





Allograft Versus Autograft Osteochondral Transplant for Chondral Defects of the Talus

Systematic Review and Meta-analysis

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Background: It is unclear whether the results of osteochondral transplant using autografts or allografts for talar osteochondral defect are equivalent.

Purpose: A systematic review of the literature was conducted to compare allografts and autografts in terms of patient-reported outcome measures (PROMs), MRI findings, and complications.

Study Design: Systematic review; Level of evidence, 4.

Methods: This study was conducted according to the PRISMA guidelines. The literature search was conducted in February 2021. All studies investigating the outcomes of allograft and/or autograft osteochondral transplant as management for osteochondral defects of the talus were accessed. The outcomes of interest were visual analog scale (VAS) score for pain, American Orthopaedic Foot and Ankle Society (AOFAS) score, and Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score. Data concerning the rates of failure and revision surgery were also collected. Continuous data were analyzed using the mean difference (MD), whereas binary data were evaluated with the odds ratio (OR) effect measure.

Results: Data from 40 studies (1174 procedures) with a mean follow-up of 46.5 ± 25 months were retrieved. There was comparability concerning the length of follow-up, male to female ratio, mean age, body mass index, defect size, VAS score, and AOFAS score ($P > .1$) between the groups at baseline. At the last follow-up, the MOCART (MD, 10.5; $P = .04$) and AOFAS (MD, 4.8; $P = .04$) scores were better in the autograft group. The VAS score was similar between the 2 groups ($P = .4$). At the last follow-up, autografts demonstrated lower rate of revision surgery (OR, 7.2; $P < .0001$) and failure (OR, 5.1; $P < .0001$).

Conclusion: Based on the main findings of the present systematic review, talar osteochondral transplant using allografts was associated with higher rates of failure and revision compared with autografts at midterm follow-up.

Keywords: talus; osteochondral defect; osteochondral transplant; OAT; allograft; autograft

Osteochondral lesions of the talus are common.⁵⁰ Given the avascular and hypocellular nature of articular cartilage, the management of talar osteochondral lesions is challenging.^{15,49} Several surgical procedures have been described.^{57,66} Smaller defects up to 1.5 cm^2 can be treated arthroscopically using the microfractures technique.^{4,52,74} For larger defects, osteochondral transplant has been commonly used.^{16,69} Osteochondral transplant can be performed using single or multiple plugs (mosaicplasty).^{13,68} Indications for osteochondral transplant are full-thickness

symptomatic defects of 1 cm^2 up to approximately 4 cm^2 .^{23,24} Both osteochondral allografts and autografts can be used.^{39,47} Common donor sites for autologous osteochondral plugs are the anterosuperior condyle region and the lateral aspect of the intercondylar notch of the ipsilateral femur.⁶⁸ The use of allografts avoids donor site morbidity.^{9,76} Several clinical studies have evaluated the outcomes of autografts and allografts.** Whether osteochondral transplant using autografts performs better than that using allografts has not been fully clarified. The present study updates current evidence concerning the use of allografts and autografts for osteochondral transplant in talar



osteocondral defects at midterm follow-up. A systematic review of the literature was conducted to compare allografts versus autografts in terms of patient-reported outcome measures (PROMs), MRI findings, and complications.

METHODS

Search Strategy

This study was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.⁵¹ The PICO algorithm was as follows:

- P (Problem): talus osteochondral defects
- I (Intervention): osteochondral transplant
- C (Comparison): autograft versus allograft
- O (Outcomes): clinical scores, MRI findings, and complications

Data Source

The literature search was conducted in February 2021. Two independent authors (F.M. and H.S.) accessed the main online databases: PubMed, Google Scholar, Embase, and Scopus. The following keywords were used in combination: *talus, ankle, chondral, cartilage, articular, osteochondral, damage, defect, injury, chondropathy, pain, autologous, allograft, autograft, transplantation, therapy, management, surgery, outcomes, failure, revision, reoperation, recurrence*. The same reviewers selected the articles of interest and accessed the full-text. The bibliographies were also checked. Disagreements were solved by a third author (N.M.).

Eligibility Criteria

All studies investigating the surgical outcomes of allograft and/or autograft osteochondral transplant as management for osteochondral defects of the talus were accessed. Given the authors' language capabilities, articles in English, German, Italian, French, and Spanish were considered. Studies with level of evidence 1 to 4, according to the Oxford Centre for Evidence-Based Medicine,³⁷ were eligible. Registries, letters, abstracts, reviews, editorials, and opinions were not considered. Animal, computational, biomechanics, and in vitro studies were excluded. Studies augmenting autologous matrix-induced chondrogenesis (AMIC) or

matrix-induced autologous chondrocyte implantation (mACI) with less committed cells (eg, mesenchymal stem cells) were not considered. Studies reporting data on patients with end-stage joint osteoarthritis were not considered. Missing data under the outcomes of interest warranted exclusion from this study.

Data Extraction

Two authors (F.M. and H.S.) separately performed data extraction. Study generalities (author, year, journal, study design) and length of follow-up were retrieved. Baseline patient data were collected: length of symptoms before intervention, number of procedures, mean body mass index (BMI), mean age, sex, and mean defect size. Further, data concerning the following scores were retrieved: visual analog scale (VAS) for pain, American Orthopaedic Foot and Ankle Society (AOFAS),⁷⁵ and Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART).⁴⁸ Rate of failures and revision surgeries were also collected.

Methodological Quality Assessment

The methodological quality assessment was performed by 2 independent authors (F.M. and H.S.). The risk of bias graph tool of the Review Manager Software (The Nordic Cochrane Collaboration) was used. Selection, detection, attrition, reporting, and other sources of bias were considered for evaluation.

Statistical Analysis

The statistical analyses were performed by the main author (F.M.) using the IBM SPSS Version 25 program. Continuous data were reported as mean difference (MD), whereas binary variables were reported using the odds ratio (OR) effect measure. The confidence interval (CI) was set at 95%. We performed *t* tests and χ^2 tests for continuous and binary data, respectively, with $P < .05$ considered statistically significant.

The meta-analyses were performed using Editorial Manager Software Version 5.3 (The Nordic Cochrane Collaboration). Dichotomous data were analyzed through the Mantel-Haenszel method and OR effect measure. The CI was set at 95% in all comparisons. A fixed model effect was set as default. If moderate or high heterogeneity was detected, a random model effect was adopted. Heterogeneity was evaluated through Higgins I^2 and χ^2 tests. Values

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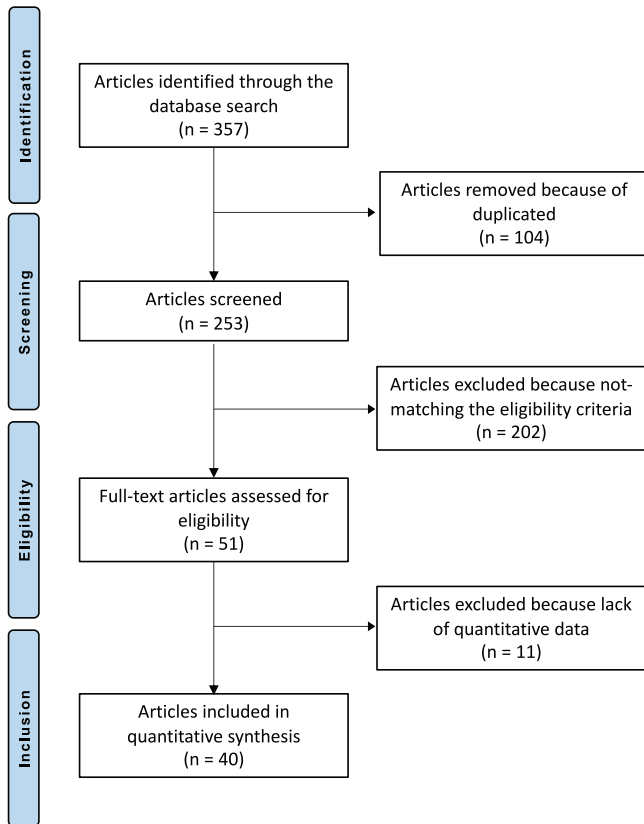


Figure 1. Flow chart of the literature search.

of Higgins I^2 were interpreted as low (<30%), moderate (30%-60%), and high (>60%). Values of $P > .05$ were considered statistically significant.

RESULTS

Search Result

The literature search resulted in 357 articles. Of them, 104 were duplicates. A further 213 articles were excluded because of incompatibility with the inclusion criteria: not matching the topic (n = 139), not focusing on the talus

(n = 17), study design (n = 21), not reporting quantitative data under the outcomes of interest (n = 11), augmented with other cells (n = 7), reporting data on patients with end-stage joint degeneration (n = 5), language limitations (n = 1), and other (n = 12). This left 40 articles for the present study: 35 retrospective and 4 prospective studies and 1 randomized clinical trial. The literature search results are shown in Figure 1.

Methodological Quality Assessment

Given the retrospective design of 85% (35/40) of the included studies, the risk of selection bias was moderate-high. Given the overall lack of blinding, detection bias was high. The risk of attrition and reporting bias among all included studies was moderate, as was the risk of other bias. The overall quality of the methodological assessment was fair. The risk of bias graph is shown in Figure 2.

Patient Characteristics

Data from 1174 procedures, with a mean follow-up of 46.5 ± 25 months, were retrieved. Study generalities and patient characteristics are shown in Table 1. There was no difference at baseline between the allograft and autograft groups (Table 2) concerning the duration of symptoms before surgery ($P = .05$), length of follow-up ($P = .6$), male to female ratio ($P = .5$), mean age ($P = .4$), mean BMI ($P = .1$), defect size ($P = .6$), VAS score ($P = .8$), and AOFAS score ($P = .1$).

Outcomes of Interest

At last follow-up, the autograft group had higher MOCART scores (MD, 10.5; $P = .04$). Similarly, the AOFAS score was higher in the autograft group (MD, 4.8; $P = .04$). The VAS score was similar between the 2 groups ($P = .4$) (Table 3).

Complications

The autograft group demonstrated lower rates of revision surgery (OR, 7.2; $P < .0001$) and failure (OR, 5.1; $P < .0001$) (Table 4).

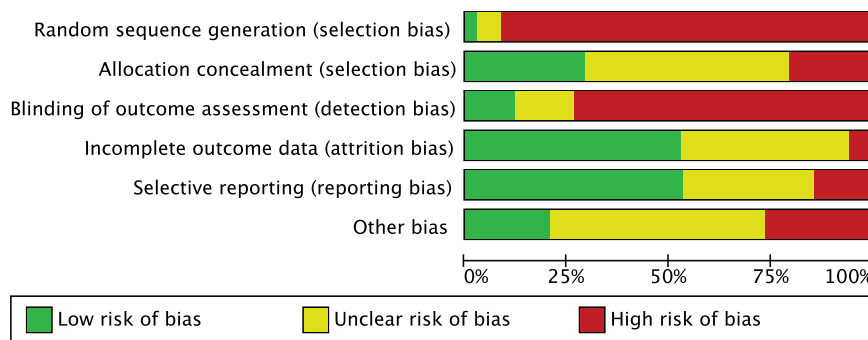


Figure 2. Methodological quality assessment.

TABLE 1
Generalities and Descriptions of the Included Studies^a

Lead Author (Year)	Journal	Design	Follow-up, mo	Treatment	Procedures	Female, %	Mean Age, y
Adams ² (2011)	<i>J Bone Joint Surg Am</i>	Retrospective	48	Osteochondral allograft transplant	8	62.5	31.4
Adams ¹ (2018)	<i>Foot Ankle Int</i>	Prospective	55.0	Osteochondral allograft transplant	14	42.9	40.0
Ahmad ³ (2016)	<i>Foot Ankle Int</i>	Randomized	40.5	Osteochondral allograft transplant	16	37.5	39.7
			35.2	Osteochondral autograft transplant	20	45.0	41.3
El-Rashidy ¹² (2011)	<i>J Bone Joint Surg Am</i>	Retrospective	37.7	Osteochondral allograft transplant	38	42.1	44.2
Emre ¹³ (2012)	<i>J Foot Ankle Surg</i>	Retrospective	16.8	Mosaicplasty	32	9.4	27.5
de l'Escalopier ¹⁰ (2015)	<i>Orthop Traumatol Surg Res</i>	Retrospective	76.0	Mosaicplasty	37	33.0	21.6
Fraser ¹⁶ (2016)	<i>Knee Surg Sports Traumatol Arthrosc</i>	Retrospective	70.8	Osteochondral autograft transplant	36	33.3	31.0
Gaul ¹⁹ (2019)	<i>Foot Ankle Int</i>	Retrospective	116.4	Osteochondral allograft transplant	20	47.0	34.7
Gaul ¹⁸ (2018)	<i>Foot Ankle Int</i>	Retrospective	123.6	Osteochondral allograft transplant	20	55.0	43.6
Gautier ²⁰ (2002)	<i>J Bone Joint Surg Br</i>	Retrospective	24.0	Osteochondral autograft transplant	11	66.5	32.0
Georgiannos ²¹ (2016)	<i>Knee Surg Sports Traumatol Arthrosc</i>	Retrospective	66	Osteochondral autograft transplant	48	19.5	36
Gobbi ²² (2006)	<i>Arthroscopy</i>	Prospective	53.0	Control group	10	40.0	24.0
				Control group	11	45.5	32.0
				Osteochondral autograft transplant	12	33.3	27.8
Gül ²⁸ (2016)	<i>J Foot Ankle Surg</i>	Retrospective	30.5	Osteochondral autograft transplant	15	33.3	32.6
			28.9	Osteochondral autograft transplant	13	8.3	36.7
Guney ²⁹ (2016)	<i>Knee Surg Sports Traumatol Arthrosc</i>	Prospective	47.3	Control group	19	37.4	47.4
			40.4	Control group	22	43.9	50.0
			30.1	Mosaicplasty	13	37.6	15.4
Haleem ³³ (2014)	<i>Am J Sports Med</i>	Retrospective	93.0	Osteochondral autograft transplant	14	50.0	42.8
			85.3	Osteochondral autograft transplant	28	39.3	44.1
Haasper ³⁰ (2008)	<i>Arch Orthop Trauma Surg</i>	Retrospective	24.0	Mosaicplasty	14	57.1	24.8
Hahn ³² (2010)	<i>Foot Ankle Int</i>	Retrospective	47.9	Osteochondral allograft transplant	13	61.5	30.4
Hangody ³⁴ (1997)	<i>Foot Ankle Int</i>	Retrospective	19.0	Mosaicplasty	11	NR	25.1
Hangody ³⁵ (2001)	<i>Foot Ankle Int</i>	Retrospective	50.4	Mosaicplasty	36	NR	27.0
Imhoff ³⁸ (2011)	<i>Am J Sports Med</i>	Retrospective	84.0	Osteochondral autograft transplant	26	46.2	33.0
Jackson ³⁹ (2019)	<i>J Foot Ankle Surg</i>	Retrospective	21.0	Osteochondral allograft transplant	31	9.7	33.6
Kreuz ⁴² (2006)	<i>Am J Sports Med</i>	Retrospective	48.9	Mosaicplasty	35	48.6	30.9
Lee ⁴⁴ (2003)	<i>Foot Ankle Int</i>	Retrospective	36.0	Mosaicplasty	18	5.6	22.7
Li ⁴⁵ (2017)	<i>BMC Musculoskelet Disord</i>	Retrospective	21.2	Osteochondral autograft transplant	11	63.6	55.4
Liu ⁴⁶ (2011)	<i>Foot Ankle Int</i>	Prospective	36.3	Osteochondral autograft transplant	16	37.5	33.9
Liu ⁴⁷ (2020)	<i>Foot Ankle Int</i>	Retrospective	18.0	Osteochondral autograft transplant	14	21.4	29.6
Nguyen ⁵⁵ (2019)	<i>Am J Sports Med</i>	Retrospective	44.7	Osteochondral autograft transplant	38	0.0	26.0
Orr ⁵⁶ (2017)	<i>Foot Ankle Spec</i>	Retrospective	28.5	Osteochondral allograft transplant	8	0.0	34.4
Park ⁵⁸ (2018)	<i>Am J Sports Med</i>	Retrospective	71.4	Osteochondral autograft transplant	18	41.6	NR
				Osteochondral autograft transplant	28	41.6	NR
Park ⁵⁷ (2020)	<i>Bone Joint J</i>	Retrospective	22.0	Osteochondral allograft transplant	25	40.0	19.6
Paul ⁵⁹ (2012)	<i>Am J Sports Med</i>	Retrospective	60.0	Osteochondral autograft transplant	131	38.2	31.0
Ross ⁶⁴ (2016)	<i>Arthroscopy</i>	Retrospective	51.0	Osteochondral autograft transplant	76	34.2	35.8
Sabaghzadeh ⁶⁵ (2020)	<i>Chin J Traumatol</i>	Retrospective	19	Mosaicplasty	19	42.1	43.0
Sadik ⁶⁶ (2017)	<i>Foot Ankle Surg</i>	Retrospective	46.4	Osteochondral autologous transposition	10	40.0	37.0
Shimozono ⁶⁹ (2018)	<i>Am J Sports Med</i>	Retrospective	52.0	Osteochondral autograft transplant	63	42.9	36.0
			45.0	Osteochondral autograft transplant	31	32.3	34.0
Shimozono ⁷⁰ (2018)	<i>J Bone Joint Surg Am</i>	Retrospective	26.3	Osteochondral autograft transplant	25	64.0	38.4
			22.3	Osteochondral allograft transplant	16	37.5	43.6
Woelfle ⁷⁷ (2013)	<i>Knee Surg Sports Traumatol Arthrosc</i>	Retrospective	29.0	Osteochondral autograft transplant	32	24.5	46.9
Yoon ⁷⁸ (2014)	<i>Am J Sports Med</i>	Retrospective	45.0	Osteochondral autograft transplant	22	31.8	37.1
			50.0	Control group	22	18.2	41.6
Zhu ⁷⁹ (2016)	<i>Foot Ankle Int</i>	Retrospective	25.4	Osteochondral autograft and cancellous allograft transfer	12	38.5	40.5

^aNR, not reported.

Meta-analysis

Two comparative studies including 77 patients were included in the meta-analysis.^{3,70} We noted statistically significant lower rates of revision surgery (OR, 12.0; $P = .02$) and failure (OR, 13.8; $P = .004$) in the autograft group. The forest plots are shown in Figure 3.

DISCUSSION

According to the main findings of the present study, osteochondral transplant for osteochondral defects of the talus

using autografts or allograft evidenced similar VAS and AOFAS scores at midterm follow-up. However, given the lower rates of failure and revision, autografts should be preferred during primary surgeries for osteochondral defects of the talus. The primary use of allograft should probably be reserved for patients who do not have a suitable donor site.

Osteochondral autograft transplant has been used for small to medium-sized defects of the talus, with a rate of satisfaction up to 95% for primary procedures.^{41,67} Osteochondral autograft transplant has been used in revision settings as well, with considerable improvement of AOFAS and VAS scores.^{42,78} Allografts show a higher rate of

TABLE 2
Characteristics of the 2 Cohorts at Baseline^a

	Allograft	Autograft	MD	P
Procedures, n	219	955		
Follow-up, mo	50.8 ± 34.3	46.0 ± 21.6	4.7	.6
Duration of symptoms, mo	54.3 ± 39.5	21.9 ± 16.8	32.4	.05
Female, %	39.6 ± 18.5	36.1 ± 16.3	3.5	.5
Mean age, y	36.0 ± 7.0	33.5 ± 8.3	2.5	.4
Body mass index	27.9 ± 2.4	25.0 ± 1.4	1.9	.1
Defect size, cm ²	1.8 ± 0.8	2.6 ± 4.3	-0.9	.6
VAS score	6.9 ± 0.9	6.7 ± 0.9	0.1	.8
AOFAS score	58.8 ± 13.8	51.5 ± 9.1	7.3	.1
Lesion site, % (n/N)				
Medial	72.9 (102/140)	72.4 (417/576)		
Central	1.4 (2/140)	0.5 (3/576)		
Lateral	25.7 (36/140)	27.1 (156/576)		

^aValues for allograft and autograft are expressed as mean ± SD unless otherwise noted. AOFAS, American Orthopaedic Foot and Ankle Society; MD, mean difference; VAS, visual analog scale.

TABLE 3
Results of VAS, MOCART, and AOFAS Scores^a

Score	Allograft	Autograft	MD	P
VAS	2.3 ± 1.3	2.5 ± 1.3	0.2	.4
MOCART	72.5 ± 4.2	83.0 ± 8.7	10.5	.04
AOFAS	81.6 ± 6.0	86.4 ± 5.6	4.8	.04

^aAOFAS, American Orthopaedic Foot and Ankle Society; MD, mean difference; MOCART, Magnetic Resonance Observation of Cartilage Repair Tissue; VAS, visual analog scale.

TABLE 4
Results of Complications

Endpoint	Allograft, % (n/N)	Autograft, % (n/N)	OR	95% CI	P
Revision	44.9 (58/129)	10.2 (50/490)	7.19	4.5665-11.3167	<.0001
Failure	14.7 (24/163)	3.3 (16/490)	5.08	2.6263-9.8367	<.0001

failure and higher costs, greater risk of disease transmission, and limited availability, whereas the autologous techniques can entail donor site morbidity.¹⁴ The effect of donor site morbidity on outcomes has not been fully clarified. Considering low-weightbearing, dimensional properties and surface curvature, only 3 harvest sites are available within the knee: the lateral side of the intercondylar notch, the superomedial trochlea, and the superolateral trochlea.^{27,36,63} In a systematic review by Bexkens et al⁷ that included 190 patients, the rate of donor site morbidity was 7.8% (10/128 patients). Of those patients, 7% (9/128 patients) reported knee pain during activity and 0.8% (1/128 patients) reported locking episodes. Shimozono et al,⁷¹ in a meta-analysis of 24 studies (915 procedures), estimated the rate of donor site morbidity to be from 6.7% to 10.8%. Nakagawa et al⁵³ investigated the clinical outcomes of donor sites in the knee after osteochondral autograft transplant. Those investigators found that 34 of

40 patients (85%) were asymptomatic at a mean follow-up of 43.1 months.

Despite the encouraging results with autografts, the use of allografts has become more prevalent to avoid donor site morbidity. Studies have shown that allografts achieve similar clinical outcomes as autografts and avoid donor site morbidity but have a greater rate of revision and failure.^{12,26} Two studies compared allografts versus autografts for osteochondral defects of the talus. Ahmad et al³ conducted a prospective study comparing 16 autograft procedures with grafts from the ipsilateral femoral condyle versus 20 fresh size-matched allografts; the mean VAS scores improved similarly in both groups. Shimozono et al⁷⁰ retrospectively evaluated 25 patients treated with autografts versus 16 patients treated with allografts for talar defects and found that AOFAS and MOCART scores were better in the autograft group. Both of these studies found higher rates of failure and revision surgery in the allograft group.

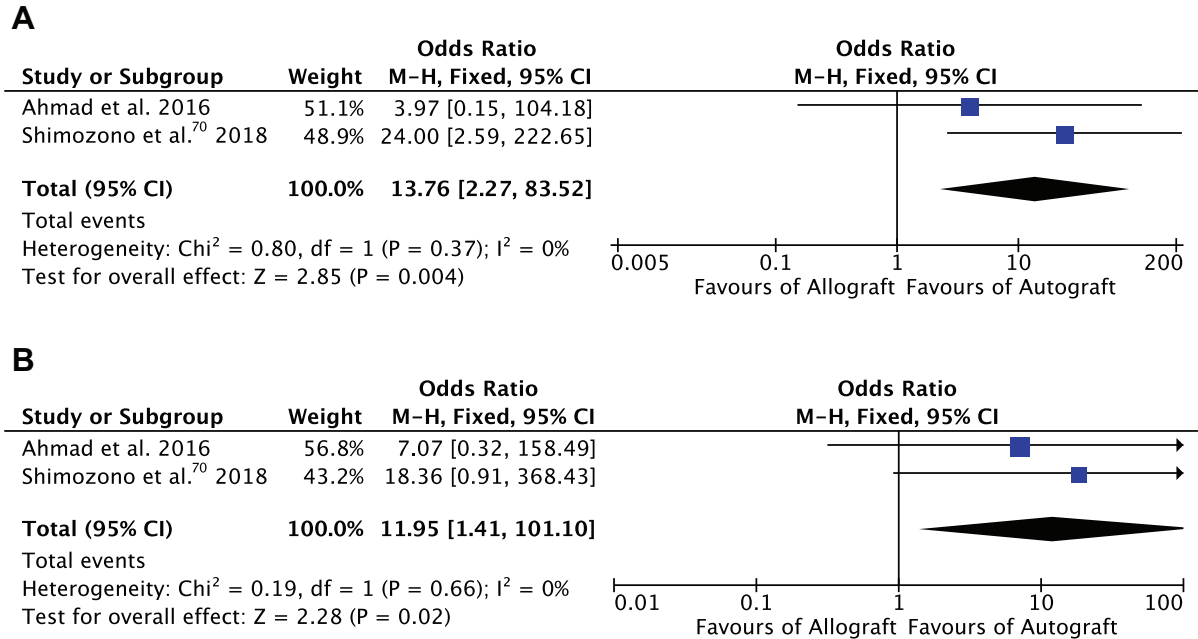


Figure 3. Forest plots of the comparison: (A) failures and (B) revision surgeries.

The present study found a rate of failure of 14.7% (24/163 patients). This finding agrees with previous evidence of failure rates between 12% and 30%. Ahmad et al³ found that 18.8% of allografts did not heal properly as shown on computed tomography scans or plain radiographs after 6 months. Gross et al²⁶ reported fragmentation and resorption of the allograft in one-third of patients (3/9). Haene et al³¹ evaluated the failure rate of allografts in 16 patients at 48 months of follow-up. Those investigators evidenced failure in graft incorporation in 13% (2/16), osteolysis in 31% (5/16), and cysts in 50% (8/16) of patients at 4 years.

The higher rate of failure in allografts may derive from immune-mediated mechanisms.⁵⁴ Immune responses similar to those implicated in allogeneic organ transplant rejections have been documented in human and animal osteochondral allograft transplant.^{17,60,72,73} Sirlin et al⁷² demonstrated that 31% (11/36) of patients who underwent allograft implantation in the knee presented anti-human antibody. These patients had a statistically significant greater rate of edema, thicker interface, abnormal graft marrow, and surface collapse.⁷² Pomajzl et al⁶¹ demonstrated a substantial loss of sulfated glycosaminoglycans and osteocalcin in the graft-host interface, along with a high osteoclast activity. They further demonstrated the presence of T-helper, T-cytotoxic, and NK cells. Moreover, Pomajzl et al demonstrated the presence of tumor necrosis factor α throughout the allograft. These features discourage the use of osteochondral allograft transplant. If a suitable harvest site is unavailable, other techniques can be used, such as AMIC, mACI, and matrix-induced stem cell transplant (mAST); these are feasible and reliable options that exploit the regenerative potential of autologous tissue.^{5,6,8,25,62} Particulated juvenile articular cartilage (PJAC) transplant has been also used to manage osteochondral defects of the talus. However, given its limited

evidence and controversial results, PJAC was not included in this analysis.^{11,40,43}

This study has some limitations. The analyses were performed regardless of the surgical approach (arthroscopy, mini-arthrotomy, arthrotomy). Furthermore, the limited number of included articles and procedures may have negatively affected our results. The retrospective design of most of the studies represents an important limitation; however, the current literature lacks high-quality studies, and further investigations are required. Furthermore, given the lack of studies directly comparing the 2 types of graft, the meta-analysis collected data from only 2 trials.^{3,70} Thus, even if no heterogeneity was detected, the reliability of the results is questionable. Most authors did not clarify the type of allograft used and did not specify its provenance or any additional procedures (eg, sterilization) before transplant. Given the lack of data, primary and revision surgeries were often mixed, and some authors combined the surgeries with other procedures. This may have influenced the results, increasing the risk of selection bias. Given the lack of data, the analyses were performed regardless of the cause of the defect or the talar location of the defect (eg, medial vs lateral). Thus, our results must be interpreted within the limitations of the present investigation. Future studies are required to overcome these limitations.

CONCLUSION

Based on the main findings of the present systematic review, talar osteochondral transplant using allografts was associated with higher rates of failure and revision compared with autografts at midterm follow-up. However,

given the limited published data, the strength of the conclusions is weak and further high-quality comparative studies are required.

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