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The role of autologous bone grafting in matrix-associated autologous chondrocyte implantation at the knee: Results from the German Cartilage Registry (KnorpelRegister DGOU)

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Abstract

Purpose: To investigate whether concomitant autologous bone grafting adversely affects clinical outcome and graft survival after matrix-associated autologous chondrocyte implantation (M-ACI).

Methods: The present study examines registry data of patients who underwent M-ACI with or without autologous bone grafting for large-sized chondral or osteochondral defects. Propensity score matching was performed to exclude potential confounders. A total of 215 patients with similar baseline characteristics were identified. Clinical outcome was assessed at the time of surgery and at 6, 12, 24, 36 and 60 months using the Knee Injury and Osteoarthritis Outcome Score (KOOS). KOOS change, clinical response rate, KOOS subcomponents and failure rate were determined.

Results: Patients treated with M-ACI and autologous bone grafting achieved comparable clinical outcomes compared with M-ACI alone. At 24 months postoperatively, the patient-reported outcome (PRO) of patients treated with M-ACI and autologous bone grafting was even significantly better as measured by KOOS (74.9 ± 18.8 vs. 79.2 ± 15.4; $p = 0.043$). However, the difference did not exceed the minimal clinically important difference (MCID). In patients with M-ACI and autologous bone grafting, a greater change in KOOS relative to baseline was observed at 6 (9.3 ± 14.7 vs. 15.0 ± 14.7; $p = 0.004$) and 12 months (12.6 ± 17.2 vs. 17.7 ± 14.6; $p = 0.035$). Overall, a high clinical response rate was observed in both groups at 24 months (75.8% vs. 82.0%; p = n.s.). The estimated survival at the endpoint of reoperation for any reason was 82.1% (SD 2.8) at 8.4 years for isolated M-ACI and 88.7% (SD 2.4) at 8.2 years for M-ACI with autologous bone grafting ($p = 0.039$).

Abbreviations: ABG, autologous bone grafting; ADL, activities of daily living; BMI, body mass index; CR, cartilage regeneration; FT, femorotibial; FU, follow-up; ICRS, International Cartilage Regeneration & Joint Preservation Society; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCID, minimal clinically important difference; MOCART, Magnetic Resonance Observation of Cartilage Repair Tissue; MRI, magnetic resonance imaging; OCA, osteochondral allograft; OCT, osteochondral transplantation; PASS, Patient Acceptable Symptomatic State; PF, patellofemoral; PRO(M), patient-reported outcome (measure); PSM, propensity score matching; QOL, quality of life; SD, standard deviation; VAS, Visual Analog Scale; (M-)ACI, (matrix-associated) autologous chondrocyte implantation.

Conclusions: Even in the challenging cohort of large osteochondral defects, the additional treatment with autologous bone grafting leads to remarkably good clinical outcomes in patients treated with M-ACI. In fact, they tend to benefit more from surgery, have lower revision rates and achieve clinical response rates earlier. Subchondral bone management is critical to the success of M-ACI and should be addressed in the treatment of borderline defects.

Level of Evidence: Level III.

KEYWORDS

ACI, autologous bone grafting, cartilage, knee, osteochondral defects, registry

INTRODUCTION

Focal cartilage damage in the knee is common, with a prevalence of up to 60% in adults. Its socioeconomic impact makes it an important public health issue [39]. Several treatment options are available, depending on the size of the defect and national differences in the availability of treatments. Symptomatic and unstable osteochondral defects with large defect size and depth are particularly challenging to treat. The subchondral bone and articular cartilage work closely together as part of the osteochondral unit. Osteochondral defects account for around 5% of focal cartilage damage and are usually trauma-related, degenerative or the result of osteochondritis dissecans [17, 26]. The osteochondral unit is thought to play an important role in articular cartilage regeneration (CR) and has been the focus of recent research [34].

As young, active patients are often affected by osteochondral defects, reconstruction of the osteochondral unit is required to prevent the early development of osteoarthritis [15]. Osteochondral transplantation (OCT) is an established procedure for smaller osteochondral defects [10, 11]. However, little is known about treatment alternatives and long-term outcomes for large and deep osteochondral defects. Refixation of large osteochondritis dissecans lesions has been associated with poor clinical outcomes and progression of osteoarthritis [20]. The good results in 80%–90% of patients at 10 years after osteochondral allograft (OCA) transplantation are compromised by limited graft availability, the risk of graft-related failure and procedure-related disease transmission [35, 36]. Cell-free implants to reconstruct the osteochondral unit improve clinical outcomes, but are associated with significant rates of degradation or delayed regeneration on magnetic resonance imaging (MRI) [6, 16].

Autologous chondrocyte implantation for large isolated cartilage defects is widely used because of its regenerative potential, with good to excellent results [7, 16, 25]. Combined with autologous bone grafting (ABG, bone augmentation), this technique can also be used to treat large, deep osteochondral defects [24]. For large osteochondral defects, primary techniques using autologous iliac crest or autologous cancellous cylinder combined with M-ACI are available [26, 40].

Initial data from a small cohort show good osteointegration, chondral regeneration and long-term survival for the combination of ABG and M-ACI [21]. However, it remains unknown whether the treatment of subchondral bone affects the cartilage regenerative potential and the patient-reported outcome (PRO) of M-ACI in a representative cohort. A recently published MRI-based study demonstrated a negative association between subchondral bone involvement and pain in patients undergoing M-ACI and ABG [14]. The extent to which the size of the bone defect and potential epidemiologic or clinical factors influence the outcome of M-ACI with concomitant ABG is still unknown.

Therefore, the aim of the proposed study was to investigate the influence of concomitant ABG on outcome after M-ACI using a matched-pairs comparison in patients with unipolar cartilage lesions.

MATERIALS AND METHODS

Prior to patient enrolment, approval was obtained from the Institutional Review Board (EK-FR 105/13_130795) of the University of Freiburg. The present study used data from the German Cartilage Registry (KnorpelRegister DGOU), an observational multicentre registry with a focus on patients undergoing CR for knee problems [19]. The registry is registered at germanctr.de (DRKS00005617) and adheres to the principles of the Declaration of Helsinki. Board-certified orthopaedic surgeons were responsible for evaluating participants when enroled in the registry. At the time of cartilage biopsy, informed written consent was obtained. Subsequently, at 6, 12, 24, 36 and 60 months postoperatively, patients were automatically contacted by e-mail to complete a patient-reported outcome measure (PROM) questionnaire [38].

A registry-based, propensity score-matched analysis of patients undergoing CR for unifocal chondral

lesions in the knee was conducted. Propensity score matching (PSM) was used to exclude certain patient-related characteristics as potential confounders and thus achieve greater comparability and homogeneity of the cohorts by adjusting for covariates that may affect the outcome of patients with unifocal chondral defects treated with M-ACI and ABG or M-ACI alone.

Patients with unifocal cartilage lesions and intact meniscal status treated with either M-ACI and ABG or M-ACI alone were included in this study. Exclusion criteria involved patients with concomitant procedures such as ligament reconstruction, meniscal repair and osteotomy (Figure 1). Patients were stratified into two treatment groups based on the procedure they received.

Data collection

To examine differences in characteristics between patients who underwent M-ACI and ABG or M-ACI alone, patient demographic and clinical data were collected, including age, sex, body mass index (BMI), smoking status, symptom duration, lesion location, lesion size, lesion aetiology, symptom duration, International Cartilage Regeneration & Joint Preservation Society (ICRS) grade, number of previous knee surgeries and time to reoperation (Table 1). Patients with osteochondral defects treated with M-ACI and additional ABG were younger, had a lower BMI, had larger defect sizes and were less likely to be traumatic but more likely to be degenerative due to other causes (e.g., osteonecrosis).

Outcome measures

Clinical outcome was primarily assessed using the Knee Injury and Osteoarthritis Outcome Score (KOOS) and was recorded at the time of surgery and at 6, 12, 24, 36 and 60 months postoperatively [32]. First, we reported the KOOS and the change in KOOS (ΔKOOS) over time in the matched groups. Subsequently, the KOOS subgroups and their change from preoperative values (ΔKOOS-Subgroup) were calculated and compared between the groups at different time points [3]. The recently published Patient Acceptable Symptomatic State (PASS) for the KOOS subscores and the minimal clinically important difference (MCID) were used to evaluate the KOOS and ΔKOOS subgroups respectively, at 12 and 24 months [5, 27]. The clinical response rate, defined as the percentage of patients achieving the MCID, was also calculated as a secondary outcome measure. The MCID for the overall KOOS was set at 10 based on recent literature and is consistent with previous recommendations [8, 27]. Failure rates and time to failure were also analysed. CR failure was defined as any type of reoperation within the follow-up period.

Statistical analysis

A 1:1 nearest neighbour PSM with replacement was performed to reduce bias from potential confounders of clinical outcome. Patients with M-ACI and ABG or M-ACI alone were then matched by PSM for age, sex, BMI, symptom duration, smoking status, previous knee surgery, lesion localization, lesion size and ICRS grading of the chondral defect. Priority was given to exact matching without minimization of memory and with shuffling enabled. The matching tolerance was set at 0.001 to obtain groups with similar baseline characteristics. This resulted in two groups of 215 subjects each with comparable baseline characteristics.

A χ^2 test was used to compare categorical variables between the two groups (sex, smoking status, defect location, previous knee surgery and ICRS grade). Continuous variables were analysed using unpaired *t* tests. For variance heterogeneity in the Levene test, the Welch test was used. *p* values of <0.05 were considered statistically significant. There was no need for Bonferroni correction for multiple testing.

Kaplan–Meier survival analysis was used to estimate the mean time to failure in each group. If revision surgery was not required, the time of the last follow-up was used. Statistical tests were performed using SPSS version 27.0 (IBM) and G-Power 3.1 (Heinrich Heine Universität).

To determine the validity of our findings, we performed a post hoc power analysis. With an estimated effect size of $\omega = 0.302$, an available patient number of $n = 178$ at 24 months postoperatively and an α of 0.05, the calculated statistical power to detect an underlying difference in KOOS was 64.1%. With an estimated effect size of $\omega = 0.171$, an available patient population of $n = 147$ at 36 months postoperatively and an α of 0.05, the calculated statistical power to detect an underlying difference in KOOS was 27.1%. This indicates a power issue when comparing the groups at 36 and 60 months.

RESULTS

Of the 1527 patients who met the inclusion and exclusion criteria, 215 were matched for similar baseline characteristics, resulting in a homogeneous cohort (Table 2).

Overall outcome

Patients requiring additional ABG had a worse initial clinical status as measured by KOOS at baseline (62.4 ± 16.7 vs. 59.2 ± 16.2; *p* = (n.s.)) than patients without significant bone involvement. Postoperatively, this trend changed in favour of the

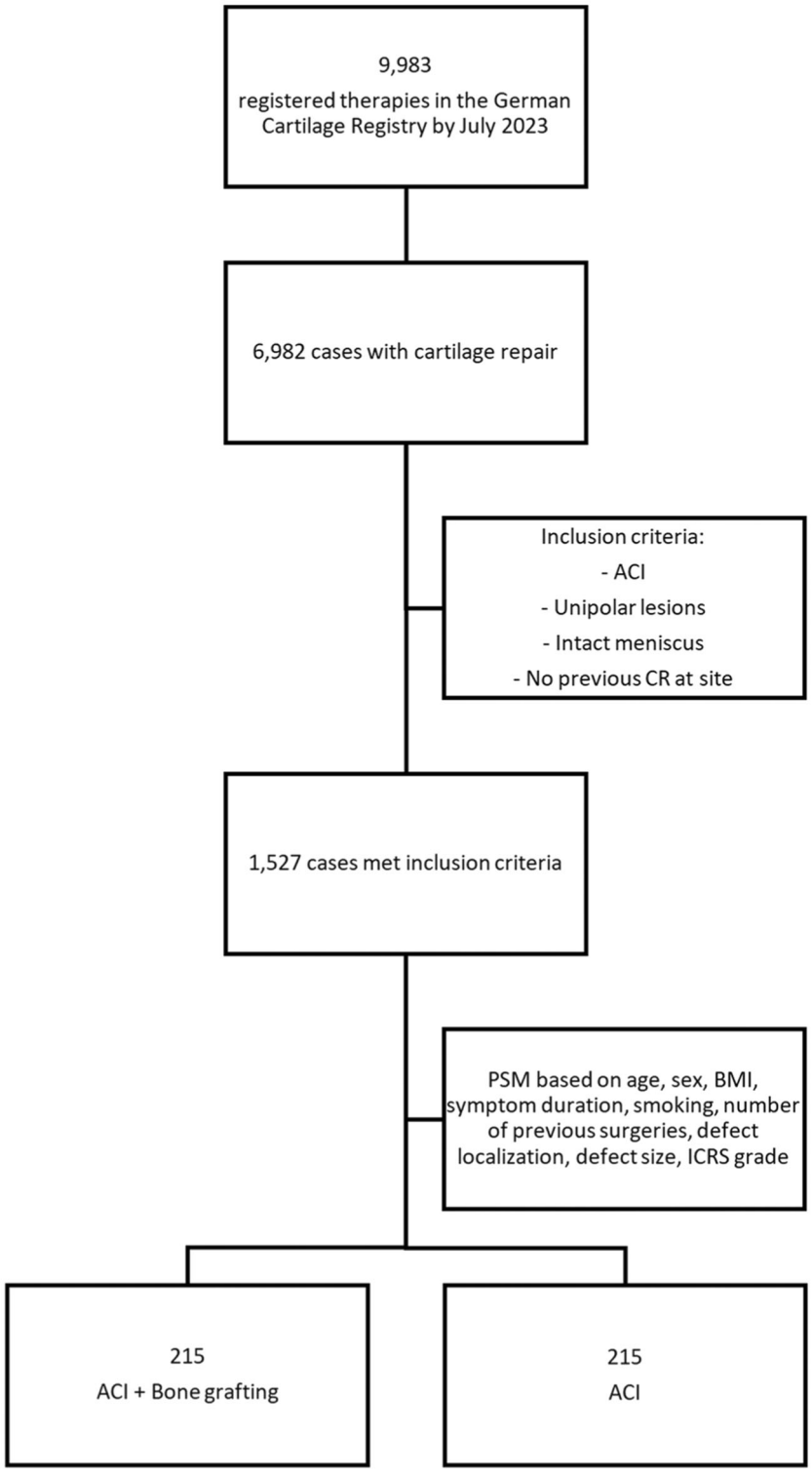

FIGURE 1 Flowchart visualizing patient selection and matching. ACI, autologous chondrocyte implantation; BMI, body mass index; CR, cartilage repair; ICRS, International Cartilage Regeneration & Joint Preservation Society; PSM, propensity score matching.

additional ABG-treated patients and peaked at 24 months (Table 3 and Figure 2).

This trend was also reflected in significant differences in ΔKOOS between the two groups at 6 and 12 months postoperatively (Table 4). The superiority in ΔKOOS in favour of patients treated with combined M-ACI and ABG also persisted at 24, 36 and 60 months, although it did not reach significance. Overall, a high clinical response rate was observed in both groups at 12 (53.9% vs. 74.7%; $p = 0.002$) and 24 months (75.8% vs. 82.0%; $p = (n.s.)$).

TABLE 1 Baseline demographic characteristics of patients with M-ACI treatment prior matching ($n = 1527$).

No. of patients	Total 1527	ACI & ABG 321	ACI 1206	*p* Value
Age, years	32.3 (10.5)	28.3 (9.5)	33.4 (10.5)	<0.0001[a]
Sex, %				
M	60.6	63.3	59.9	(n.s.)
F	39.4	36.7	40.1	
BMI (kg/m²)	25.8 (4.2)	25.1 (4.0)	25.9 (4.3)	0.002[a]
Smoker, %				
Y	22.5	24.2	22.1	(n.s.)
N	77.5	75.8	77.9	
Symptom duration, m.	24.6 (64.3)	25.8 (64.3)	24.3 (64.3)	(n.s.)
Defect size, cm²	4.35 (2.0)	4.57 (2.26)	4.29 (1.92)	0.029[a]
Genesis, %				<0.0001[a]
Traumatic	26.9	10.3	31.3	
Degenerative	41.1	32.2	43.5	
Post-traumatic	17.9	12.8	19.3	
Other	14.1	44.7	5.9	
ICRS, %				<0.0001[a]
I	0	0	0	
II	0	0	0	
III	33.8	6.9	40.9	
IV	66.3	93.1	59.1	

Note: Mean (SD).

Abbreviations: ABG, autologous bone grafting; ACI, autologous chondrocyte implantation; BMI, body mass index; ICRS, International Cartilage Regeneration & Joint Preservation Society.

[a]Significance.

Differences in the KOOS subcomponent analysis indicate that patients with additional ABG benefit particularly in terms of symptom improvement (72.9 [18.7] vs. 78.5 [15.9]) and pain reduction (76.6 [19.3] vs. 82.6 [15.4]) at 24 months (Table 5). The differences in KOOS subscores at 12 and 24 months are visualized in Figure 3 and plotted against PASS as a reference parameter.

Differences in ΔKOOS subscores were also determined for all follow-ups. Differences in ΔKOOS mainly concern pain (10.1 [16.5] vs. 15.7 [18.6] at 6 months and 12.0 [19.6] vs. 18.6 [16.6] at 12 months), activities of daily living (8. 9 [15.2] vs. 14.5 [17.9] at 6 months and 11.0 [17.8] vs. 17.3 [19.8] at 12 months) and QOL (16.1 [22.7] vs. 23.0 [21.3] at 6 months; Table 6). The differences in ΔKOOS subscores at 12 and 24 months are also visualized in Figure 4 and related to the respective MCID.

Reoperation rate and time to reoperation

In the present cohort, a total of 56 reoperations were performed, 35 (16.2%) in patients with isolated M-ACI and 21 (9.8%) in patients with combined M-ACI and ABG ($p = 0.045$). There was no difference in time to reoperation (1.6 ± 1.3 vs. 2.1 ± 1.7 years; $p = $ (n.s.)). Estimated survival to the endpoint of reoperation for any reason was 82.1% (SD 2.8) at 8.4 years for isolated M-ACI and 88.7% (SD 2.4) at 8.2 years for M-ACI and concomitant ABG ($p = 0.039$, $\chi^2 = 4.3$; Figure 5).

DISCUSSION

The main finding of this study is that matched patients treated with combined M-ACI and ABG for osteochondral defects have comparable outcomes to those treated with M-ACI for chondral defects in the knee. In fact, they tend to benefit more from surgery and tend to have lower revision rates. PASS is widely achieved in both groups [5]. The clinical response rate of patients receiving combined treatment is achieved earlier [27].

M-ACI is a safe procedure for large chondral defects in the knee, leads to improved clinical outcomes and has a positive impact on the progression of osteoarthritis [1, 7, 15, 22, 25, 30]. Functional outcome, subjective satisfaction, reoperation and clinical failure rates are comparable when treating chondral defects with M-ACI or OCAs [31]. In the treatment of large chondral defects with bone involvement, OCA achieves excellent functional results in long-term follow-up with survival rates of 95% at 5 years and 93% at 10 years [4, 33]. In this context, a potential advantage of OCA over M-ACI with ABG for the treatment of large osteochondral defects has been repeatedly mentioned in the literature [12, 23]. Accordingly, M-ACI should be considered as an alternative, although less effective, when subchondral changes are present [12]. The combination of M-ACI and ABG is the standard treatment for large osteochondral defects due to the limited availability of OCA in Europe. In addition, OCAs carry the risk of graft-versus-host reactions, disease transmission and potential graft failure over time [2].

However, more recent studies also show good results for the combination of ABG and M-ACI in both clinical and radiological follow-up [13, 21, 40]. However, the results of these studies are limited by their small sample sizes and lack of control groups. Zellner and colleagues demonstrated significant improvements in International Knee Documentation Committee (IKDC)

TABLE 2 Baseline demographic characteristics of M-ACI patients with or without concomitant autologous bone grafting ($n = 430$).

No. of patients	ACI 215				ACI & ABG 215				*p* Value
Age, y	29.8 (9.8)				30.1 (9.7)				(n.s.)
Sex, %									
M	65.1								(n.s.)
F	34.9								
BMI (kg/m²)	25.8 (4.4)				25.3 (4.0)				(n.s.)
Symptom duration, m.	25.1 (36.8)				29.0 (75.7)				(n.s.)
Defect size, cm²	4.5 (2.5)				4.6 (2.4)				(n.s.)
Localization, %	FT		PF		FT		PF		(n.s.)
	149		66		166		49		
ICRS grade	III		IV		III		IV		(n.s.)
	18		197		20		195		
Previous knee surgeries	0	1	2	≥3	0	1	2	≥3	(n.s.)
	84	77	34	19	92	82	25	16	

Note: Mean (SD).

Abbreviations: ABG, autologous bone grafting; ACI, autologous chondrocyte implantation; BMI, body mass index; FT, femorotibial; ICRS, International Cartilage Regeneration & Joint Preservation Society; PF, patellofemoral.

TABLE 3 Comparison of the mean KOOS Scores at the various FUs of the matched cohort.

	Total *n* (ACI/ ACI&ABG)	ACI	ACI & ABG	*p* Value
Baseline	266 (141/125)	62.4 (16.7)	59.2 (16.2)	(n.s.)
6 months	241 (123/118)	70.6 (18.2)	73.0 (16.0)	(n.s.)
12 months	195 (95/100)	75.0 (18.4)	77.0 (14.5)	(n.s.)
24 months	178 (88/90)	74.9 (18.8)	79.2 (15.4)	0.043[a]
36 months	147 (74/73)	77.5 (18.4)	80.2 (18.0)	(n.s.)
60 months	104 (55/49)	79.3 (16.6)	79.9 (17.1)	(n.s.)

Note: Mean (SD).

Abbreviations: ABG, autologous bone grafting; ACI, autologous chondrocyte implantation; FU, follow-up; KOOS, Knee Injury and Osteoarthritis Outcome Score.

[a]Significance.

scores, Cincinnati scores and Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scores in patients with large and deep osteochondral defects over two years of follow-up [40]. IKDC-measured PASS was achieved at 1 year in the observed population [40]. This is consistent with the results of the present study where PASS is achieved after 6–12 months. In the present study, we were able to demonstrate in a large, controlled cohort a comparable clinical outcome with a low risk of reoperation for patients treated with M-ACI and ABG compared with patients treated with M-ACI alone. The combined treatment resulted in a good PRO and exceeded the PASS and MCID thresholds of the KOOS and ΔKOOS subscores, respectively. This finding is supported by Minas et al. In their controlled cohort study, they found a favourable survival rate of 87% 5 years after combined M-ACI and ABG versus ABG alone and a significant improvement in clinical outcome as measured by the modified Cincinnati Knee Score and VAS [21].

An interesting finding of the present study is certainly the dynamics in the improvement of clinically meaningful changes in outcome in patients with combined bone–cartilage treatment regarding symptoms, pain, sport, activities of daily living (ADL) and quality of life (QOL). Previously, good clinical outcomes, even if achieved, were attributed to prolonged rehabilitation after combined treatment [12]. Furthermore, it is noteworthy that despite the size and depth of the osteochondral defects, patients with additive ABG tend to have a more favourable clinical outcome compared to M-ACI alone, as measured by the KOOS score 1–2 years postoperatively. This hypothesis, which has previously been discussed in the literature but not yet supported with data from comparable, controlled study cohorts, has now been supported for the first time by the present study [18, 37]. This may be due to the adequate reconstruction of the biomechanically important subchondral layer in patients treated with M-ACI and ABG [9, 28]. However, the present study lacks MRI data to support this assumption. The subchondral layer plays an important role in

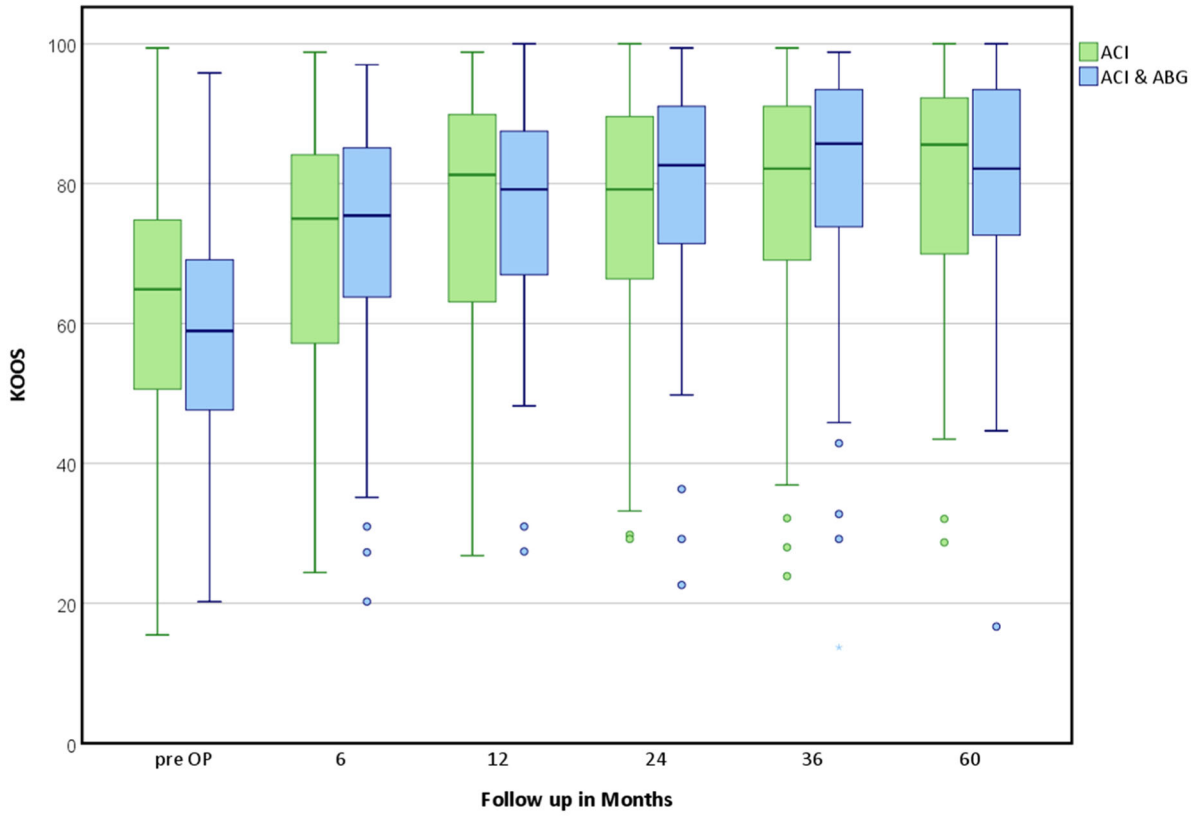

FIGURE 2 Differences in mean Knee Injury and Osteoarthritis Outcome Score (KOOS) Scores at various follow-ups (FUs) in the matched cohort.

TABLE 4 Comparison of mean ΔKOOS scores from baseline to the different FUs in the matched cohort.

	Total *n* (ACI/ ACI&ABG)	ACI	ACI & ABG	*p* Value
6 months	194 (106/88)	9.3 (14.7)	15.0 (14.7)	0.004[a]
12 months	156 (82/74)	12.6 (17.2)	17.7 (14.6)	0.035[a]
24 months	135 (72/63)	14.0 (18.3)	16.4 (15.6)	(n.s.)
36 months	115 (61/54)	14.9 (19.6)	19.9 (17.7)	(n.s.)
60 months	80 (44/36)	15.5 (17.5)	16.5 (17.8)	(n.s.)

Note: Mean (SD).

Abbreviations: ABG, autologous bone grafting; ACI, autologous chondrocyte implantation; KOOS, Knee Injury and Osteoarthritis Outcome Score.

[a]Significance.

TABLE 5 KOOS subcomponent analysis indicating significant differences between both groups ($p = 0.05$).

	Symptoms	Pain	ADL	Sports	QOL
Baseline	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)
6 months	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)
12 months	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)
24 months	0.034[a]	0.022[a]	(n.s.)	(n.s.)	(n.s.)
36 months	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)
60 months	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)

Note: *p* values.

Abbreviations: ADL, activities of daily living; KOOS, Knee Injury and Osteoarthritis Outcome Score; QOL, quality of life.

[a]Significance.

establishing graft nutrition and restructuring the subchondral plate, which allows M-ACI integration and healing [29]. It is known that subchondral bone is not only the cause of osteochondral pathology but also plays a fundamental role in CR [34].

The studied cohort of the present study is relatively large compared with other studies that have investigated the outcome of CR [21]. However, the power of the study is insufficient to reliably detect an underlying intergroup difference in clinical outcomes, especially after more than 2 years. The desired power of 80% was not achieved. It should also be noted that the ABG group also included ICRS grade III lesions. According to the ICRS articular cartilage injury classification, IIIC defects extend down to but not through the subchondral bone, which in fact does not necessarily require the addition of ABG to M-ACI as a therapy. Therefore, confusion with the ICRS OCD classification, mislabelling or other reasons for concomitant bone grafting may

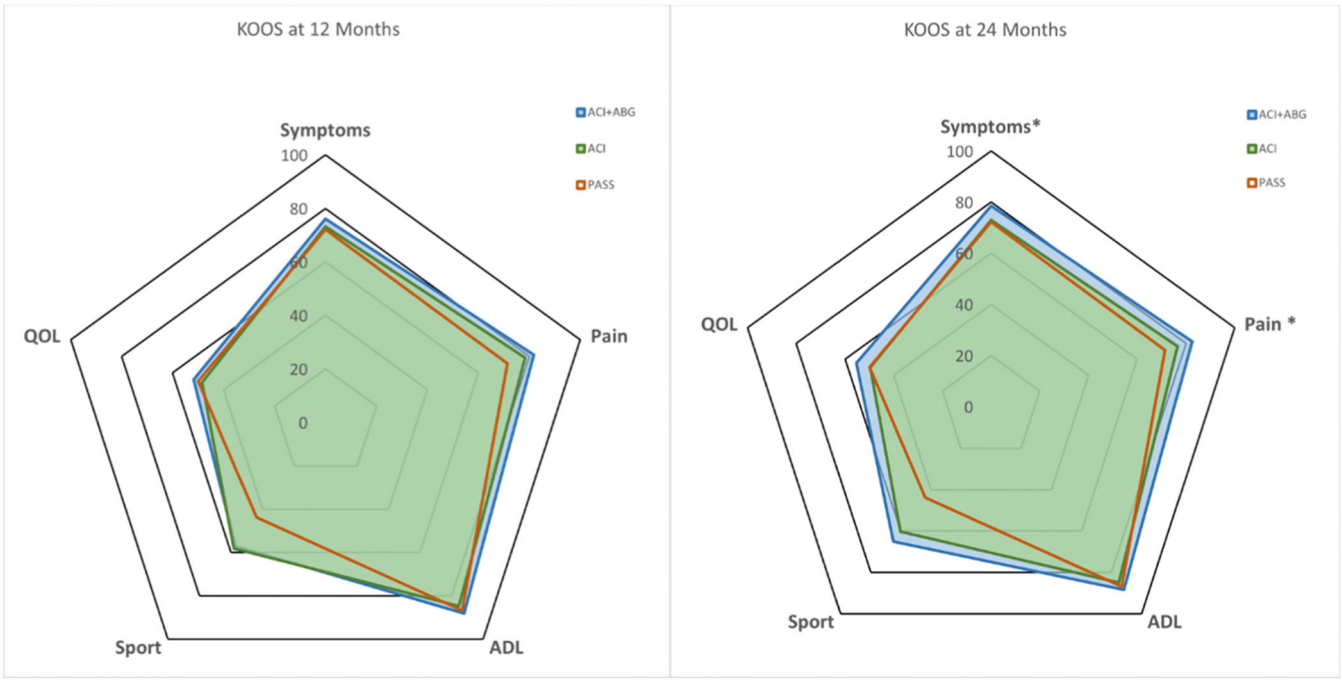

FIGURE 3 Differences in Knee Injury and Osteoarthritis Outcome Score (KOOS) subscores between the two groups at 12 and 24 months—plotted against PASS. * indicates significance; ABG, autologous bone grafting; ADL, activities of daily living; PASS, patient acceptable symptomatic state; QOL, quality of life.

TABLE 6 ΔKOOS subcomponent analysis indicating significant differences between both groups ($p = 0.05$).

	Symptoms	Pain	ADL	Sports	QOL
6 months	(n.s.)	0.023[a]	0.016[a]	(n.s.)	(n.s.)
12 months	(n.s.)	0.018[a]	0.026[a]	(n.s.)	0.040[a]
24 months	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)
36 months	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)
60 months	(n.s.)	(n.s.)	(n.s.)	(n.s.)	(n.s.)

Note: *p* values.

Abbreviations: ABG, autologous bone grafting; ADL, activities of daily living; KOOS, Knee Injury and Osteoarthritis Outcome Score; QOL, quality of life.

[a]Significance.

have occurred in these cases. Each of these is a potential source of bias in our matching. However, the number of patients with ICRS III lesions is very low at 8% of the matched ABG cohort. As one of nine matching factors in the PSM, it is a rather negligible confounder. Furthermore, this study was not able to compare the different ABG techniques accompanying CR with M-ACI due to structural limitations. The cartilage registry (KnorpelRegister DGOU) does not specify the procedure used to perform ABG. A comparison of combined M-ACI and ABG or OCA was not possible due to the low use of OCA in Europe and would have missed the study objective. The study was limited by comparing two different entities of chondral or osteochondral defects with their respective treatment techniques. In clinical practice, these are usually not competing, but complementary, stage-appropriate treatment options. Nevertheless, the data from this study help to demonstrate the clinical efficacy and safety of combined CR while providing insight into borderline defects.

In addition, the study population has insufficient baseline MRI data and no follow-up MRI data for analysis. This is unfortunate because it misses the opportunity to examine for the first time MRI data from a substantial cohort undergoing M-ACI and additional ABG [13, 14]. Recently, a correlation between subchondral bone parameters, cartilage MRI signal and outcome after CR has been suggested [14]. Thus, the good clinical results of the studied population suggest adequate bone and cartilage healing, even if this finding cannot be supported by MRI data.

The present study demonstrates the efficacy of combined M-ACI and ABG in the treatment of osteochondral lesions, achieving at least comparable clinical results to M-ACI in chondral defects. ABG ensures good graft healing and may therefore improve CR and clinical outcome even in cartilage defects with minor bone involvement or previous bone marrow stimulation. In these cases, the indication for additional bone grafting should be generously considered. The combination of M-ACI and ABG is a reliable alternative to OCA for the treatment of osteochondral defects not limited to regions with limited allograft availability.

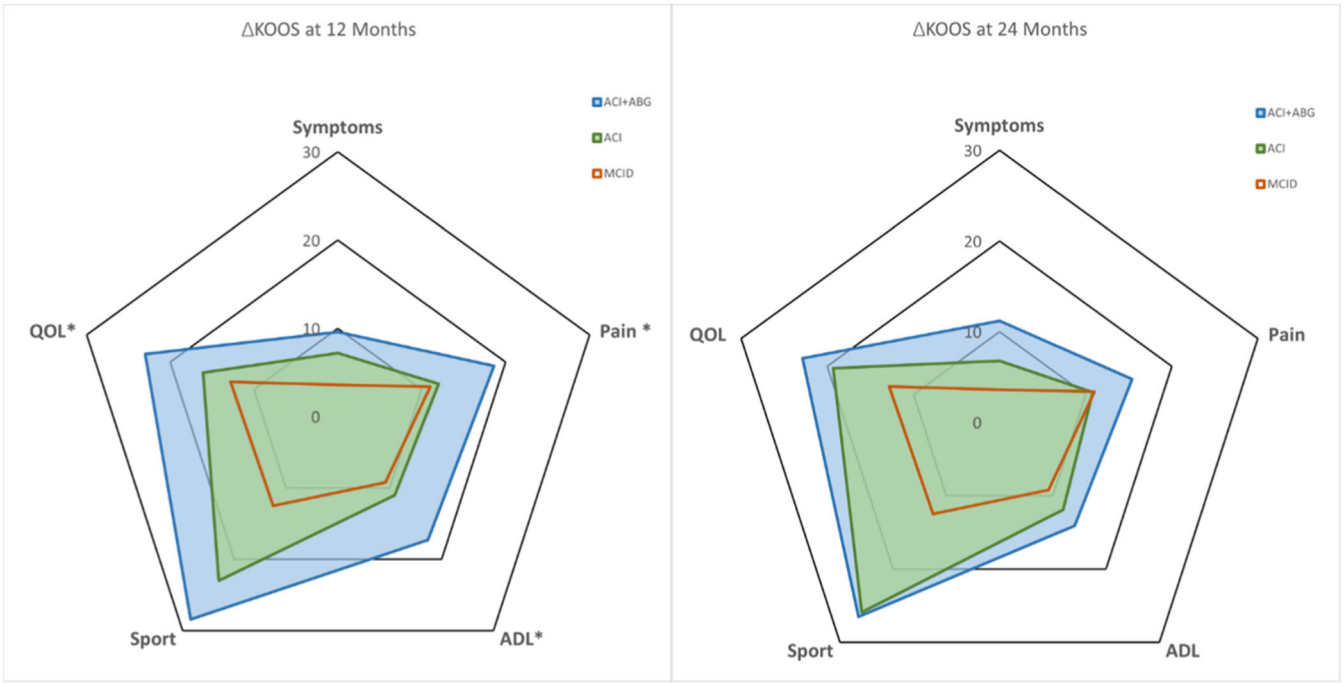

FIGURE 4 Differences in Knee Injury and Osteoarthritis Outcome Score (ΔKOOS) subscores between the two groups at 12 and 24 months—plotted against MCID. * indicates significance; ABG, autologous bone grafting; ADL, activities of daily living; MCID, minimal clinically important difference; QOL, quality of life.

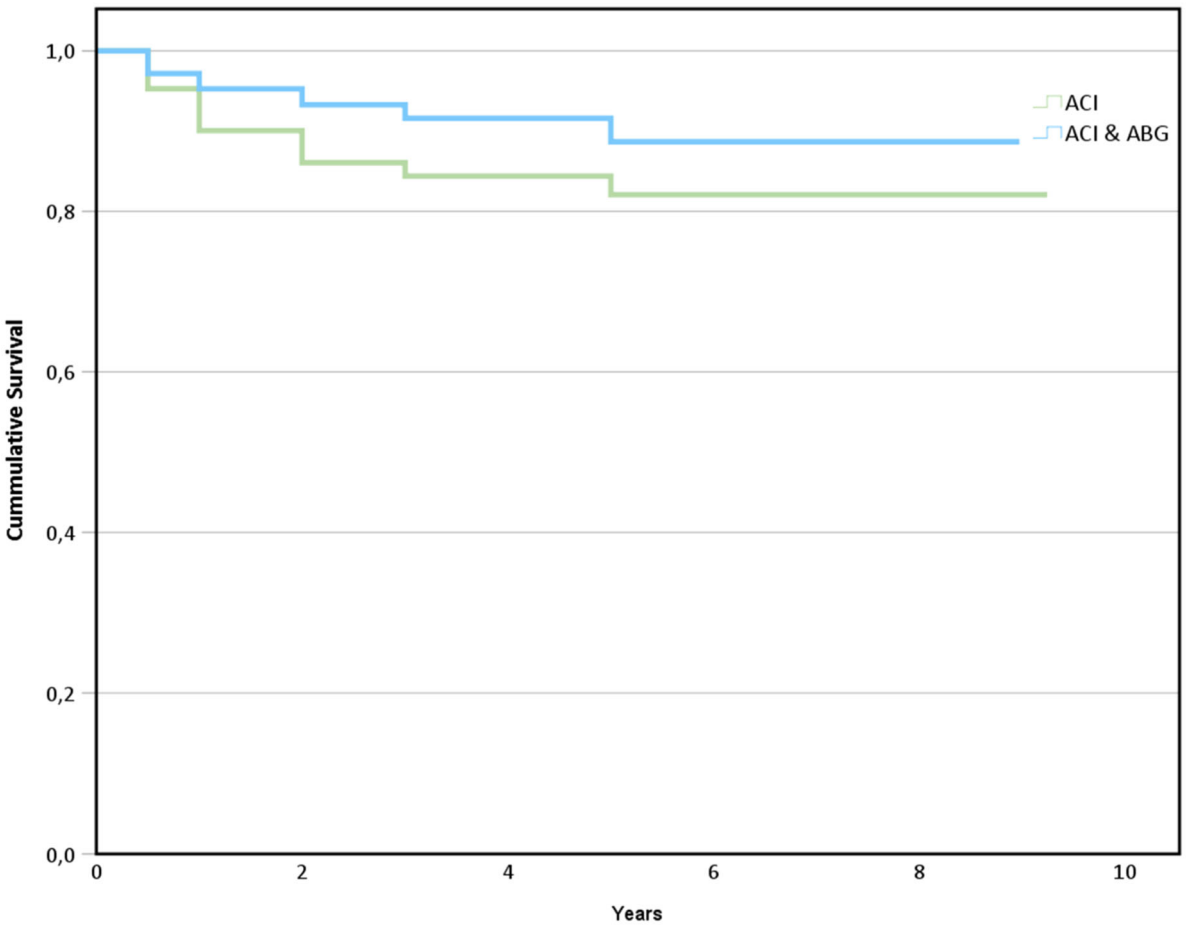

FIGURE 5 Kaplan–Meier Plot illustrating estimated survival at Revision for any reason.

CONCLUSION

Patients treated with combined M-ACI and ABG for osteochondral defects have comparable outcomes to those treated with M-ACI for chondral defects in the knee. In fact, they tend to benefit more from surgery, have lower revision rates and achieve clinical response rates earlier. Specifically, at 6 and 12 months, patients treated with the combined treatment showed greater benefits in terms of KOOS Pain, ADL and QOL. Subchondral bone management is critical to the success of M-ACI and should be addressed in the treatment of borderline defects.

AUTHOR CONTRIBUTIONS

Johannes Weishorn performed the data extraction and statistical analysis and drafted the manuscript. Philipp Niemeyer and Thomas Tischer were involved in reviewing and drafting the manuscript. Tobias Renkawitz critically reviewed and revised the manuscript. Yannic Bangert served as supervisor of the study and was involved in interpreting the statistical results and drafting the manuscript.

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CONFLICT OF INTEREST STATEMENT

Tobias Renkawitz declares the following conflicts of interest: Financial interests: Research funding at personal disposal: DePuy, Zimmer, Aesculap, German Federal Ministry of Education and Research, Deutsche Arthrose-Hilfe, OttoBock-Stiftung, German Federal Ministry of Economic and Development, Oskar-Helene-Heim Foundation in Berlin, Vielberth Foundation, Deutsche Forschungsgemeinschaft (DFG). Reimbursement of costs: DePuy, Zimmer, Aesculap, Federal Ministry of Education and Research, Deutsche Arthrose-Hilfe, OttoBock-Stiftung, Federal Ministry for Economic Co-operation and Cooperation and Development, Oskar-Helene-Heim Foundation in Berlin, Vielberth Foundation, DGOOC, BVOU, DGOU. - Reimbursement of costs for training/lectures: DePuy, Zimmer, Aesculap, German Society for Endoprosthetics (AE), Bavarian Association of General Practitioners. Philipp Niemeyer is an independent consultant for Arthrex, Stryker, Geistlich and Tetec. The remaining authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data will be available upon reasonable request.

ETHICS STATEMENT

The current study was approved by the Ethics Commission of the Medical Center, University of Freiburg: EK-FR 105/13_130795. Written informed consent was obtained from every patient before inclusion.

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