictors of 105 cases. Arthroscopy. 2008;24(1):106–12. https://doi.org/10.1016/j.arthro.2007.07.022.
33. Kubosch EJ, Erdle B, Izadpanah K, Kubosch D, Uhl M, Sudkamp NP, Niemeyer P. Clinical outcome and T2 assessment following autologous matrix-induced chondrogenesis in osteochondral lesions of the talus. Int Orthop. 2016;40(1):65–71. https://doi.org/10.1007/s00264-015-2988-z.
34. Weigelt L, Hartmann R, Pfirrmann C, Espinosa N, Wirth SH. Autologous matrix-induced chondrogenesis for osteochondral lesions of the talus: a clinical and radiological 2- to 8-year follow-up study. Am J Sports Med. 2019;47(7):1679–86. https://doi.org/10.1177/0363546519841574.
35. Jaiswal PK, Bentley G, Carrington RW, Skinner JA, Briggs TW. The adverse effect of elevated body mass index on outcome after autologous chondrocyte implantation. J Bone Joint Surg Br. 2012;94(10):1377–81. https://doi.org/10.1302/0301-620X.94B10.29388.
36. Cicuttini F, Forbes A, Morris K, Darling S, Bailey M, Stuckey S. Gender differences in knee cartilage volume as measured by magnetic resonance imaging. Osteoarthritis Cartilage. 1999;7(3):265–71. https://doi.org/10.1053/joca.1998.0200.
37. Kreuz PC, Muller S, von Keudell A, Tischer T, Kaps C, Niemeyer P, Erggelet C. Influence of sex on the outcome of autologous chondrocyte implantation in chondral defects of the knee. Am J Sports Med. 2013;41(7):1541–8. https://doi.org/10.1177/0363546513489262.
38. Dugard MN, Kuiper JH, Parker J, Roberts S, Robinson E, Harrison P, Richardson JB. Development of a tool to predict outcome of autologous chondrocyte implantation. Cartilage. 2017;8(2):119–30. https://doi.org/10.1177/1947603516650002.
39. Jungmann PM, Salzmann GM, Schmal H, Pestka JM, Sudkamp NP, Niemeyer P. Autologous chondrocyte implantation for treatment of cartilage defects of the knee: what predicts the need for

reintervention? Am J Sports Med. 2012;40(1):58–67. https://doi.org/10.1177/0363546511423522.
40. Pestka JM, Luu NH, Sudkamp NP, Angele P, Spahn G, Zinser W, Niemeyer P. Revision surgery after cartilage repair: data from the German cartilage registry (Knorpelregister DGOU). Orthop J Sports Med. 2018;6(2):2325967117752623. https://doi.org/10.1177/2325967117752623.
41. Niemeyer P, Pestka JM, Kreuz PC, Erggelet C, Schmal H, Suedkamp NP, Steinwachs M. Characteristic complications after autologous chondrocyte implantation for cartilage defects of the knee joint. Am J Sports Med. 2008;36(11):2091–9. https://doi.org/10.1177/0363546508322131.
42. Adams SB Jr, Viens NA, Easley ME, Stinnett SS, Nunley JA 2nd. Midterm results of osteochondral lesions of the talar shoulder treated with fresh osteochondral allograft transplantation. J Bone Joint Surg Am. 2011;93(7):648–54. https://doi.org/10.2106/JBJS.J.00141.
43. Adams SB, Dekker TJ, Schiff AP, Gross CP, Nunley JA, Easley ME. Prospective evaluation of structural allograft transplantation for osteochondral lesions of the Talar shoulder. Foot Ankle Int. 2018;39(1):28–34. https://doi.org/10.1177/1071100717732342.
44. Ahmad J, Jones K. Comparison of osteochondral autografts and allografts for treatment of recurrent or large Talar osteochondral lesions. Foot Ankle Int. 2016;37(1):40–50. https://doi.org/10.1177/1071100715603191.
45. Akgun I, Unlu MC, Erdal OA, Ogut T, Erturk M, Ovali E, Kantarci F, Caliskan G, Akgun Y. Matrix-induced autologous mesenchymal stem cell implantation versus matrix-induced autologous chondrocyte implantation in the treatment of chondral defects of the knee: a 2-year randomized study. Arch Orthop Trauma Surg. 2015;135(2):251–63. https://doi.org/10.1007/s00402-014-2136-z.
46. Albano D, Martinelli N, Bianchi A, Messina C, Malerba F, Sconfienza LM. Clinical and imaging outcome of osteochondral lesions of the talus treated using autologous matrix-induced chondrogenesis technique with a biomimetic scaffold. BMC Musculoskelet Disord. 2017;18(1):306. https://doi.org/10.1186/s12891-017-1679-x.
47. Anders S, Goetz J, Schubert T, Grifka J, Schaumburger J. Treatment of deep articular talus lesions by matrix associated autologous chondrocyte implantation—results at five years. Int Orthop. 2012;36(11):2279–85. https://doi.org/10.1007/s00264-012-1635-1.
48. Anders S, Volz M, Frick H, Gellissen J. A Randomized, controlled trial comparing autologous matrix-induced chondrogenesis (AMIC(R)) to microfracture: analysis of 1- and 2-year follow-up data of 2 centers. Open Orthop J. 2013;7:133–43. https://doi.org/10.2174/1874325001307010133.
49. Apprich S, Trattnig S, Welsch GH, Noebauer-Huhmann IM, Sokolowski M, Hirschfeld C, Stelzeneder D, Domayer S. Assessment of articular cartilage repair tissue after matrix-associated autologous chondrocyte transplantation or the microfracture technique in the ankle joint using diffusion-weighted imaging at 3 Tesla. Osteoarthritis Cartilage. 2012;20(7):703–11. https://doi.org/10.1016/j.joca.2012.03.008.
50. Astur DC, Lopes JC, Santos MA, Kaleka CC, Amaro JT, Cohen M. Surgical treatment of chondral knee defects using a collagen membrane—autologus matrix-induced chondrogenesis. Rev Bras Ortop. 2018;53(6):733–9. https://doi.org/10.1016/j.rboe.2018.09.005.
51. Aurich M, Bedi HS, Smith PJ, Rolauffs B, Muckley T, Clayton J, Blackney M. Arthroscopic treatment of osteochondral lesions of the ankle with matrix-associated chondrocyte implantation: early clinical and magnetic resonance imaging results. Am J Sports Med. 2011;39(2):311–9. https://doi.org/10.1177/0363546510381575.
52. Bartlett W, Skinner JA, Gooding CR, Carrington RW, Flanagan AM, Briggs TW, Bentley G. Autologous chondrocyte implantation versus matrix-induced autologous chondrocyte implantation for osteochondral defects of the knee: a prospective, randomised study. J Bone Joint Surg Br. 2005;87(5):640–5. https://doi.org/10.1302/0301-620X.87B5.15905.
53. Basad E, Ishaque B, Bachmann G, Sturz H, Steinmeyer J. Matrix-induced autologous chondrocyte implantation versus microfracture in the treatment of cartilage defects of the knee: a 2-year randomised study. Knee Surg Sports Traumatol Arthrosc. 2010;18(4):519–27. https://doi.org/10.1007/s00167-009-1028-1.
54. Basad E, Wissing FR, Fehrenbach P, Rickert M, Steinmeyer J, Ishaque B. Matrix-induced autologous chondrocyte implantation (MACI) in the knee: clinical outcomes and challenges. Knee Surg Sports Traumatol Arthrosc. 2015;23(12):3729–35. https://doi.org/10.1007/s00167-014-3295-8.
55. Battaglia M, Vannini F, Buda R, Cavallo M, Ruffilli A, Monti C, Galletti S, Giannini S. Arthroscopic autologous chondrocyte implantation in osteochondral lesions of the talus: midterm T2-mapping MRI evaluation. Knee Surg Sports Traumatol Arthrosc. 2011;19(8):1376–84. https://doi.org/10.1007/s00167-011-1509-x.
56. Baumfeld T, Baumfeld D, Prado M, Nery C. All-arthroscopic AMIC((R)) (AT-AMIC) for the treatment of talar osteochondral defects: a short follow-up case series. Foot (Edinb). 2018;37:23–7. https://doi.org/10.1016/j.foot.2018.07.006.
57. Baums MH, Heidrich G, Schultz W, Steckel H, Kahl E, Klinger HM. Autologous chondrocyte transplantation for treating cartilage defects of the talus. J Bone Joint Surg Am. 2006;88(2):303–8. https://doi.org/10.2106/JBJS.E.00033.
58. Becher C, Ettinger M, Ezechieli M, Kaps C, Ewig M, Smith T. Repair of retropatellar cartilage defects in the knee with microfracture and a cell-free polymer-based implant. Arch Orthop Trauma Surg. 2015;135(7):1003–10. https://doi.org/10.1007/s00402-015-2235-5.
59. Becher C, Laute V, Fickert S, Zinser W, Niemeyer P, John T, Diehl P, Kolombe T, Siebold R, Fay J. Safety of three different product doses in autologous chondrocyte implantation: results of a prospective, randomised, controlled trial. J Orthop Surg Res. 2017;12(1):71. https://doi.org/10.1186/s13018-017-0570-7.
60. Becher C, Malahias MA, Ali MM, Maffulli N, Thermann H. Arthroscopic microfracture vs. arthroscopic autologous matrix-induced chondrogenesis for the treatment of articular cartilage defects of the talus. Knee Surg Sports Traumatol Arthrosc 2019;27(9):2731–6. https://doi.org/10.1007/s00167-018-5278-7
61. Behrens P, Bitter T, Kurz B, Russlies M. Matrix-associated autologous chondrocyte transplantation/implantation (MACT/MACI)–5-year follow-up. Knee. 2006;13(3):194–202. https://doi.org/10.1016/j.knee.2006.02.012.
62. Bentley G, Biant LC, Vijayan S, Macmull S, Skinner JA, Carrington RW. Minimum ten-year results of a prospective randomised study of autologous chondrocyte implantation versus mosaicplasty for symptomatic articular cartilage lesions of the knee. J Bone Joint Surg Br. 2012;94(4):504–9. https://doi.org/10.1302/0301-620X.94B4.27495.
63. Berruto M, Ferrua P, Pasqualotto S, Uboldi F, Maione A, Tradati D, Usellini E. Long-term follow-up evaluation of autologous chondrocyte implantation for symptomatic cartilage lesions of the knee: a single-centre prospective study. Injury. 2017;48(10):2230–4. https://doi.org/10.1016/j.injury.2017.08.005.
64. Bode G, Schmal H, Pestka JM, Ogon P, Sudkamp NP, Niemeyer P. A non-randomized controlled clinical trial on autologous

chondrocyte implantation (ACI) in cartilage defects of the medial femoral condyle with or without high tibial osteotomy in patients with varus deformity of less than 5 degrees. Arch Orthop Trauma Surg. 2013;133(1):43–9. https://doi.org/10.1007/s00402-012-1637-x.
65. Brittberg M, Recker D, Ilgenfritz J, Saris DBF, Group SES. Matrix-applied characterized autologous cultured chondrocytes versus microfracture: five-year follow-up of a prospective randomized trial. Am J Sports Med 2018;46(6):1343–51. https://doi.org/10.1177/0363546518756976
66. Browne JE, Anderson AF, Arciero R, Mandelbaum B, Moseley JB Jr, Micheli LJ, Fu F, Erggelet C. Clinical outcome of autologous chondrocyte implantation at 5 years in US subjects. Clin Orthop Relat Res. 2005;436:237–45. https://doi.org/10.1097/00003086-200507000-00036.
67. Buda R, Vannini F, Cavallo M, Grigolo B, Cenacchi A, Giannini S. Osteochondral lesions of the knee: a new one-step repair technique with bone-marrow-derived cells. J Bone Joint Surg Am. 2010;92(Suppl 2):2–11. https://doi.org/10.2106/JBJS.J.00813.
68. Buda R, Vannini F, Castagnini F, Cavallo M, Ruffilli A, Ramponi L, Pagliazzi G, Giannini S. Regenerative treatment in osteochondral lesions of the talus: autologous chondrocyte implantation versus one-step bone marrow derived cells transplantation. Int Orthop. 2015;39(5):893–900. https://doi.org/10.1007/s00264-015-2685-y.
69. Buda R, Baldassarri M, Perazzo L, Ghinelli D, Pagliazzi G. A useful combination for the treatment of patellofemoral chondral lesions: realignment procedure plus mesenchymal stem cell-retrospective analysis and clinical results at 48 months of follow-up. Eur J Orthop Surg Traumatol. 2019;29(2):461–70. https://doi.org/10.1007/s00590-018-2310-z.
70. Chan KW, Ferkel RD, Kern B, Chan SS, Applegate GR. Correlation of MRI appearance of autologous chondrocyte implantation in the ankle with clinical outcome. Cartilage. 2018;9(1):21–9. https://doi.org/10.1177/1947603516681131.
71. Chung JY, Lee DH, Kim TH, Kwack KS, Yoon KH, Min BH. Cartilage extra-cellular matrix biomembrane for the enhancement of microfractured defects. Knee Surg Sports Traumatol Arthrosc. 2014;22(6):1249–59. https://doi.org/10.1007/s00167-013-2716-4.
72. Cole BJ, Farr J, Winalski CS, Hosea T, Richmond J, Mandelbaum B, De Deyne PG. Outcomes after a single-stage procedure for cell-based cartilage repair: a prospective clinical safety trial with 2-year follow-up. Am J Sports Med. 2011;39(6):1170–9. https://doi.org/10.1177/0363546511399382.
73. Cvetanovich GL, Riboh JC, Tilton AK, Cole BJ. Autologous chondrocyte implantation improves knee-specific functional outcomes and health-related quality of life in adolescent patients. Am J Sports Med. 2017;45(1):70–6. https://doi.org/10.1177/0363546516663711.
74. D'Ambrosi R, Maccario C, Serra N, Liuni F, Usuelli FG. Osteochondral lesions of the talus and autologous matrix-induced chondrogenesis: is age a negative predictor outcome? Arthroscopy. 2017;33(2):428–35. https://doi.org/10.1016/j.arthro.2016.09.030.
75. D'Ambrosi R, Villafane JH, Indino C, Liuni FM, Berjano P, Usuelli FG. Return to sport after arthroscopic autologous matrix-induced chondrogenesis for patients with osteochondral lesion of the talus. Clin J Sport Med. 2019;29(6):470–5. https://doi.org/10.1097/JSM.0000000000000560.
76. de l'Escalopier N, Barbier O, Mainard D, Mayer J, Ollat D, Versier G. Outcomes of talar dome osteochondral defect repair using osteocartilaginous autografts: 37 cases of mosaicplasty (R). Orthop Traumatol Surg Res. 2015;101(1):97–102. https://doi.org/10.1016/j.otsr.2014.11.006.
77. de Windt TS, Vonk LA, Slaper-Cortenbach IC, van den Broek MP, Nizak R, van Rijen MH, de Weger RA, Dhert WJ, Saris DB. Allogeneic mesenchymal stem cells stimulate cartilage regeneration and are safe for single-stage cartilage repair in humans upon mixture with recycled autologous chondrons. Stem Cells. 2017;35(1):256–64. https://doi.org/10.1002/stem.2475.
78. de Windt TS, Vonk LA, Slaper-Cortenbach ICM, Nizak R, van Rijen MHP, Saris DBF. Allogeneic MSCs and recycled autologous chondrons mixed in a one-stage cartilage cell transplantion: a first-in-man trial in 35 patients. Stem Cells. 2017;35(8):1984–93. https://doi.org/10.1002/stem.2657.
79. de Girolamo L, Schonhuber H, Vigano M, Bait C, Quaglia A, Thiebat G, Volpi P. Autologous matrix-induced chondrogenesis (AMIC) and AMIC enhanced by autologous concentrated bone marrow aspirate (BMAC) allow for stable clinical and functional improvements at up to 9 years follow-up: results from a randomized controlled study. J Clin Med. 2019; 8(3). https://doi.org/10.3390/jcm8030392.
80. Desando G, Bartolotti I, Vannini F, Cavallo C, Castagnini F, Buda R, Giannini S, Mosca M, Mariani E, Grigolo B. Repair potential of matrix-induced bone marrow aspirate concentrate and matrix-induced autologous chondrocyte implantation for talar osteochondral repair: patterns of some catabolic, inflammatory, and pain mediators. Cartilage. 2017;8(1):50–60. https://doi.org/10.1177/1947603516642573.
81. Dhollander AA, Verdonk PC, Lambrecht S, Verdonk R, Elewaut D, Verbruggen G, Almqvist KF. Short-term outcome of the second generation characterized chondrocyte implantation for the treatment of cartilage lesions in the knee. Knee Surg Sports Traumatol Arthrosc. 2012;20(6):1118–27. https://doi.org/10.1007/s00167-011-1759-7.
82. Dixon S, Harvey L, Baddour E, Janes G, Hardisty G. Functional outcome of matrix-associated autologous chondrocyte implantation in the ankle. Foot Ankle Int. 2011;32(4):368–74. https://doi.org/10.3113/FAI.2011.0368.
83. Domayer SE, Apprich S, Stelzeneder D, Hirschfeld C, Sokolowski M, Kronnerwetter C, Chiari C, Windhager R, Trattnig S. Cartilage repair of the ankle: first results of T2 mapping at 7.0 T after microfracture and matrix associated autologous cartilage transplantation. Osteoarthritis Cartilage 2012;20(8):829–36. https://doi.org/10.1016/j.joca.2012.04.015
84. Duramaz A, Baca E. Microfracture provides better clinical results than debridement in the treatment of acute talar osteochondral lesions using arthroscopic assisted fixation of acute ankle fractures. Knee Surg Sports Traumatol Arthrosc. 2018;26(10):3089–95. https://doi.org/10.1007/s00167-018-4963-x.
85. Ebert JR, Robertson WB, Woodhouse J, Fallon M, Zheng MH, Ackland T, Wood DJ. Clinical and magnetic resonance imaging-based outcomes to 5 years after matrix-induced autologous chondrocyte implantation to address articular cartilage defects in the knee. Am J Sports Med. 2011;39(4):753–63. https://doi.org/10.1177/0363546510390476.
86. Ebert JR, Fallon M, Ackland TR, Wood DJ, Janes GC. Arthroscopic matrix-induced autologous chondrocyte implantation: 2-year outcomes. Arthroscopy 2012;28 (7):952–964 e951–952. https://doi.org/10.1016/j.arthro.2011.12.022
87. Ebert JR, Fallon M, Smith A, Janes GC, Wood DJ. Prospective clinical and radiologic evaluation of patellofemoral matrix-induced autologous chondrocyte implantation. Am J Sports Med. 2015;43(6):1362–72. https://doi.org/10.1177/0363546515574063.
88. Ebert JR, Fallon M, Wood DJ, Janes GC. A prospective clinical and radiological evaluation at 5 years after arthroscopic matrix-induced autologous chondrocyte implantation. Am J Sports Med. 2017;45(1):59–69. https://doi.org/10.1177/0363546516663493.

89. Efe T, Theisen C, Fuchs-Winkelmann S, Stein T, Getgood A, Rominger MB, Paletta JR, Schofer MD. Cell-free collagen type I matrix for repair of cartilage defects-clinical and magnetic resonance imaging results. Knee Surg Sports Traumatol Arthrosc. 2012;20(10):1915–22. https://doi.org/10.1007/s00167-011-1777-5.
90. El-Rashidy H, Villacis D, Omar I, Kelikian AS. Fresh osteochondral allograft for the treatment of cartilage defects of the talus: a retrospective review. J Bone Joint Surg Am. 2011;93(17):1634–40. https://doi.org/10.2106/JBJS.J.00900.
91. Emre TY, Ege T, Cift HT, Demircioglu DT, Seyhan B, Uzun M. Open mosaicplasty in osteochondral lesions of the talus: a prospective study. J Foot Ankle Surg. 2012;51(5):556–60. https://doi.org/10.1053/j.jfas.2012.05.006.
92. Enea D, Cecconi S, Calcagno S, Busilacchi A, Manzotti S, Kaps C, Gigante A. Single-stage cartilage repair in the knee with microfracture covered with a resorbable polymer-based matrix and autologous bone marrow concentrate. Knee. 2013;20(6):562–9. https://doi.org/10.1016/j.knee.2013.04.003.
93. Enea D, Cecconi S, Calcagno S, Busilacchi A, Manzotti S, Gigante A. One-step cartilage repair in the knee: collagen-covered microfracture and autologous bone marrow concentrate. A pilot study. Knee. 2015;22(1):30–5. https://doi.org/10.1016/j.knee.2014.10.003.
94. Espregueira-Mendes J, Pereira H, Sevivas N, Varanda P, da Silva MV, Monteiro A, Oliveira JM, Reis RL. Osteochondral transplantation using autografts from the upper tibio-fibular joint for the treatment of knee cartilage lesions. Knee Surg Sports Traumatol Arthrosc. 2012;20(6):1136–42. https://doi.org/10.1007/s00167-012-1910-0.
95. Ferruzzi A, Buda R, Faldini C, Vannini F, Di Caprio F, Luciani D, Giannini S. Autologous chondrocyte implantation in the knee joint: open compared with arthroscopic technique. Comparison at a minimum follow-up of five years. J Bone Joint Surg Am 2008;90 Suppl 4:90–101. https://doi.org/10.2106/JBJS.H.00633
96. Filardo G, Kon E, Di Martino A, Iacono F, Marcacci M. Arthroscopic second-generation autologous chondrocyte implantation: a prospective 7-year follow-up study. Am J Sports Med. 2011;39(10):2153–60. https://doi.org/10.1177/0363546511415658.
97. Fraser EJ, Harris MC, Prado MP, Kennedy JG. Autologous osteochondral transplantation for osteochondral lesions of the talus in an athletic population. Knee Surg Sports Traumatol Arthrosc. 2016;24(4):1272–9. https://doi.org/10.1007/s00167-015-3606-8.
98. Galla M, Duensing I, Kahn TL, Barg A. Open reconstruction with autologous spongiosa grafts and matrix-induced chondrogenesis for osteochondral lesions of the talus can be performed without medial malleolar osteotomy. Knee Surg Sports Traumatol Arthrosc. 2019;27(9):2789–95. https://doi.org/10.1007/s00167-018-5063-7.
99. Gaul F, Tirico LEP, McCauley JC, Pulido PA, Bugbee WD. Osteochondral allograft transplantation for osteochondral lesions of the talus: midterm follow-up. Foot Ankle Int. 2019;40(2):202–9. https://doi.org/10.1177/1071100718805064.
100. Gaul F, Tirico LEP, McCauley JC, Bugbee WD. Long-term follow-up of revision osteochondral allograft transplantation of the ankle. Foot Ankle Int. 2018;39(5):522–9. https://doi.org/10.1177/1071100717750578.
101. Gautier E, Kolker D, Jakob RP. Treatment of cartilage defects of the talus by autologous osteochondral grafts. J Bone Joint Surg Br. 2002;84(2):237–44. https://doi.org/10.1302/0301-620x.84b2.11735.
102. Georgiannos D, Bisbinas I, Badekas A. Osteochondral transplantation of autologous graft for the treatment of osteochondral lesions of talus: 5- to 7-year follow-up. Knee Surg Sports Traumatol Arthrosc. 2016;24(12):3722–9. https://doi.org/10.1007/s00167-014-3389-3.
103. Giannini S, Buda R, Vannini F, Di Caprio F, Grigolo B. Arthroscopic autologous chondrocyte implantation in osteochondral lesions of the talus: surgical technique and results. Am J Sports Med. 2008;36(5):873–80. https://doi.org/10.1177/0363546507312644.
104. Giannini S, Battaglia M, Buda R, Cavallo M, Ruffilli A, Vannini F. Surgical treatment of osteochondral lesions of the talus by open-field autologous chondrocyte implantation: a 10-year follow-up clinical and magnetic resonance imaging T2-mapping evaluation. Am J Sports Med. 2009;37(Suppl 1):112S-118S. https://doi.org/10.1177/0363546509349928.
105. Giannini S, Buda R, Ruffilli A, Cavallo M, Pagliazzi G, Bulzamini MC, Desando G, Luciani D, Vannini F. Arthroscopic autologous chondrocyte implantation in the ankle joint. Knee Surg Sports Traumatol Arthrosc. 2014;22(6):1311–9. https://doi.org/10.1007/s00167-013-2640-7.
106. Giannini S, Mazzotti A, Vannini F. Bipolar fresh total osteochondral allograft in the ankle: is it a successful long-term solution? Injury. 2017;48(7):1319–24. https://doi.org/10.1016/j.injury.2017.05.011.
107. Gille J, Behrens P, Volpi P, de Girolamo L, Reiss E, Zoch W, Anders S. Outcome of autologous matrix induced chondrogenesis (AMIC) in cartilage knee surgery: data of the AMIC Registry. Arch Orthop Trauma Surg. 2013;133(1):87–93. https://doi.org/10.1007/s00402-012-1621-5.
108. Giza E, Sullivan M, Ocel D, Lundeen G, Mitchell ME, Veris L, Walton J. Matrix-induced autologous chondrocyte implantation of talus articular defects. Foot Ankle Int. 2010;31(9):747–53. https://doi.org/10.3113/FAI.2010.0747.
109. Gobbi A, Francisco RA, Lubowitz JH, Allegra F, Canata G. Osteochondral lesions of the talus: randomized controlled trial comparing chondroplasty, microfracture, and osteochondral autograft transplantation. Arthroscopy. 2006;22(10):1085–92. https://doi.org/10.1016/j.arthro.2006.05.016.
110. Gobbi A, Kon E, Berruto M, Filardo G, Delcogliano M, Boldrini L, Bathan L, Marcacci M. Patellofemoral full-thickness chondral defects treated with second-generation autologous chondrocyte implantation: results at 5 years' follow-up. Am J Sports Med. 2009;37(6):1083–92. https://doi.org/10.1177/0363546509331419.
111. Gobbi A, Karnatzikos G, Scotti C, Mahajan V, Mazzucco L, Grigolo B. One-step cartilage repair with bone marrow aspirate concentrated cells and collagen matrix in full-thickness knee cartilage lesions: results at 2-year follow-up. Cartilage. 2011;2(3):286–99. https://doi.org/10.1177/1947603510392023.
112. Gobbi A, Karnatzikos G, Sankineani SR. One-step surgery with multipotent stem cells for the treatment of large full-thickness chondral defects of the knee. Am J Sports Med. 2014;42(3):648–57. https://doi.org/10.1177/0363546513518007.
113. Gobbi A, Scotti C, Karnatzikos G, Mudhigere A, Castro M, Peretti GM. One-step surgery with multipotent stem cells and Hyaluronan-based scaffold for the treatment of full-thickness chondral defects of the knee in patients older than 45 years. Knee Surg Sports Traumatol Arthrosc. 2017;25(8):2494–501. https://doi.org/10.1007/s00167-016-3984-6.
114. Gomoll AH, Gillogly SD, Cole BJ, Farr J, Arnold R, Hussey K, Minas T. Autologous chondrocyte implantation in the patella: a multicenter experience. Am J Sports Med. 2014;42(5):1074–81. https://doi.org/10.1177/0363546514523927.
115. Gooding CR, Bartlett W, Bentley G, Skinner JA, Carrington R, Flanagan A. A prospective, randomised study comparing two techniques of autologous chondrocyte implantation for osteochondral defects in the knee: periosteum covered versus type I/

III collagen covered. Knee. 2006;13(3):203–10. https://doi.org/10.1016/j.knee.2006.02.011.
116. Gottschalk O, Altenberger S, Baumbach S, Kriegelstein S, Dreyer F, Mehlhorn A, Horterer H, Topfer A, Roser A, Walther M. Functional medium-term results after autologous matrix-induced chondrogenesis for osteochondral lesions of the talus: a 5-year prospective cohort study. J Foot Ankle Surg. 2017;56(5):930–6. https://doi.org/10.1053/j.jfas.2017.05.002.
117. Gudas R, Stankevicius E, Monastyreckiene E, Pranys D, Kalesinskas RJ. Osteochondral autologous transplantation versus microfracture for the treatment of articular cartilage defects in the knee joint in athletes. Knee Surg Sports Traumatol Arthrosc. 2006;14(9):834–42. https://doi.org/10.1007/s00167-006-0067-0.
118. Gudas R, Simonaityte R, Cekanauskas E, Tamosiunas R. A prospective, randomized clinical study of osteochondral autologous transplantation versus microfracture for the treatment of osteochondritis dissecans in the knee joint in children. J Pediatr Orthop. 2009;29(7):741–8. https://doi.org/10.1097/BPO.0b013e3181b8f6c7.
119. Gudas R, Gudaite A, Pocius A, Gudiene A, Cekanauskas E, Monastyreckiene E, Basevicius A. Ten-year follow-up of a prospective, randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint of athletes. Am J Sports Med. 2012;40(11):2499–508. https://doi.org/10.1177/0363546512458763.
120. Gudas R, Maciulaitis J, Staskunas M, Smailys A. Clinical outcome after treatment of single and multiple cartilage defects by autologous matrix-induced chondrogenesis. J Orthop Surg (Hong Kong). 2019;27(2):2309499019851011. https://doi.org/10.1177/2309499019851011.
121. Gul M, Cetinkaya E, Aykut US, Ozkul B, Saygili MS, Akman YE, Kabukcuoglu YS. Effect of the presence of subchondral cysts on treatment results of autologous osteochondral graft transfer in osteochondral lesions of the talus. J Foot Ankle Surg. 2016;55(5):1003–6. https://doi.org/10.1053/j.jfas.2016.05.012.
122. Guney A, Yurdakul E, Karaman I, Bilal O, Kafadar IH, Oner M. Medium-term outcomes of mosaicplasty versus arthroscopic microfracture with or without platelet-rich plasma in the treatment of osteochondral lesions of the talus. Knee Surg Sports Traumatol Arthrosc. 2016;24(4):1293–8. https://doi.org/10.1007/s00167-015-3834-y.
123. Haleem AM, Singergy AA, Sabry D, Atta HM, Rashed LA, Chu CR, El Shewy MT, Azzam A, Abdel Aziz MT. The clinical use of human culture-expanded autologous bone marrow mesenchymal stem cells transplanted on platelet-rich fibrin glue in the treatment of articular cartilage defects: a pilot study and preliminary results. Cartilage. 2010;1(4):253–61. https://doi.org/10.1177/1947603510366027.
124. Haleem AM, Ross KA, Smyth NA, Duke GL, Deyer TW, Do HT, Kennedy JG. Double-plug autologous osteochondral transplantation shows equal functional outcomes compared with single-plug procedures in lesions of the talar dome: a minimum 5-year clinical follow-up. Am J Sports Med. 2014;42(8):1888–95. https://doi.org/10.1177/0363546514535068.
125. Haasper C, Zelle BA, Knobloch K, Jagodzinski M, Citak M, Lotz J, Krettek C, Zeichen J. No mid-term difference in mosaicplasty in previously treated versus previously untreated patients with osteochondral lesions of the talus. Arch Orthop Trauma Surg. 2008;128(5):499–504. https://doi.org/10.1007/s00402-007-0513-6.
126. Hahn DB, Aanstoos ME, Wilkins RM. Osteochondral lesions of the talus treated with fresh talar allografts. Foot Ankle Int. 2010;31(4):277–82. https://doi.org/10.3113/FAI.2010.0277.
127. Hangody L, Kish G, Karpati Z, Szerb I, Eberhardt R. Treatment of osteochondritis dissecans of the talus: use of the mosaicplasty technique—a preliminary report. Foot Ankle Int. 1997;18(10):628–34. https://doi.org/10.1177/107110079701801005.
128. Hangody L, Kish G, Modis L, Szerb I, Gaspar L, Dioszegi Z, Kendik Z. Mosaicplasty for the treatment of osteochondritis dissecans of the talus: two to seven year results in 36 patients. Foot Ankle Int. 2001;22(7):552–8. https://doi.org/10.1177/107110070102200704.
129. Hoburg A, Loer I, Korsmeier K, Siebold R, Niemeyer P, Fickert S, Ruhnau K. Matrix-associated autologous chondrocyte implantation is an effective treatment at midterm follow-up in adolescents and young adults. Orthop J Sports Med. 2019;7(4):2325967119841077. https://doi.org/10.1177/2325967119841077.
130. Horas U, Pelinkovic D, Herr G, Aigner T, Schnettler R. Autologous chondrocyte implantation and osteochondral cylinder transplantation in cartilage repair of the knee joint. A prospective, comparative trial. J Bone Joint Surg Am. 2003;85(2):185–92. https://doi.org/10.2106/00004623-200302000-00001
131. Imhoff AB, Paul J, Ottinger B, Wortler K, Lammle L, Spang J, Hinterwimmer S. Osteochondral transplantation of the talus: long-term clinical and magnetic resonance imaging evaluation. Am J Sports Med. 2011;39(7):1487–93. https://doi.org/10.1177/0363546510397726.
132. Jackson AT, Drayer NJ, Samona J, Dukes CA, Chen CS, Arrington EA, Ryan PM. Osteochondral allograft transplantation surgery for osteochondral lesions of the talus in athletes. J Foot Ankle Surg. 2019;58(4):623–7. https://doi.org/10.1053/j.jfas.2018.11.020.
133. Kim TY, Song SH, Baek JH, Hwang YG, Jeong BO. Analysis of the changes in the clinical outcomes according to time after arthroscopic microfracture of osteochondral lesions of the talus. Foot Ankle Int. 2019;40(1):74–9. https://doi.org/10.1177/1071100718794944.
134. Knutsen G, Drogset JO, Engebretsen L, Grontvedt T, Ludvigsen TC, Loken S, Solheim E, Strand T, Johansen O. A randomized multicenter trial comparing autologous chondrocyte implantation with microfracture: long-term follow-up at 14 to 15 years. J Bone Joint Surg Am. 2016;98(16):1332–9. https://doi.org/10.2106/JBJS.15.01208.
135. Koh YG, Kwon OR, Kim YS, Choi YJ, Tak DH. Adipose-derived mesenchymal stem cells with microfracture versus microfracture alone: 2-year follow-up of a prospective randomized trial. Arthroscopy. 2016;32(1):97–109. https://doi.org/10.1016/j.arthro.2015.09.010.
136. Kon E, Gobbi A, Filardo G, Delcogliano M, Zaffagnini S, Marcacci M. Arthroscopic second-generation autologous chondrocyte implantation compared with microfracture for chondral lesions of the knee: prospective nonrandomized study at 5 years. Am J Sports Med. 2009;37(1):33–41. https://doi.org/10.1177/0363546508323256.
137. Kon E, Filardo G, Condello V, Collarile M, Di Martino A, Zorzi C, Marcacci M. Second-generation autologous chondrocyte implantation: results in patients older than 40 years. Am J Sports Med. 2011;39(8):1668–75. https://doi.org/10.1177/0363546511404675.
138. Kretzschmar M, Bieri O, Miska M, Wiewiorski M, Hainc N, Valderrabano V, Studler U. Characterization of the collagen component of cartilage repair tissue of the talus with quantitative MRI: comparison of T2 relaxation time measurements with a diffusion-weighted double-echo steady-state sequence (dwDESS). Eur Radiol. 2015;25(4):980–6. https://doi.org/10.1007/s00330-014-3490-5.
139. Kreulen C, Giza E, Walton J, Sullivan M. Seven-year follow-up of matrix-induced autologous implantation in talus articular

defects. Foot Ankle Spec. 2018;11(2):133–7. https://doi.org/10.1177/1938640017713614.
140. Kreuz PC, Steinwachs M, Erggelet C, Lahm A, Henle P, Niemeyer P. Mosaicplasty with autogenous talar autograft for osteochondral lesions of the talus after failed primary arthroscopic management: a prospective study with a 4-year follow-up. Am J Sports Med. 2006;34(1):55–63. https://doi.org/10.1177/0363546505278299.
141. Kwak SK, Kern BS, Ferkel RD, Chan KW, Kasraeian S, Applegate GR. Autologous chondrocyte implantation of the ankle: 2- to 10-year results. Am J Sports Med. 2014;42(9):2156–64. https://doi.org/10.1177/0363546514540587.
142. Lahner M, Ull C, Hagen M, von Schulze PC, Daniilidis K, von Engelhardt LV, Lahner N, Teske W. Cartilage surgery in overweight patients: clinical and MRI results after the autologous matrix-induced chondrogenesis procedure. Biomed Res Int. 2018;2018:6363245. https://doi.org/10.1155/2018/6363245.
143. Lee CH, Chao KH, Huang GS, Wu SS. Osteochondral autografts for osteochondritis dissecans of the talus. Foot Ankle Int. 2003;24(11):815–22. https://doi.org/10.1177/107110070302401102.
144. Li X, Zhu Y, Xu Y, Wang B, Liu J, Xu X. Osteochondral autograft transplantation with biplanar distal tibial osteotomy for patients with concomitant large osteochondral lesion of the talus and varus ankle malalignment. BMC Musculoskelet Disord. 2017;18(1):23. https://doi.org/10.1186/s12891-016-1367-2.
145. Liu W, Liu F, Zhao W, Kim JM, Wang Z, Vrahas MS. Osteochondral autograft transplantation for acute osteochondral fractures associated with an ankle fracture. Foot Ankle Int. 2011;32(4):437–42. https://doi.org/10.3113/FAI.2011.0437.
146. Liu X, An J, Zhang H, Li Y, Chen Y, Zhang W. Autologous osteochondral graft for early posttraumatic arthritis of tibiotalar joints after comminuted pilon fractures in young patients. Foot Ankle Int. 2020;41(1):69–78. https://doi.org/10.1177/1071100719875728.
147. Lopez-Alcorocho JM, Aboli L, Guillen-Vicente I, Rodriguez-Inigo E, Guillen-Vicente M, Fernandez-Jaen TF, Arauz S, Abelow S, Guillen-Garcia P. Cartilage defect treatment using high-density autologous chondrocyte implantation: two-year follow-up. Cartilage. 2018;9(4):363–9. https://doi.org/10.1177/1947603517693045.
148. Lopez-Alcorocho JM, Guillen-Vicente I, Rodriguez-Inigo E, Navarro R, Caballero-Santos R, Guillen-Vicente M, Casqueiro M, Fernandez-Jaen TF, Sanz F, Arauz S, Abelow S, Guillen-Garcia P. High-density autologous chondrocyte implantation as treatment for ankle osteochondral defects. Cartilage. 2019:1947603519835898. https://doi.org/10.1177/1947603519835898.
149. Macmull S, Parratt MT, Bentley G, Skinner JA, Carrington RW, Morris T, Briggs TW. Autologous chondrocyte implantation in the adolescent knee. Am J Sports Med. 2011;39(8):1723–30. https://doi.org/10.1177/0363546511404202.
150. Macmull S, Jaiswal PK, Bentley G, Skinner JA, Carrington RW, Briggs TW. The role of autologous chondrocyte implantation in the treatment of symptomatic chondromalacia patellae. Int Orthop. 2012;36(7):1371–7. https://doi.org/10.1007/s00264-011-1465-6.
151. Magnan B, Samaila E, Bondi M, Vecchini E, Micheloni GM, Bartolozzi P. Three-dimensional matrix-induced autologous chondrocytes implantation for osteochondral lesions of the talus: midterm results. Adv Orthop. 2012;2012: 942174. https://doi.org/10.1155/2012/942174.
152. Marlovits S, Aldrian S, Wondrasch B, Zak L, Albrecht C, Welsch G, Trattnig S. Clinical and radiological outcomes 5 years after matrix-induced autologous chondrocyte implantation in patients with symptomatic, traumatic chondral defects. Am J Sports Med. 2012;40(10):2273–80. https://doi.org/10.1177/0363546512457008.
153. McNickle AG, L'Heureux DR, Yanke AB, Cole BJ. Outcomes of autologous chondrocyte implantation in a diverse patient population. Am J Sports Med. 2009;37(7):1344–50. https://doi.org/10.1177/0363546509332258.
154. Mehl J, Huck J, Bode G, Hohloch L, Schmitt A, Sudkamp NP, Niemeyer P. Clinical mid- to long-term outcome after autologous chondrocyte implantation for patellar cartilage lesions and its correlation with the geometry of the femoral trochlea. Knee. 2019;26(2):364–73. https://doi.org/10.1016/j.knee.2019.01.019.
155. Meyerkort D, Ebert JR, Ackland TR, Robertson WB, Fallon M, Zheng MH, Wood DJ. Matrix-induced autologous chondrocyte implantation (MACI) for chondral defects in the patellofemoral joint. Knee Surg Sports Traumatol Arthrosc. 2014;22(10):2522–30. https://doi.org/10.1007/s00167-014-3046-x.
156. Micheli LJ, Browne JE, Erggelet C, Fu F, Mandelbaum B, Moseley JB, Zurakowski D. Autologous chondrocyte implantation of the knee: multicenter experience and minimum 3-year follow-up. Clin J Sport Med. 2001;11(4):223–8. https://doi.org/10.1097/00042752-200110000-00003.
157. Minas T, Von Keudell A, Bryant T, Gomoll AH. The John Insall Award: a minimum 10-year outcome study of autologous chondrocyte implantation. Clin Orthop Relat Res. 2014;472(1):41–51. https://doi.org/10.1007/s11999-013-3146-9.
158. Moseley JB Jr, Anderson AF, Browne JE, Mandelbaum BR, Micheli LJ, Fu F, Erggelet C. Long-term durability of autologous chondrocyte implantation: a multicenter, observational study in US patients. Am J Sports Med. 2010;38(2):238–46. https://doi.org/10.1177/0363546509348000.
159. Murphy EP, Fenelon C, Egan C, Kearns SR. Matrix-associated stem cell transplantation is successful in treating talar osteochondral lesions. Knee Surg Sports Traumatol Arthrosc. 2019;27(9):2737–43. https://doi.org/10.1007/s00167-019-05452-z.
160. Nam EK, Ferkel RD, Applegate GR. Autologous chondrocyte implantation of the ankle: a 2- to 5-year follow-up. Am J Sports Med. 2009;37(2):274–84. https://doi.org/10.1177/0363546508325670.
161. Nawaz SZ, Bentley G, Briggs TW, Carrington RW, Skinner JA, Gallagher KR, Dhinsa BS. Autologous chondrocyte implantation in the knee: mid-term to long-term results. J Bone Joint Surg Am. 2014;96(10):824–30. https://doi.org/10.2106/JBJS.L.01695.
162. Nehrer S, Domayer SE, Hirschfeld C, Stelzeneder D, Trattnig S, Dorotka R. Matrix-associated and autologous chondrocyte transplantation in the ankle: clinical and MRI follow-up after 2 to 11 years. Cartilage. 2011;2(1):81–91. https://doi.org/10.1177/1947603510381095.
163. Nejadnik H, Hui JH, Feng Choong EP, Tai BC, Lee EH. Autologous bone marrow-derived mesenchymal stem cells versus autologous chondrocyte implantation: an observational cohort study. Am J Sports Med. 2010;38(6):1110–6. https://doi.org/10.1177/0363546509359067.
164. Nguyen A, Ramasamy A, Walsh M, McMenemy L, Calder JDF. Autologous osteochondral transplantation for large osteochondral lesions of the talus is a viable option in an athletic population. Am J Sports Med. 2019;47(14):3429–35. https://doi.org/10.1177/0363546519881420.
165. Niemeyer P, Steinwachs M, Erggelet C, Kreuz PC, Kraft N, Kostler W, Mehlhorn A, Sudkamp NP. Autologous chondrocyte implantation for the treatment of retropatellar cartilage defects: clinical results referred to defect localisation. Arch Orthop Trauma Surg. 2008;128(11):1223–31. https://doi.org/10.1007/s00402-007-0413-9.

166. Niemeyer P, Lenz P, Kreuz PC, Salzmann GM, Sudkamp NP, Schmal H, Steinwachs M. Chondrocyte-seeded type I/III collagen membrane for autologous chondrocyte transplantation: prospective 2-year results in patients with cartilage defects of the knee joint. Arthroscopy. 2010;26(8):1074–82. https://doi.org/10.1016/j.arthro.2009.12.028.
167. Niemeyer P, Porichis S, Steinwachs M, Erggelet C, Kreuz PC, Schmal H, Uhl M, Ghanem N, Sudkamp NP, Salzmann G. Long-term outcomes after first-generation autologous chondrocyte implantation for cartilage defects of the knee. Am J Sports Med. 2014;42(1):150–7. https://doi.org/10.1177/0363546513506593.
168. Niemeyer P, Laute V, John T, Becher C, Diehl P, Kolombe T, Fay J, Siebold R, Niks M, Fickert S, Zinser W. The effect of cell dose on the early magnetic resonance morphological outcomes of autologous cell implantation for articular cartilage defects in the knee: a randomized clinical trial. Am J Sports Med. 2016;44(8):2005–14. https://doi.org/10.1177/0363546516646092.
169. Niemeyer P, Laute V, Zinser W, Becher C, Kolombe T, Fay J, Pietsch S, Kuzma T, Widuchowski W, Fickert S. A prospective, randomized, open-label, multicenter, phase III noninferiority trial to compare the clinical efficacy of matrix-associated autologous chondrocyte implantation with spheroid technology versus arthroscopic microfracture for cartilage defects of the knee. Orthop J Sports Med. 2019;7(7):2325967119854442. https://doi.org/10.1177/2325967119854442.
170. Ogura T, Mosier BA, Bryant T, Minas T. A 20-year follow-up after first-generation autologous chondrocyte implantation. Am J Sports Med. 2017;45(12):2751–61. https://doi.org/10.1177/0363546517716631.
171. Ogura T, Merkely G, Bryant T, Winalski CS, Minas T. Autologous chondrocyte implantation "segmental-sandwich" technique for deep osteochondral defects in the knee: clinical outcomes and correlation with magnetic resonance imaging findings. Orthop J Sports Med. 2019;7(5):2325967119847173. https://doi.org/10.1177/2325967119847173.
172. Orr JD, Dunn JC, Heida KA Jr, Kusnezov NA, Waterman BR, Belmont PJ Jr. Results and functional outcomes of structural fresh osteochondral allograft transfer for treatment of osteochondral lesions of the talus in a highly active population. Foot Ankle Spec. 2017;10(2):125–32. https://doi.org/10.1177/1938640016666924.
173. Pagliazzi G, Vannini F, Battaglia M, Ramponi L, Buda R. Autologous chondrocyte implantation for talar osteochondral lesions: comparison between 5-year follow-up magnetic resonance imaging findings and 7-year follow-up clinical results. J Foot Ankle Surg. 2018;57(2):221–5. https://doi.org/10.1053/j.jfas.2017.05.013.
174. Park KH, Hwang Y, Han SH, Park YJ, Shim DW, Choi WJ, Lee JW. Primary versus secondary osteochondral autograft transplantation for the treatment of large osteochondral lesions of the talus. Am J Sports Med. 2018;46(6):1389–96. https://doi.org/10.1177/0363546518758014.
175. Park CH, Song KS, Kim JR, Lee SW. Retrospective evaluation of outcomes of bone peg fixation for osteochondral lesion of the talus. Bone Joint J 2020;102-B(10):1349–53. https://doi.org/10.1302/0301-620X.102B10.BJJ-2020-0527.R1
176. Paul J, Sagstetter M, Lammle L, Spang J, El-Azab H, Imhoff AB, Hinterwimmer S. Sports activity after osteochondral transplantation of the talus. Am J Sports Med. 2012;40(4):870–4. https://doi.org/10.1177/0363546511435084.
177. Peterson L, Vasiliadis HS, Brittberg M, Lindahl A. Autologous chondrocyte implantation: a long-term follow-up. Am J Sports Med. 2010;38(6):1117–24. https://doi.org/10.1177/0363546509357915.
178. Polat G, Ersen A, Erdil ME, Kizilkurt T, Kilicoglu O, Asik M. Long-term results of microfracture in the treatment of talus osteochondral lesions. Knee Surg Sports Traumatol Arthrosc. 2016;24(4):1299–303. https://doi.org/10.1007/s00167-016-3990-8.
179. Quirbach S, Trattnig S, Marlovits S, Zimmermann V, Domayer S, Dorotka R, Mamisch TC, Bohndorf K, Welsch GH. Initial results of in vivo high-resolution morphological and biochemical cartilage imaging of patients after matrix-associated autologous chondrocyte transplantation (MACT) of the ankle. Skeletal Radiol. 2009;38(8):751–60. https://doi.org/10.1007/s00256-009-0682-1.
180. Randsborg PH, Brinchmann J, Loken S, Hanvold HA, Aae TF, Aroen A. Focal cartilage defects in the knee—a randomized controlled trial comparing autologous chondrocyte implantation with arthroscopic debridement. BMC Musculoskelet Disord. 2016;17:117. https://doi.org/10.1186/s12891-016-0969-z.
181. Richter M, Zech S, Andreas Meissner S. Matrix-associated stem cell transplantation (MAST) in chondral defects of the 1st metatarsophalangeal joint is safe and effective-2-year-follow-up in 20 patients. Foot Ankle Surg. 2017;23(3):195–200. https://doi.org/10.1016/j.fas.2016.05.318.
182. Richter M, Zech S, Meissner S, Naef I. Comparison matrix-associated stem cell transplantation (MAST) with autologous matrix induced chondrogenesis plus peripheral blood concentrate (AMIC+PBC) in chondral lesions at the ankle—a clinical matched-patient analysis. Foot Ankle Surg. 2020;26(6):669–75. https://doi.org/10.1016/j.fas.2019.08.009.
183. Rosa D, Balato G, Ciaramella G, Soscia E, Improta G, Triassi M. Long-term clinical results and MRI changes after autologous chondrocyte implantation in the knee of young and active middle aged patients. J Orthop Traumatol. 2016;17(1):55–62. https://doi.org/10.1007/s10195-015-0383-6.
184. Ross AW, Murawski CD, Fraser EJ, Ross KA, Do HT, Deyer TW, Kennedy JG. Autologous osteochondral transplantation for osteochondral lesions of the talus: does previous bone marrow stimulation negatively affect clinical outcome? Arthroscopy. 2016;32(7):1377–83. https://doi.org/10.1016/j.arthro.2016.01.036.
185. Sabaghzadeh A, Mirzaee F, Shahriari Rad H, Bahramian F, Alidousti A, Aslani H. Osteochondral autograft transfer (mosaicplasty) for treatment of patients with osteochondral lesions of talus. Chin J Traumatol. 2020;23(1):60–2. https://doi.org/10.1016/j.cjtee.2019.12.001.
186. Sadlik B, Kolodziej L, Blasiak A, Szymczak M, Warchal B. Biological reconstruction of large osteochondral lesions of the talar dome with a modified "sandwich" technique—midterm results. Foot Ankle Surg. 2017;23(4):290–5. https://doi.org/10.1016/j.fas.2016.09.001.
187. Saris DB, Vanlauwe J, Victor J, Almqvist KF, Verdonk R, Bellemans J, Luyten FP, Tig/Act, Group EXTS. Treatment of symptomatic cartilage defects of the knee: characterized chondrocyte implantation results in better clinical outcome at 36 months in a randomized trial compared to microfracture. Am J Sports Med 2009;37 Suppl 1:10S-9S. https://doi.org/10.1177/0363546509350694.
188. Saris D, Price A, Widuchowski W, Bertrand-Marchand M, Caron J, Drogset JO, Emans P, Podskubka A, Tsuchida A, Kili S, Levine D, Brittberg M, Group S. Matrix-applied characterized autologous cultured chondrocytes versus microfracture: two-year follow-up of a prospective randomized trial. Am J Sports Med. 2014;42(6):1384–94. https://doi.org/10.1177/0363546514528093.
189. Schagemann J, Behrens P, Paech A, Riepenhof H, Kienast B, Mittelstadt H, Gille J. Mid-term outcome of arthroscopic AMIC for the treatment of articular cartilage defects in the knee joint is equivalent to mini-open procedures. Arch Orthop

Trauma Surg. 2018;138(6):819–25. https://doi.org/10.1007/s00402-018-2887-z.
190. Schiavone Panni A, Del Regno C, Mazzitelli G, D'Apolito R, Corona K, Vasso M. Good clinical results with autologous matrix-induced chondrogenesis (Amic) technique in large knee chondral defects. Knee Surg Sports Traumatol Arthrosc. 2018;26(4):1130–6. https://doi.org/10.1007/s00167-017-4503-0.
191. Schneider TE, Karaikudi S. Matrix-induced autologous chondrocyte implantation (MACI) grafting for osteochondral lesions of the talus. Foot Ankle Int. 2009;30(9):810–4. https://doi.org/10.3113/FAI.2009.0810.
192. Schneider U, Rackwitz L, Andereya S, Siebenlist S, Fensky F, Reichert J, Loer I, Barthel T, Rudert M, Noth U. A prospective multicenter study on the outcome of type I collagen hydrogel-based autologous chondrocyte implantation (CaReS) for the repair of articular cartilage defects in the knee. Am J Sports Med. 2011;39(12):2558–65. https://doi.org/10.1177/0363546511423369.
193. Schneider U. Controlled, randomized multicenter study to compare compatibility and safety of ChondroFiller liquid (cell free 2-component collagen gel) with microfracturing of patients with focal cartilage defects of the knee joint. J Ortop Surg. 2016;1:1–8.
194. Schuttler KF, Gotschenberg A, Klasan A, Stein T, Pehl A, Roessler PP, Figiel J, Heyse TJ, Efe T. Cell-free cartilage repair in large defects of the knee: increased failure rate 5 years after implantation of a collagen type I scaffold. Arch Orthop Trauma Surg. 2019;139(1):99–106. https://doi.org/10.1007/s00402-018-3028-4.
195. Siebold R, Suezer F, Schmitt B, Trattnig S, Essig M. Good clinical and MRI outcome after arthroscopic autologous chondrocyte implantation for cartilage repair in the knee. Knee Surg Sports Traumatol Arthrosc. 2018;26(3):831–9. https://doi.org/10.1007/s00167-017-4491-0.
196. Shimozono Y, Donders JCE, Yasui Y, Hurley ET, Deyer TW, Nguyen JT, Kennedy JG. Effect of the containment type on clinical outcomes in osteochondral lesions of the talus treated with autologous osteochondral transplantation. Am J Sports Med. 2018;46(9):2096–102. https://doi.org/10.1177/0363546518776659.
197. Shimozono Y, Hurley ET, Nguyen JT, Deyer TW, Kennedy JG. Allograft compared with autograft in osteochondral transplantation for the treatment of osteochondral lesions of the talus. J Bone Joint Surg Am. 2018;100(21):1838–44. https://doi.org/10.2106/JBJS.17.01508.
198. Skowronski J, Rutka M. Osteochondral lesions of the knee reconstructed with mesenchymal stem cells—results. Ortop Traumatol Rehabil. 2013;15(3):195–204. https://doi.org/10.5604/15093492.1058409.
199. Solheim E, Hegna J, Strand T, Harlem T, Inderhaug E. Randomized study of long-term (15–17 years) outcome after microfracture versus mosaicplasty in knee articular cartilage defects. Am J Sports Med. 2018;46(4):826–31. https://doi.org/10.1177/0363546517745281.
200. Steinwachs M, Cavalcanti N, Mauuva Venkatesh Reddy S, Werner C, Tschopp D, Choudur HN. Arthroscopic and open treatment of cartilage lesions with BST-CARGEL scaffold and microfracture: a cohort study of consecutive patients. Knee. 2019;26(1):174–84. https://doi.org/10.1016/j.knee.2018.11.015.
201. Teo BJ, Buhary K, Tai BC, Hui JH. Cell-based therapy improves function in adolescents and young adults with patellar osteochondritis dissecans. Clin Orthop Relat Res. 2013;471(4):1152–8. https://doi.org/10.1007/s11999-012-2338-z.
202. Tohyama H, Yasuda K, Minami A, Majima T, Iwasaki N, Muneta T, Sekiya I, Yagishita K, Takahashi S, Kurokouchi K, Uchio Y, Iwasa J, Deie M, Adachi N, Sugawara K, Ochi M. Atelocollagen-associated autologous chondrocyte implantation for the repair of chondral defects of the knee: a prospective multicenter clinical trial in Japan. J Orthop Sci. 2009;14(5):579–88. https://doi.org/10.1007/s00776-009-1384-1.
203. Usuelli FG, D'Ambrosi R, Maccario C, Boga M, de Girolamo L. All-arthroscopic AMIC((R)) (AT-AMIC((R))) technique with autologous bone graft for talar osteochondral defects: clinical and radiological results. Knee Surg Sports Traumatol Arthrosc. 2018;26(3):875–81. https://doi.org/10.1007/s00167-016-4318-4.
204. Valderrabano V, Miska M, Leumann A, Wiewiorski M. Reconstruction of osteochondral lesions of the talus with autologous spongiosa grafts and autologous matrix-induced chondrogenesis. Am J Sports Med. 2013;41(3):519–27. https://doi.org/10.1177/0363546513476671.
205. Van Assche D, Staes F, Van Caspel D, Vanlauwe J, Bellemans J, Saris DB, Luyten FP. Autologous chondrocyte implantation versus microfracture for knee cartilage injury: a prospective randomized trial, with 2-year follow-up. Knee Surg Sports Traumatol Arthrosc. 2010;18(4):486–95. https://doi.org/10.1007/s00167-009-0955-1.
206. Vanlauwe J, Saris DB, Victor J, Almqvist KF, Bellemans J, Luyten FP, Tig/Act, Group EXTS. Five-year outcome of characterized chondrocyte implantation versus microfracture for symptomatic cartilage defects of the knee: early treatment matters. Am J Sports Med 2011;39(12):2566–74. https://doi.org/10.1177/0363546511422220.
207. Vanlauwe JJ, Claes T, Van Assche D, Bellemans J, Luyten FP. Characterized chondrocyte implantation in the patellofemoral joint: an up to 4-year follow-up of a prospective cohort of 38 patients. Am J Sports Med. 2012;40(8):1799–807. https://doi.org/10.1177/0363546512452712.
208. Volz M, Schaumburger J, Frick H, Grifka J, Anders S. A randomized controlled trial demonstrating sustained benefit of autologous matrix-induced chondrogenesis over microfracture at five years. Int Orthop. 2017;41(4):797–804. https://doi.org/10.1007/s00264-016-3391-0.
209. Whittaker JP, Smith G, Makwana N, Roberts S, Harrison PE, Laing P, Richardson JB. Early results of autologous chondrocyte implantation in the talus. J Bone Joint Surg Br. 2005;87(2):179–83. https://doi.org/10.1302/0301-620x.87b2.15376.
210. Wiewiorski M, Miska M, Kretzschmar M, Studler U, Bieri O, Valderrabano V. Delayed gadolinium-enhanced MRI of cartilage of the ankle joint: results after autologous matrix-induced chondrogenesis (AMIC)-aided reconstruction of osteochondral lesions of the talus. Clin Radiol. 2013;68(10):1031–8. https://doi.org/10.1016/j.crad.2013.04.016.
211. Wiewiorski M, Werner L, Paul J, Anderson AE, Barg A, Valderrabano V. Sports activity after reconstruction of osteochondral lesions of the talus with autologous spongiosa grafts and autologous matrix-induced chondrogenesis. Am J Sports Med. 2016;44(10):2651–8. https://doi.org/10.1177/0363546516659643.
212. Wolf MT, Zhang H, Sharma B, Marcus NA, Pietzner U, Fickert S, Lueth A, Albers GHR, Elisseeff JH. Two-year follow-up and remodeling kinetics of ChonDux hydrogel for full-thickness cartilage defect repair in the knee. Cartilage. 2020;11(4):447–57. https://doi.org/10.1177/1947603518800547.
213. Woelfle JV, Reichel H, Nelitz M. Indications and limitations of osteochondral autologous transplantation in osteochondritis dissecans of the talus. Knee Surg Sports Traumatol

Arthrosc. 2013;21(8):1925–30. https://doi.org/10.1007/s00167-013-2483-2.

214. Yontar NS, Aslan L, Can A, Ogut T. One step treatment of talus osteochondral lesions with microfracture and cell free hyaluronic acid based scaffold combination. Acta Orthop Traumatol Turc. 2019;53(5):372–5. https://doi.org/10.1016/j.aott.2019.04.002.
215. Yoon HS, Park YJ, Lee M, Choi WJ, Lee JW. Osteochondral autologous transplantation is superior to repeat arthroscopy for the treatment of osteochondral lesions of the talus after failed primary arthroscopic treatment. Am J Sports Med. 2014;42(8):1896–903. https://doi.org/10.1177/0363546514535186.
216. Zaslav K, Cole B, Brewster R, DeBerardino T, Farr J, Fowler P, Nissen C, Investigators SSP. A prospective study of autologous chondrocyte implantation in patients with failed prior treatment for articular cartilage defect of the knee: results of the study of the treatment of articular repair (STAR) clinical trial. Am J Sports Med. 2009;37(1):42–55. https://doi.org/10.1177/0363546508322897.
217. Zeifang F, Oberle D, Nierhoff C, Richter W, Moradi B, Schmitt H. Autologous chondrocyte implantation using the original periosteum-cover technique versus matrix-associated autologous chondrocyte implantation: a randomized clinical trial. Am J Sports Med. 2010;38(5):924–33. https://doi.org/10.1177/0363546509351499.
218. Zhu Y, Xu X. Osteochondral autograft transfer combined with cancellous allografts for large cystic osteochondral defect of the talus. Foot Ankle Int. 2016;37(10):1113–8. https://doi.org/10.1177/1071100716655345.