Does Prior Cartilage Restoration Impact Outcomes Following Knee Arthroplasty?

Rachel M. Frank, MD*, Craig J. Della Valle, MD,
Darren R. Plummer, MD, MBA, Peter N. Chalmers, MD,
Brian J. Cole, MD, MBA

KEYWORDS

• Cartilage restoration • Meniscus transplantation • Knee joint preservation • Arthroplasty

KEY POINTS

- When compared with matched control subjects, patients undergoing arthroplasty after prior cartilage/meniscal restoration have significantly less pain relief, lower functional outcomes, and less improvement following partial or total knee arthroplasty.
- Patients undergoing arthroplasty after prior cartilage/meniscal restoration have significantly less severe arthritic findings on radiographs as measured by the Kellegren and Lawrence grade compared with matched control subjects.
- In this study, patients who underwent arthroplasty after failed prior cartilage/meniscal restoration did not experience symptom relief after cartilage/meniscal restoration, which is atypical of the typical patient undergoing cartilage/meniscal restoration.

INTRODUCTION

Injuries to the articular cartilage of the knee are seen in up to 63% of arthroscopies.[1,2] Articular cartilage defects do not reliably heal and can lead to degenerative joint disease,[3–5] ultimately resulting in significant pain and disability.[6–10] The optimal treatment strategy for these defects, one that provides the highest likelihood of a painless return to activity, remains unknown.[6–10] In particular, young, active patients with symptomatic articular cartilage defects are challenging, because arthroplasty may lead to wear-related complications and a need for multiple revisions over an individual's lifetime[11] and hence articular cartilage and meniscal restoration procedures are being performed with increasing frequency.[12–14]

Techniques including autologous chondrocyte implantation or variations thereof (Fig. 1), osteochondral autograft transfer, osteochondral allograft transplantation, and meniscus allograft transplantation (MAT) provide alternatives to arthroplasty to help improve function and reduce pain.[15–31] In some settings, both cartilage restoration and arthroplasty may be viable surgical alternatives for these patients. Given that patients' status-post cartilage restoration can be revised to arthroplasty and arthroplasty cannot be revised back to native cartilage, cartilage restoration has been advocated as a "conservative" surgical approach that does not "burn any bridges."[15–31] If cartilage restoration fails, patients may progress to knee arthroplasty, including total knee arthroplasty (TKA) and

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Department of Orthopaedic Surgery, Rush University Medical Center, 1611 West Harrison, Suite 300, Chicago, IL 60612, USA
* Corresponding author.
E-mail address: rmfrank3@gmail.com

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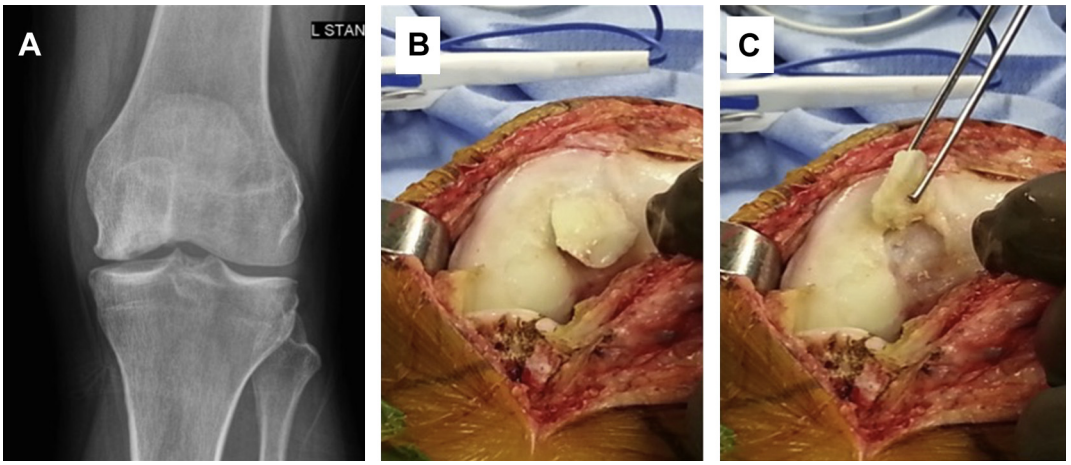

Fig. 1. A 39-year-old woman with continued left knee medial compartment pain after undergoing medial femoral condyle osteochondral allograft transplantation. (*A*) A 45° flexion weight-bearing posteroanterior radiograph demonstrating cystic changes of the left knee medial femoral condyle. (*B*, *C*) Osteochondral graft not healed at the time of unicompartmental knee arthroplasty, approximately 1.5 years following transplantation.

unicompartmental knee arthroplasty (UKA), as their definitive pain-relieving surgical solution. It remains unknown whether the outcome of knee arthroplasty after cartilage restoration is equivalent to the outcome had the knee arthroplasty been performed primarily.

To date, no data are available regarding clinical outcomes following conversion of a joint preservation procedure, such as cartilage/meniscal restoration, to TKA. Such information would be especially important with respect to preoperative counseling for patients related to the outcomes following arthroplasty procedures. Therefore, the purpose of this study was to compare the clinical outcomes of patients with a history of cartilage or meniscal restorative procedures with age-, sex-, and procedure-matched control patients undergoing primary TKA or UKA. The authors hypothesized that outcomes following primary TKA will be equivalent to those with TKA following cartilage and/or meniscus restoration.

METHODS

This study underwent approval by our university's institutional review board. A retrospective review of prospectively collected data on consecutive patients who underwent cartilage restoration by a single surgeon and subsequently progressed to arthroplasty was performed. Inclusion criteria included patients with a history of a prior open or arthroscopic cartilage and/or meniscal restoration procedure and subsequent ipsilateral UKA or TKA. The cartilage/meniscal restoration procedures included osteochondral autograft transfer, osteochondral allograft transplantation, and/or MAT of the same condyle and joint. All cartilage patients were matched with control patients based on sex, age ± 5 years, body mass index (BMI) ± 5, smoking status, and arthroplasty type. All patients in both the cartilage and the control groups were followed for a minimum of 2 years. Exclusion criteria in the cartilage group included patients whose cartilage/meniscal procedure was complicated by infection or chondrolysis as a complication of the index cartilage procedure and patients undergoing revision cartilage/meniscal restoration.

In the cartilage group, indications for cartilage/meniscal restoration versus primary knee arthroplasty included symptomatic, unipolar, full-thickness articular cartilage lesions and/or symptomatic meniscal deficiency not amenable to repair, in patients without diffuse arthritic changes in the affected compartment. Patients were also required to be ligamentously stable (or correctable) with neutral (or correctable) coronal plane alignment. In the cartilage group and the control groups, indications for arthroplasty were symptomatic medial or lateral tibiofemoral pain (UKA) or diffuse symptomatic bicompartmental or tricompartmental degenerative changes (TKA), unresponsive to prior treatment. In addition, indications for UKA included intact cruciate ligament status, lack of patellofemoral arthritis greater than grade III or IV on radiographs, lack of coronal plane deformity greater than 5°, and lack of knee flexion contracture

greater than 5°. All patients in both groups underwent preoperative physical therapy.

Data collected for all patients included age, sex, laterality, comorbidities, preoperative and final follow-up Knee Society Score (KSS),[32–34] Quality of Life Short-Form-12 score, Hospital for Special Surgery scores, and range of motion (ROM). Prearthroplasty radiographs were graded according to the Kellgren and Lawrence scale.[35] In addition, the cartilage patients were assessed pre–cartilage procedure and post–cartilage procedure (prearthroplasty) with the following outcomes assessments: Tegner, Lysholm, International Knee Documentation Committee (IKDC), and Knee Injury and Osteoarthritis Outcome Score (KOOS) for pain. The control patients were not analyzed with the Tegner, Lysholm, IKDC, or KOOS scores because these outcomes instruments are not used in the preoperative or postoperative assessment of patients undergoing primary knee arthroplasty for osteoarthritis.

Statistical Analysis

All analyses were performed in Excel X (Microsoft Inc, Redmond, WA) and SPSS version 21 (IBM Inc, Armonk, NY). Categorical data were compared between study and control groups using chi-square and Fisher exact tests as appropriate. For continuous variables Komolgorov-Smirnov testing was performed. To compare between study and control groups Student *t* tests and Mann-Whitney *U* tests were performed as appropriate. Within study and control groups preoperative and postoperative data were compared using paired Student *t* tests and related-samples Wilcoxon signed rank tests as appropriate. Because a limited number of patients are available who have undergone both cartilage restoration and knee arthroplasty on the same knee, all eligible patients were included and no *a priori* power analysis was conducted. A post hoc power analysis was performed; based on the means and standard deviations for the difference in preoperative and postoperative KSS the effect size was 1.67. With this study size the study's power was found to be 98%.

RESULTS

A total of 26 patients were included, with 13 patients (eight TKA and five UKA) in each group. The average clinical follow-up was 3.7 years (range, 2.0–7.2 years). There were no significant differences in age, sex, BMI, smoking status, worker's compensation status, preoperative physical therapy participation, preoperative ROM, postoperative ROM, or preoperative KSS scores between groups ($P > .05$ in all cases), suggesting adequate matching (Table 1). There were no intraoperative or postoperative complications, and there were no differences in tourniquet time between the cartilage and control groups (average of 82 vs 90 minutes, respectively; $P = .08$).

Before arthroplasty, the patients in the cartilage group underwent the following cartilage/meniscal restoration procedures: medial femoral condyle osteochondral allograft (n = 8), medial femoral condyle osteochondral allograft with corrective osteotomy (n = 1), MAT with anterior cruciate ligament reconstruction (n = 1), MAT with corrective osteotomy (n = 2), and patella osteochondral allograft with corrective osteotomy (n = 1). For the 10 patients with focal chondral lesions, the average defect size was

Table 1
Demographic data in the control group and the group status-post cartilage reconstruction

	Control Group	Cartilage Group	*P* Value
Age, y	44 ± 5	42 ± 6	.567
BMI	32 ± 7	31 ± 6	.576
Length of follow-up, y	3.3 ± 1.5	4 ± 1.7	.239
Time from cartilage restoration to arthroplasty, y	N/A	2.6 ± 1.8	N/A
Female, %	46	46	1.000
Smokers, %	15	15	1.000
Worker's compensation, %	23	38	.673
Arthroplasty type	5 UKA, 8 TKA	5 UKA, 8 TKA	N/A
Tourniquet time, min	90 ± 13	81 ± 10	.08

Data are displayed as means ± standard deviation.
Abbreviation: N/A, not applicable.

331 ± 204 mm^2 (range, 100–625 mm^2). Before cartilage/meniscal restoration, patients had undergone an average 2 ± 2 prior surgeries (range, 1–7 surgeries) on the ipsilateral knee, including diagnostic arthroscopy, arthroscopic chondroplasty, arthroscopic partial meniscectomy, medial collateral ligament reconstruction, anterior cruciate ligament reconstruction, tibial plateau open reduction internal fixation, and medial patellofemoral ligament imbrication. Following cartilage/meniscal restoration, all patients underwent a standardized rehabilitation protocol at the direction of the senior author, including 6 to 8 weeks of protected weightbearing, physical therapy, and return to full activities by 4 to 6 months following surgery. The duration of time between the cartilage/meniscal restoration procedure and the arthroplasty averaged 2.6 ± 1.8 years (range, 7.8 months to 7.7 years).

In the cartilage group, there were no significant differences in precartilage scores to postcartilage (prearthroplasty) scores for any of the outcomes assessments. Specifically, there were no postcartilage restoration improvements in the Tegner (2.4 ± 2.4–2.3 ± 0.8; P = .729), Lysholm (30.8 ± 17.1–38.2 ± 20.0; P = .474), IKDC (26.4 ± 10.3–33.0 ± 10.3; P = .847), or KOOS-pain (41.7 ± 19.4–59.0 ± 19.9; P = .672) scores.

Patients in the cartilage group had a significantly lower prearthroplasty (postcartilage) Kellgren and Lawrence grade (average, 2.6 ± 0.9) compared with matched control subjects (average, 3.7 ± 0.5; P = .004).

Patients in the cartilage group had significantly lower postoperative KSS scores (78 ± 13 vs 91 ± 5; P = .005) (Table 2) and experienced significantly less improvement in KSS scores (30 ± 10 vs 46 ± 10; P<.001). Two patients (15%) in the cartilage group required revision TKA at 1.9 years (for pain) and 4.7 years (for infection) following the index TKA. There were no reoperations in the control group.

DISCUSSION

Given the rise in the number of cartilage and meniscal restorative procedures being performed, it is important to understand the potential impact that these procedures may have on a subsequent arthroplasty. Our results suggest, that when compared with matched control subjects, patients undergoing arthroplasty after prior cartilage/meniscal restoration have significantly less pain relief, lower functional outcomes, and less improvement following UKA or TKA.

Patients undergoing cartilage and/or meniscal restoration procedures are difficult to treat. These patients are young, have high expectations, and have high activity levels. However, the surgical options for these patients are often salvage procedures, aimed at improving function for activities of daily living and relieving pain. Thus, the durability of joint preservation procedures may be limited. Arthroplasty is usually considered an option of last resort given the higher rates of complications and lower survivability of arthroplasty in young patients.[11,36–39] A recent study by Aggarwal and colleagues[11] compared 84 patients aged 50 years or younger with a sex- and BMI-matched cohort consisting of 84 patients aged 60 to 70 years (average, 62 years). Within the younger cohort revision TKA survivorship at 6 years was disappointingly low at 71%. Within this study, arthroplasty failure was more commonly attributed to aseptic loosening in the younger cohort and more commonly attributed to infection in the older cohort. The authors attributed these findings to younger patients being healthier and having a higher likelihood of subjecting their implants to higher levels of activities and loads. In the present study, we attempted to control for patient age to identify other potential risk factors for poor outcomes by matching both groups based on age, such that the average age for all patients (including the cartilage and the control groups) was 42 years, similar to the cohort in the Aggarwal study.[11]

Prior studies have suggested that, in general, prior knee surgery results in inferior outcomes following arthroplasty. Recently, Piedade and colleagues[40] reported on outcomes, complications, and failures in patients undergoing TKA after having undergone prior knee surgery (bone and soft tissue) compared with patients undergoing primary TKA alone (n = 1119). Prior procedures in the surgery group included bone procedures (n = 85), such as high tibial osteotomy, patellar realignment, and/or tibial plateau fracture surgery, and soft tissue procedures (n = 146), including arthroscopy and meniscectomy. At a minimum follow-up of 2 years, the authors reported worse postoperative flexion in the bone procedure group and a significantly increased complication rate in the soft tissue group, but an overall similar survivorship (and thus revision rate) in all three groups. In a separate study, the same group[41] reported in greater detail on the outcomes of the arthroscopy group (n = 60). Specifically, the authors reported a 30% local complication rate in the

Table 2
Outcome data in the control group and the group status-post cartilage reconstruction

	Control Group (n = 13)			Cartilage Group (n = 13)			Preoperative	Postoperative
	Preoperative	Postoperative	*P* Value	Preoperative	Postoperative	*P* Value	*P* Value	*P* Value
Range of motion	110 ± 17	119 ± 10	.074	116 ± 17	117 ± 15	.872	.431	.703
Knee Society Score	45 ± 10	91 ± 5	<.001	48 ± 8	78 ± 13	<.001	.304	.005
Knee Society Score - Functional	47 ± 10	91 ± 6	<.001	50 ± 8	76 ± 20	<.001	.396	.016
Revised, %	N/A	0.00	N/A	N/A	15	N/A	N/A	N/A
With a complication, %	N/A	0.00	N/A	N/A	15	N/A	N/A	N/A

Data are displayed as means ± standard deviation.
Abbreviation: N/A, not applicable.

arthroscopy group, with 8.3% of those cases requiring revision TKA. Together, these reports indicate increased complications, but not necessarily worse overall clinical outcomes, in patients undergoing TKA after undergoing previous knee surgery. However, in these studies,[40,41] arthroplasty survivorship did not seem to be impacted by prior surgery. Longer follow-up is necessary to see if prior cartilage restoration impacts knee arthroplasty survivorship. To date, only a single study has analyzed outcomes in patients undergoing TKA after prior osteochondral allograft transplantation. In their cohort of 35 knees in 35 patients with an average age of 63 years, Morag and colleagues[42] reported improvements in KSS scores following arthroplasty at an average 92-month follow-up in 18 patients (KSS 45 preoperatively, KSS 82 postoperatively). Similar to the revision rate noted in our study, Morag and colleagues[42] described revision arthroplasty in six patients (17%) for aseptic loosening, with two revisions performed within 2 years following the index arthroplasty.

An important difference between the two groups of patients was that the control group had more severe disease preoperatively as measured by the Kellegren and Lawrence grade of their prearthroplasty radiographs. Other authors have shown a correlation between the severity of preoperative arthritis and final outcome following TKA.[43–45] Riis and colleagues[43] conducted a prospective study of 176 undergoing TKA and found that a low radiologic severity of osteoarthritis was associated with an inferior level of function ($P = .007$), but was not associated with pain. In a separate study, Dowsey and colleagues[45] evaluated 478 patients undergoing primary TKA and found that patients with a lower radiologic severity of arthritis at the time of arthroplasty were significantly more likely to report poor function and had significantly higher odds of postoperative moderate to severe pain ($P = .002$). Hence, it is important for surgeons to counsel patients preoperatively that the absence of full-thickness cartilage loss as seen on radiographs may be associated with a higher risk of dissatisfaction postoperatively.

Patients in the present study undergoing arthroplasty after prior cartilage/meniscal restoration still had significant improvements in KSS, despite lower preoperative Kellgren and Lawrence grades. In these patients, before arthroplasty, cartilage restoration did not improve functional outcomes, as evidenced by no clinical and statistical differences between preoperative and postoperative Tegner, Lysholm, IKDC, and KOOS outcome scores. This is not typical of most cartilage restoration patients, who more commonly experience significant statistical and clinical improvements in these outcomes measures following cartilage and/or meniscal restoration.[12,46–49] Together, these findings suggest that knee arthroplasty is an effective procedure in patients who fail cartilage restoration, but that expectations must be tempered from the almost uniformly excellent outcomes that are achieved with primary knee arthroplasty.

This study has several limitations, including its small sample size, retrospective case-control design, and short-term follow-up. Our observations are not synonymous with cartilage restoration procedures being the sole cause of worse outcomes following revision to arthroplasty. Although increasing in overall incidence, cartilage restoration procedures are infrequently performed and even more infrequently revised to a knee arthroplasty, and thus large studies of this patient population are difficult to perform. A post hoc power analysis (based on KSS scores) demonstrated that the study is currently powered to 98% because the difference in outcomes between the groups is so large. The case-control design also introduces the potential for unmeasured residual bias between groups even though no significant differences were found between the groups preoperatively. A single patient in the cartilage group underwent revision arthroplasty because of infection, whereas no patients in the control group sustained an infection, and thus some of the differences in outcomes (especially reoperation rate) may be attributable to this factor. Of note, a second control group of patients undergoing cartilage restoration but without progression to arthroplasty was not evaluated as part of this study. The information that would be provided by such a control group was not thought to be relevant to the goal of this study, which was to determine how outcomes following knee arthroplasty are impacted by history of prior cartilage restoration, and instead would simply allow for the comparison of successful and failed cartilage restoration patients, which has been previously analyzed in a variety of cartilage/meniscal restoration studies.[15–31] Another limitation to this study is the relatively short-term follow-up, and certainly a study of longer-duration follow-up is necessary to see if these results are maintained over time.

Finally, and perhaps most important, patients undergoing arthroplasty for osteoarthritis (control subjects) may represent a different patient

population compared with the patients undergoing arthroplasty for articular cartilage defects and thus the underlying diagnosis must be considered when extrapolating the results from this study to a specific patient. The purpose of this study was to determine whether the outcomes of arthroplasty performed for an indication of a failed cartilage procedure differ from the outcomes of arthroplasty performed for an indication of osteoarthritis. This information is useful prognostically and helps to guide knee arthroplasty expectations in patients with failed cartilage procedures. Underlying differences in preoperative indications, demographics, pathology, postoperative protocols, and numerous other factors likely play a role in outcomes determination, and thus the findings of this study cannot be used to determine whether cartilage restoration or arthroplasty provides superior outcomes for similar pathology. Notably, no patients in the control group underwent prior ipsilateral knee surgery, whereas patients in the cartilage group underwent an average of 2.2 prior ipsilateral knee surgeries, and although the number of prior knee surgeries may introduce bias, this is also typical of the cartilage patient population.

Explanations for why patients without osteoarthritis but who present with localized cartilage damage or following a functional meniscectomy have significant pain and functional limitations remain elusive. This coupled with the knowledge that patients with lesser degrees of arthritis have inferior outcomes following arthroplasty suggests that patients traditionally indicated for arthroplasty are inherently much different than those indicated for cartilage restoration. Identifying who will respond favorably among those who undergo cartilage restoration with minimal degrees of arthritis continues to be a significant knowledge gap among cartilage repair specialists.

SUMMARY

Although patients with a failed cartilage procedure do still derive benefit from knee arthroplasty, the magnitude of improvement and final scores are lower than matched control subjects. These patients also experienced little to no benefit from cartilage restoration, suggesting that unmeasured shared patient characteristics may play a role. This information can be used to counsel this difficult patient population on expected outcomes following arthroplasty procedures. Further research identifying characteristics of responders to treatment remains critical to refine clinical decision-making for this difficult patient group.

REFERENCES

1. Curl WW, Krome J, Gordon ES, et al. Cartilage injuries: a review of 31,516 knee arthroscopies. Arthroscopy 1997;13(4):456–60.
2. Hjelle K, Solheim E, Strand T, et al. Articular cartilage defects in 1,000 knee arthroscopies. Arthroscopy 2002;18(7):730–4.
3. Maletius W, Messner K. The effect of partial meniscectomy on the long-term prognosis of knees with localized, severe chondral damage. A twelve- to fifteen-year followup. Am J Sports Med 1996; 24(3):258–62.
4. Mankin HJ. The response of articular cartilage to mechanical injury. J Bone Joint Surg Am 1982; 64(3):460–6.
5. Messner K, Maletius W. The long-term prognosis for severe damage to weight-bearing cartilage in the knee: a 14-year clinical and radiographic follow-up in 28 young athletes. Acta Orthop Scand 1996;67(2): 165–8.
6. Heir S, Nerhus TK, Rotterud JH, et al. Focal cartilage defects in the knee impair quality of life as much as severe osteoarthritis: a comparison of knee injury and osteoarthritis outcome score in 4 patient categories scheduled for knee surgery. Am J Sports Med 2010;38(2):231–7.
7. Gudas R, Kalesinskas RJ, Kimtys V, et al. 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.
8. Kon E, Gobbi A, Filardo G, et al. 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.
9. Mithoefer K, Hambly K, Villa Della S, et al. Return to sports participation after articular cartilage repair in the knee: scientific evidence. Am J Sports Med 2009;37(Suppl 1):167S–76S.
10. Steadman JR, Miller BS, Karas SG, et al. The microfracture technique in the treatment of full-thickness chondral lesions of the knee in National Football League players. J Knee Surg 2003;16(2):83–6.
11. Aggarwal VK, Goyal N, Deirmengian G, et al. Revision total knee arthroplasty in the young patient: is there trouble on the horizon? J Bone Joint Surg Am 2014;96(7):536–42.
12. McCormick F, Harris JD, Abrams GD, et al. Survival and reoperation rates after meniscal allograft transplantation: analysis of failures for 172 consecutive transplants at a minimum 2-year follow-up. Am J Sports Med 2014;42(4):892–7.
13. McCormick F, Harris JD, Abrams GD, et al. Trends in the surgical treatment of articular cartilage

lesions in the United States: an analysis of a large private-payer database over a period of 8 years. Arthroscopy 2014;30(2):222–6.
14. Abrams GD, Frank RM, Gupta AK, et al. Trends in meniscus repair and meniscectomy in the United States, 2005-2011. Am J Sports Med 2013;41(10): 2333–9.
15. Gudas R, Stankevicius E, Monastyreckienė E, et al. 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.
16. Kon E, Filardo G, Berruto M, et al. Articular cartilage treatment in high-level male soccer players: a prospective comparative study of arthroscopic second-generation autologous chondrocyte implantation versus microfracture. Am J Sports Med 2011;39(12):2549–57.
17. Basad E, Ishaque B, Bachmann G, et al. 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.
18. Cerynik DL, Lewullis GE, Joves BC, et al. Outcomes of microfracture in professional basketball players. Knee Surg Sports Traumatol Arthrosc 2009;17(9): 1135–9.
19. Cole BJ, Farr J, Winalski CS, et al. 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.
20. Ebert JR, Fallon M, Zheng MH, et al. A randomized trial comparing accelerated and traditional approaches to postoperative weightbearing rehabilitation after matrix-induced autologous chondrocyte implantation: findings at 5 years. Am J Sports Med 2012;40(7):1527–37.
21. Gooding CR, Bartlett W, Bentley G, et al. 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.
22. Horas U, Pelinkovic D, Herr G, et al. Autologous chondrocyte implantation and osteochondral cylinder transplantation in cartilage repair of the knee joint. A prospective, comparative trial. J Bone Joint Surg Am 2003;85A(2):185–92.
23. Knutsen G, Engebretsen L, Ludvigsen TC, et al. Autologous chondrocyte implantation compared with microfracture in the knee. A randomized trial. J Bone Joint Surg Am 2004;86A(3):455–64.
24. Kreuz PC, Steinwachs M, Erggelet C, et al. Importance of sports in cartilage regeneration after autologous chondrocyte implantation: a prospective study with a 3-year follow-up. Am J Sports Med 2007;35(8):1261–8.
25. Lim HC, Bae J-H, Song S-H, et al. Current treatments of isolated articular cartilage lesions of the knee achieve similar outcomes. Clin Orthop Relat Res 2012;470(8):2261–7.
26. Marder RA, Hopkins G, Timmerman LA. Arthroscopic microfracture of chondral defects of the knee: a comparison of two postoperative treatments. Arthroscopy 2005;21(2):152–8.
27. Niemeyer P, Köstler W, Salzmann GM, et al. Autologous chondrocyte implantation for treatment of focal cartilage defects in patients age 40 years and older: a matched-pair analysis with 2-year follow-up. Am J Sports Med 2010;38(12):2410–6.
28. Panagopoulos A, van Niekerk L, Triantafillopoulos I. Autologous chondrocyte implantation for knee cartilage injuries: moderate functional outcome and performance in patients with high-impact activities. Orthopedics 2012;35(1):e6–14.
29. Pestka JM, Bode G, Salzmann G, et al. Clinical outcome of autologous chondrocyte implantation for failed microfracture treatment of full-thickness cartilage defects of the knee joint. Am J Sports Med 2012;40(2):325–31.
30. Vanlauwe J, Saris DBF, Victor J, et al. 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.
31. Zaslav K, Cole B, Brewster R, et al. 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.
32. Ghanem E, Pawasarat I, Lindsay A, et al. Limitations of the Knee Society Score in evaluating outcomes following revision total knee arthroplasty. J Bone Joint Surg Am 2010;92(14):2445–51.
33. Insall JN, Dorr LD, Scott RD, et al. Rationale of the Knee Society clinical rating system. Clin Orthop Relat Res 1989;(248):13–4.
34. Liow RY, Walker K, Wajid MA, et al. The reliability of the American Knee Society Score. Acta Orthop Scand 2000;71(6):603–8.
35. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957;16(4): 494–502.
36. Meehan JP, Danielsen B, Kim SH, et al. Younger age is associated with a higher risk of early periprosthetic joint infection and aseptic mechanical failure after total knee arthroplasty. J Bone Joint Surg Am 2014;96(7):529–35.
37. Stambough JB, Clohisy JC, Barrack RL, et al. Increased risk of failure following revision total knee replacement in patients aged 55 years and younger. Bone Joint J 2014;96B(12):1657–62.

38. W-Dahl A, Robertsson O, Lidgren L. Surgery for knee osteoarthritis in younger patients. Acta Orthop 2010;81(2):161–4.
39. Diduch DR, Insall JN, Scott WN, et al. Total knee replacement in young, active patients. Long-term follow-up and functional outcome. J Bone Joint Surg Am 1997;79(4):575–82.
40. Piedade SR, Pinaroli A, Servien E, et al. TKA outcomes after prior bone and soft tissue knee surgery. Knee Surg Sports Traumatol Arthrosc 2013; 21(12):2737–43.
41. Piedade SR, Pinaroli A, Servien E, et al. Is previous knee arthroscopy related to worse results in primary total knee arthroplasty? Knee Surg Sports Traumatol Arthrosc 2009;17(4):328–33.
42. Morag G, Kulidjian A, Zalzal P, et al. Total knee replacement in previous recipients of fresh osteochondral allograft transplants. J Bone Joint Surg Am 2006;88(3):541–6.
43. Riis A, Rathleff MS, Jensen MB, et al. Low grading of the severity of knee osteoarthritis preoperatively is associated with a lower functional level after total knee replacement: a prospective cohort study with 12 months' follow-up. Bone Joint J 2014;96B(11):1498–502.
44. Dowsey MM, Dieppe P, Lohmander S, et al. The association between radiographic severity and pre-operative function in patients undergoing primary knee replacement for osteoarthritis. Knee 2012;19(6):860–5.
45. Dowsey MM, Nikpour M, Dieppe P, et al. Associations between pre-operative radiographic changes and outcomes after total knee joint replacement for osteoarthritis. Osteoarthr Cartil 2012;20(10):1095–102.
46. Chahal J, Gross AE, Gross C, et al. Outcomes of osteochondral allograft transplantation in the knee. Arthroscopy 2013;29(3):575–88.
47. Abrams GD, Hussey KE, Harris JD, et al. Clinical results of combined meniscus and femoral osteochondral allograft transplantation: minimum 2-year follow-up. Arthroscopy 2014;30(8):964–70.e1.
48. McCulloch PC, Kang RW, Sobhy MH, et al. Prospective evaluation of prolonged fresh osteochondral allograft transplantation of the femoral condyle: minimum 2-year follow-up. Am J Sports Med 2007;35(3):411–20.
49. Frank RM, Lee S, Levy D, et al. Osteochondral Allograft Transplantation of the Knee: Analysis of Failures at 5 Years. Am J Sports Med 2017;45(4): 864–74.