Failure of Bone Marrow Stimulation Techniques

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Abstract: Marrow stimulation techniques, including microfracture, are among the most commonly performed cartilage restoration procedures for symptomatic chondral defects of the knee. For the vast majority of patients, marrow stimulation results in reduced pain and improved function, providing overall satisfactory outcomes. In some cases, however, marrow stimulation fails, resulting in symptom recurrence and often, the need for repeat surgery. This review will describe the indications and outcomes of microfracture as a primary surgical treatment for focal chondral defects of the knee, identify patient and procedure-specific factors associated with poor clinical outcomes, and will discuss treatment options and their respective outcomes for patients with a failed prior microfracture surgery.

Key Words: cartilage restoration, microfracture failure, marrow stimulation failure, autologous chondrocyte implantation, osteochondral allograft transplantation

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Mature articular cartilage is relatively avascular and aneural, composed of predominantly type II collagen mixed with proteoglycans and relatively few cells. Without vascularity, articular cartilage is dependent on diffusion to obtain nutrients and oxygen, making intrinsic repair of articular cartilage defects exceedingly difficult in vivo.[1] Focal cartilage defects of the knee are relatively common, found in over 60% of patients undergoing arthroscopy of the knee.[2,3] It has been estimated that cartilage injuries of the knee affect approximately 900,000 Americans annually, resulting in >200,000 surgical procedures.[4] Regardless of whether the defect is acute, chronic, or degenerative in nature, articular cartilage has not demonstrated quality spontaneous healing.[5–8] When left untreated, focal chondral lesions, particularly those involving the weight-bearing surfaces of the medial or lateral compartments as well as those involving the patellofemoral joint, can result to pain, effusions, mechanical symptoms, and low levels of function. For appropriately indicated patients, surgical intervention for symptomatic cartilage lesions is not only helpful in reducing these symptoms, but also, is needed to restore near normal joint mechanics and congruence, and in some cases, to prevent further joint deterioration. The limitations in intrinsic articular cartilage physiology and regeneration has led to an influx of research into surgical cartilage restoration techniques.

There are numerous surgical options available for the treatment of focal chondral defects, which can be broadly categorized into 4 groups: palliative options, including arthroscopic debridement and lavage; reparative options, including microfracture and other bone marrow stimulation techniques; restorative options including osteochondral autograft transfer (OATS) and autologous chondrocyte implantation (ACI) procedures; and reconstructive options including osteochondral allograft transplantation.[9] Regardless of the specific technique chosen, the goals of surgical treatment are similar, including the ability to improve joint function, relieve pain, and allow patients to return to activity or in the case of athletes, return to sport. The appropriate treatment decision for any given patient presenting with a symptomatic cartilage defect of the knee must be made on a case-by-case basis, and certainly, several defect-specific and patient-specific factors will aid in clinical decision-making. Specifically, the size and location of the lesion, the activity level of the patient, the expectations and goals of the patient, prior surgical/treatment history, body mass index, and other concomitant knee pathologies are all considerations in determining which procedure is best for each patient.[9]

Bone marrow stimulation techniques were first described by Pridie,[10] who demonstrated that drilling subchondral bone could stimulate bone marrow substrates to repopulate articular cartilage defects, a technique that was later termed spongialization by Ficat et al.[11] Building on the concept of drilling, Johnson[12,13] first described abrasion arthroplasty where one performs multiple tissue debridement including surgical penetration through subchondral bone to enhance bleeding to create a repair response. These early techniques eventually gave rise to microfracture, which was popularized by Steadman et al[14] and is now considered the gold standard surgical procedure for small, isolated, articular cartilage defects of the knee. Microfracture has gained popularity as it is a minimally invasive, single-stage, low-cost, and relatively straightforward surgical procedure (Fig. 1).[15] Microfracture and other marrow stimulation techniques induce an influx of marrow substrates to repopulate the cartilage defect by removing the subchondral bone and exposing cancellous bone.[16] This results in clot formation with marrow elements that is remodeled and organized into a fibrocartilage plug, comprised primary of type I collagen. Although fibrocartilage is superior to no cartilage, the long-term efficacy of microfracture has been called into question due to the lack of true, articular, hyaline-type cartilage filling the void. Fibrocartilage repair tissue lacks many of the intrinsic biochemical and viscoelastic properties of normal hyaline cartilage. As a result of its biochemical and viscoelastic properties, fibrocartilage is more stiff compared with

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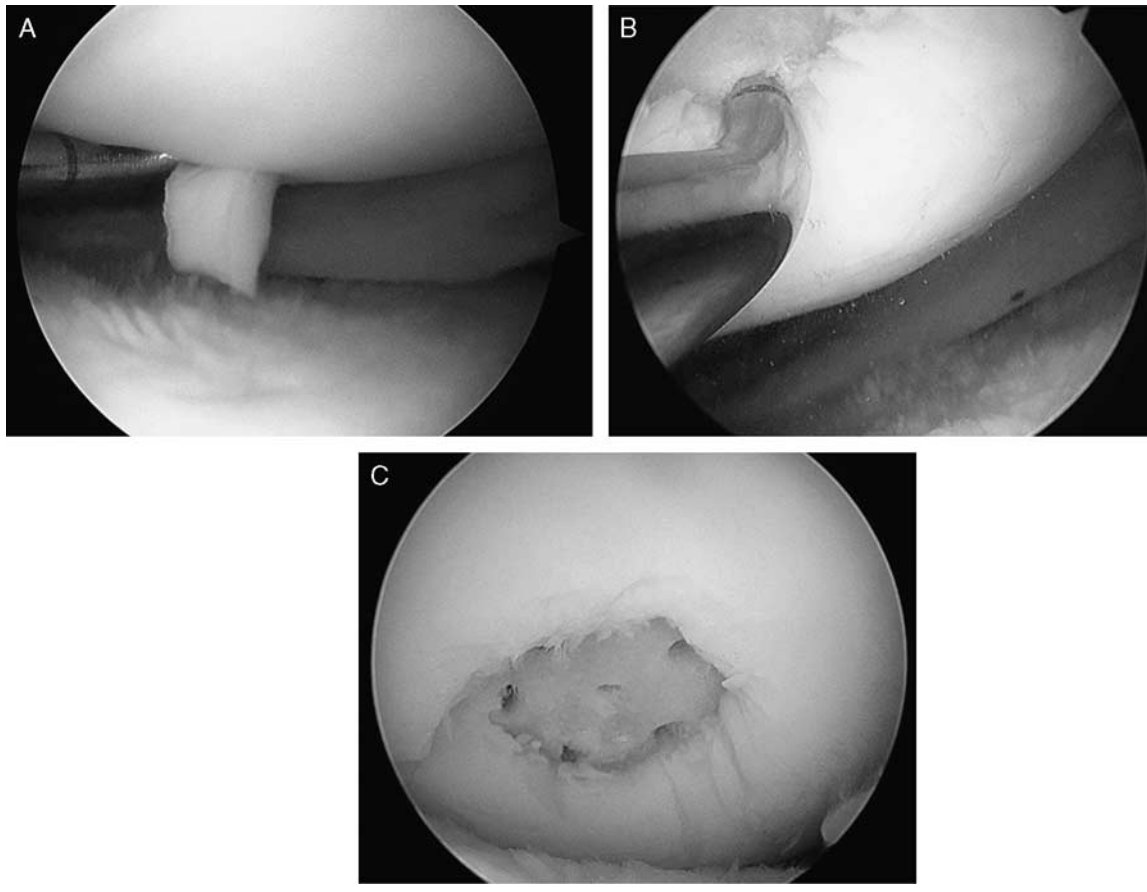

FIGURE 1. Intraoperative arthroscopic photographs demonstrating the use of the microfracture procedure to a 1.8 cm × 1.8 m lesion of the weight-bearing portion of the lateral femoral condyle in a 24-year-old woman.

articular hyaline cartilage, which does not afford it the same shock absorption and force distribution capabilities seen in normal hyaline cartilage.[10,17–19] The remainder of this review will describe the indications and outcomes of microfracture as a primary surgical treatment for focal chondral defects of the knee, identify patient and procedure-specific factors associated with poor clinical outcomes, and will discuss treatment options and their respective outcomes for patients with a failed prior microfracture surgery.

INDICATIONS AND OUTCOMES

Marrow stimulation techniques, including microfracture, are among the most commonly performed cartilage restoration procedures in the United States for symptomatic chondral defects of the knee.[20] These techniques are indicated for patients with symptomatic, full-thickness, isolated chondral defects.[21] Numerous authors have nicely delineated which patients may benefit most from microfracture, while also reporting on possible negative prognostic factors. In a systematic review of 28 studies with over 3000 patients, Mithoefer et al[22] reported patient age above 40 years, preoperative symptomatic intervals < 12 months, lesion size $\leq 4\,cm^2$ for nonathletes and $< 2\,cm^2$ for athletes, and body mass index $< 30\,kg/m^2$ were associated with better outcomes. Overall they reported knee function was consistently improved in the first 24 months after microfracture. Specifically, at 2-year, patient-reported outcomes (PROs) were improved compared with preoperative scores; however, only 67% to 85% of patients continued to report improved outcomes between 2 and 5 years postoperatively. In a more recent systematic review only of level I and II studies, Goyal et al[23] confirmed the factors described by Mithoefer et al.[22] However, Goyal et al[23] noted progression to osteoarthritis was observed frequently in patients who received microfracture for lesions $> 4\,cm^2$ just 5 years after the procedure. Other authors have demonstrated successful outcomes following microfracture for lesions $> 4\,cm^2$; however, that improvement has not been shown to last as long as for smaller lesions, which may explain why many surgeons reserve the use of microfracture for isolated lesions $< 4\,cm^2$.[22,24] Finally, microfracture typically has better outcomes used as a first-line treatment, as opposed to when it is performed as a revision operation.[25–27]

For patients with symptomatic chondral defects of the knee, often, concomitant knee pathology may be present, including meniscal deficiency, coronal or sagittal plane malalignment, and/or ligamentous instability.[21] Such concomitant knee pathology may actually contribute to the development of focal cartilage defects, as any combination of meniscal deficiency, malalignment, and ligamentous insufficiency may alter normal joint biomechanics, placing

excessive strain on the articular surfaces. In either a single or staged fashion, it is essential to address all symptomatic pathologies adequately to prevent failure of microfracture or other cartilage restoration techniques. In meniscus-deficient patients, concurrent meniscal allograft transplantation with cartilage restoration has been shown to have equivalent outcomes compared with isolated cartilage restoration.[28,29] Likewise, corrective osteotomy for malalignment concurrent with microfracture has been demonstrated to improve patient satisfaction scores with a 91% survivorship at 7 years.[30,31]

In a prospective study evaluating the long-term outcomes of microfracture in 110 patients, Solheim et al[32] reported a relatively high rate of reoperation, including conversion to knee arthroplasty, at a median follow-up of 12 years. Specifically, 50 of the 110 patients (45%) were noted to have had a poor outcome, defined by conversion to knee arthroplasty (N = 7) and/or Lysholm score < 64. The authors found that poor results were more common in patients with mild degenerative changes in the cartilage surrounding the defect, concurrent partial meniscectomy, poor baseline Lysholm score, or long-standing knee symptoms.[32]

In 2014, Gobbi and Karnatzikos[33] also reported on long-term outcomes following microfracture. In their prospective study of 61 athletes with an average 15-year follow-up, the authors found significant improvements in PRO scores at 2 years, with a gradual drop in scores over time. A total of 7 patients (11%) were considered failures as defined by undergoing another operation, either due to reinjury, or due to persistent pain within the first 5 years following the index microfracture. The authors concluded that lesion size was a more important prognostic factors than patient age, with lesions $\leq 400\,mm^2$ associated with superior outcomes.

In addition to the long-term studies following microfracture, several studies have compared microfracture with other cartilage restoration procedures. Ulstein et al[34] conducted a prospective randomized clinical trial of 11 patients undergoing microfracture versus 14 undergoing OATS for full-thickness defects of the femoral condyle. At a median 10-year follow-up, there were no significant long-term differences in Lysholm scores, Knee Injury and Osteoarthritis Scores, isokinetic muscle strength, reoperation rates, or radiographic osteoarthritis between the 2 groups.[34] Similarly, Gudas et al[35] conducted a prospective randomized clinical trial of 60 athletes with articular cartilage defects of the knee in which 30 patients were randomized to OATS and 30 were randomized to microfracture. The authors reported 4 failures in the OATS treatment group and 11 failures in the microfracture treatment group at an average of 10-year follow-up, which correlated with a statistically significant difference in International Cartilage Repair Society and Tegner scores between the 2 groups. In addition, 25% of OATS patients and 48% of microfracture patients were found to have radiographic evidence of Kellgren-Lawrence grade 1 osteoarthritis at 10 years. In a recent meta-analysis, Pareek et al[36] summated the literature comparing OATS and microfracture. A total of 6 studies met inclusion criteria consisting of a total of 249 patients with an average of 67-month follow-up. Their results demonstrated patients treated with OATS had higher activity levels as measured by Tegner score and lower risk of failure for treatment of lesions $> 3\,cm^2$ whereas there was no difference in outcomes between the two treatment group for lesions $< 3\,cm^2$.

Knutsen et al[37–39] conducted a randomized controlled trial of 80 patients randomized to either microfracture or ACI. The authors reported both 2 and 5-year outcomes following surgery, with no significant differences in PROs between the groups, and with both groups exhibiting 23% failure rates at 5-year.[38] Their most recent study evaluated outcomes at 14 + years following surgery, with 42.5% of patients in the ACI group and 32.5% of patients in the microfracture group found to be failures. One of the more significant findings of these studies is that approximately 50% of patients who failed surgery, regardless of the whether it was ACI or microfracture, were found to have early radiographic signs of osteoarthritis.[37] In a systematic review of activity-related outcomes of cartilage surgery that included a total of 1375 patients, Chalmers et al[40] reported that ACI and OATS demonstrate significant advantages over microfracture with respect to the majority of reported PROs. Specifically, ACI was found to result in superior Tegner scores at 1 year and International Knee Documentation Committee scores at 2 years, while OATS was found to have superior Lysholm scores at 1 year and Marx scores at 2 years. The only score measure favoring microfracture was the Lysholm at 1 year when comparing microfracture to ACI.[40] Thus, based on the results of that systematic review, ACI and OATS may be more advantageous than microfracture at improving activity levels short-term following surgery.

Special Consideration—Athletes Undergoing Microfracture

High-level athletes undergoing microfracture surgery within the knee warrant additional consideration, as they often challenge the fibrocartilage repair site with increased load and more frequent impact. On the basis of the findings of Mithoefer et al,[41] microfracture should be used for smaller lesions in athletes, with smaller lesions, or those $< 2\,cm^2$ being predictive of return to sport. In addition, the location of the chondral defect in a non–weight-bearing area of the knee, as well as a shorter duration of symptoms (< 12 mo) have been shown to predict better outcomes after microfracture.[22,41]

Numerous studies have been conducted in athletes participating in a variety of sports in an effort to analyze the efficacy of microfracture and its impact on return-to-play (RTP). In a study of 41 National Basketball Association players who underwent microfracture, Harris et al[42] reported an 83% RTP rate with respect to professional basketball, with 73% RTP in the National Basketball Association specifically. In a prospective cohort study of 20 professional alpine ski racers, Steadman et al[43] reported 95% RTP rate at an average 13 months after undergoing microfracture. Mai et al[44] assessed 32 National Football League athletes who underwent microfracture, and at 1-year there was a 75% National Football League RTP rate with the average time to RTP being 330 days. Finally, Mithoefer and Steadman[45] evaluated 21 professional male soccer players, 12 with single cartilage defects and 9 with multiple cartilage defects, all treated with microfracture. The authors reported 95% RTP rate for professional soccer at an average of 5 years following surgery.

Recently, Krych et al[46] published a meta-analysis specifically analyzing RTP rates after surgical management of articular cartilage lesions of the knee. In this analysis of 44 studies (18 level I/II studies and 26 level III/IV) with 2549 patients, 34% underwent microfracture. Of the

patients undergoing microfracture, there was a 58% RTP rate at an average of 9.1 months following surgery. Of note, Krych et al[46] also evaluated osteochondral allograft transplantation, OATS, and ACI in athletes with chondral defects of the knee, with RTP rates of 88%, 93%, and 82%, respectively. Microfracture was associated with the lowest RTP rates, with the next lowest procedure being ACI (82%).[46] The results of that meta-analysis[46] reinforce the findings of Mithoefer et al,[41] who reported a 73% RTP rate in 1363 patients undergoing microfracture, as well as of Campbell et al,[47] who reported a 75% RTP rate in 529 athletes undergoing microfracture in a systematic review of level I-IV studies. Of note, in their study, Campbell et al[47] demonstrated RTP rates of 89%, 88%, and 84% for OATS, osteochondral allograft transplantation, and ACI, respectively. Certainly, the demands of the specific sport in question require consideration when evaluating overall RTP rates, as sports such as football or rugby are more likely to subject athletes to stronger and more frequent stressors across the knee joint.[48] When analyzed as a group, the various systematic reviews and meta-analyses evaluating outcomes and RTP rates of cartilage restoration procedures for the knee have consistently reported concerning outcomes following microfracture, particularly in athletes, with failure rates approaching approximately 25% and higher. As such, more recent research efforts have focused on improving our understanding of why microfracture fails, and what treatment options exist for those patients who do, unfortunately, experience fail.

WHY MICROFRACTURE MAY FAIL

Compared with hyaline cartilage, the fibrocartilage produced by microfracture imparts less compressive stiffness under normal load, inferior resilience, and poorer wear characteristics.[49] In addition to the previously described patient-specific characteristics associated with better outcomes following microfracture, several authors have conducted studies to more closely examine which molecular properties of fibrocartilage repair tissue may be associated with better or worse outcomes. In a second-look study, Kaul et al[50] examined the repair tissue of 5 human patients at an average of 8.8 months following microfracture to better describe the cellular and molecular properties of the repair tissue. Polarized light microscopy revealed collagen fibrils in a disorganized or vertical pattern relative to the joint surface, and further, found the fibrocartilage tissue to be cell-rich compared with surrounding, normal hyaline articular cartilage. In addition, the authors noted that the proteoglycan content of the repair tissue was, on average, less than adjacent healthy cartilage. In another study, Richter[1] described how the cellular and molecular properties of the clot induced by microfracture is not conducive to healing back to normal hyaline cartilage in large part due to the limited scaffolding on which marrow derived stem cells can attach as well as the relatively low concentration of stem cells elicited by microfracture compared with the defect size. Clearly, the cellular and molecular properties of the fibrocartilage plug elicited by microfracture do not replicate the native hyaline cartilage properties.

Interestingly, despite the clear improvement of hyaline cartilage over fibrocartilage with respect to native joint function, it is unclear if the hyaline-type cartilage produced with ACI translates to improved clinical outcomes when compared with the clinical outcomes following microfracture. For example, in a randomized controlled trial comparing the outcomes of ACI (n = 51) to microfracture (n = 61), Vanlauwe et al[51] reported relatively equivalent clinical outcomes between the groups at 5 years of follow-up, with the only notable difference being that if microfracture failed, it usually occurred earlier than when ACI failed.

The development of subchondral bone overgrowth following microfracture has also been implicated as a possible etiology of failure. In a prospective study of 84 patients undergoing microfracture, Mithoefer et al[52] assessed the postoperative magnetic resonance imaging findings of the defect site at an average 22 months following surgery. The authors noted subchondral bone overgrowth in 62% of patients, with the majority of cases classified as "low grade." Importantly, 93% of the patients who failed their microfracture procedure were found to have evidence of osseous overgrowth, and statistically, the presence of overgrowth was associated with an increased rate of failure ($P < 0.01$).[52]

Other factors that may lead to a failed microfracture procedure include poor surgical technique (ie, not establishing vertical walls), poor patient indications (ie, treating an uncontained defect, treating "kissing lesions," etc.), as well as patient noncompliance with postoperative rehabilitation protocols (ie, lack of adherence to weight-bearing restrictions). Patient noncompliance is more likely to lead to early failure, whereas progressive breakdown of the weaker, fibrocartilaginous repair tissue over time is more likely to lead to late failure.[25]

Given the limitations of microfracture, recent research efforts have focused on modification and augmentation techniques for improving the quality of the repair tissue produced by microfracture, in an effort to reduce failure rates and improve outcomes.[4,49,53] Many of these techniques attempt to improve the availability of stem cells and growth factors and/or provide an additional scaffold on which the repair tissue can adhere to and proliferate.[54–56] For example, in a basic science equine model, Fortier et al[56] demonstrated that the delivery of bone marrow aspirate concentrate as augmentation to microfracture induces superior cartilage defect healing compared with microfracture alone.

Overall, a clear understanding of the underlying factor(s) associated with a failed microfracture is essential to provide the patient with the best treatment options moving forward. The workup of these patients can be complex, and involves meticulous review of prior treatment/surgical records, including any arthroscopic imaging; a complete history, physical examination, and assessment of advanced imaging findings; and treatment of any concomitant knee pathologies, including meniscus deficiency, ligamentous insufficiency, and/or malalignment. Certainly, additional research in this area is needed, as it remains unclear as to what specifically leads some patients to fail microfracture.[57]

REVISION CARTILAGE RESTORATION AFTER FAILED MICROFRACTURE

For those patients who fail microfracture, revision cartilage restoration options exist, including cell transplantation (ie, ACI), OATS, and osteochondral allograft transplantation (Fig. 2). Typically, the choice of revision procedure is determined by the location of the cartilage

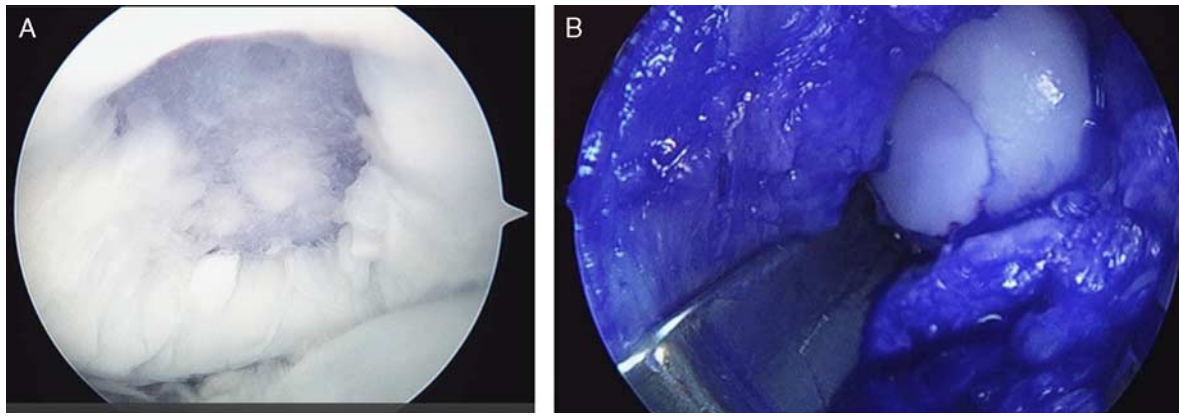

FIGURE 2. Intraoperative arthroscopic photographs demonstrating the appearance of a failed microfracture of the weight-bearing portion of the lateral femoral condyle (A) and salvage to an osteochondral allograft transplantation in a 25-year-old woman (B).

defect. Recently, Chahal et al[25] described a treatment algorithm for patients who failed microfracture. Specifically, the authors recommended ACI or other cell transplant procedures such as DeNovo for failed microfracture of the patellofemoral joint, and OATS (for defects $< 2\,cm^2$) or osteochondral allograft transplantation (for defects $\geq 2\,cm^2$) for failed microfracture of the tibiofemoral joint.

ACI was first introduced in Sweden more than 20 years ago,[58,59] and is certainly a viable treatment option for large full-thickness cartilage defects. Unlike the fibrocartilage tissue produced by microfracture, ACI results in a hyaline-type cartilage tissue, which more closely mimics the natural articular surface of the knee joint. The disadvantages of ACI include its cost and the need to perform 2 operations—1 to harvest the cells and 1 to reimplant them 4 to 6 weeks later. Procedures such as ACI have been described as a revision option following a failed microfracture procedure. Unfortunately, several authors have reported unpredictable cartilage volume and higher failure rates for cell transplantation surgery following failed prior microfracture compared with primary cell transplantation surgery, suggesting that microfracture is not a benign procedure, and may "burn bridges" and lower the likelihood of successful outcomes following revision ACI.[22,60]

Zaslav et al[57] conducted a prospective cohort study of 154 patients who failed a previous cartilage restoration procedure (microfracture in 42 patients) and went onto receive ACI. The authors reported that 76% of patients had successful outcomes at an average 48 months following ACI, with no difference in outcomes in patients with a prior microfracture versus a prior debridement.[57] In a match-paired cohort study of 28 patients receiving ACI after failed microfracture of the knee compared with primary ACI, Pestka et al[61] reported significantly higher failure rates and inferior clinical outcomes following ACI as a revision cartilage procedure compared with ACI as first-line therapy. Seven of the 28 patients in the revision ACI group ultimately failed their ACI procedure, whereas only 1 patient in the primary ACI cohort failed. PROs, including Knee Injury and Osteoarthritis Scores and International Knee Documentation Committee scores were found to be significantly higher in the primary ACI cohort versus the revision group.[61] In a separate study of 522 chondral defects in 321 patients treated with ACI, Minas et al[62] demonstrated that patients who had previously undergone treatment affecting subchondral bone, had a failure rate three times higher than patients undergoing a primary ACI. Of note, 110 of the 321 patients in this study had a previous treatment affecting subchondral bone, which included microfracture among other techniques. Microfracture specifically had a 20% failure rate in this study, albeit the microfracture cohort comprised only 25 of the 110 patients who had previously undergone treatment affecting subchondral bone.[62]

Overall, these studies and others call into question the utility of ACI as a revision cartilage restoration procedure following failed microfracture surgery. Recent authors have demonstrated subchondral changes in up to one third of patients treated with microfracture, including thickening of subchondral bone, osseous overgrowth, and the formation of subchondral cysts.[63,64] Some have looked at modifications to drilling that may decrease the likelihood of these complications. Eldracher et al[65] recently reported that application of 1.0 mm subchondral drill holes led to significantly improved osteochondral repair of cartilage defects in a sheep model compared with 1.8 mm drill holes. Specifically, the authors demonstrated higher bone volume and reduced thickening of the subchondral bone plate. Alternatively, Chen et al[49,66] evaluated drilling depth as a factor influencing defect repair. Utilizing a rabbit model, the authors reported deep drilling to 6 mm compared with 2 mm induced a larger volume of repaired and remodeled subchondral bone which correlated with improved cartilage repair even though the presence of many atypical features such as residual holes, cysts, and bony overgrowth were still frequent. Although novel variations to marrow stimulation techniques as well as procedure augmentations are promising ways to improve this treatments going forward, overall there remains concern that microfracture and other marrow stimulation techniques alter the subchondral bone to such an extent that subsequent procedures may have a lower likelihood of success.

Osteochondral allograft transplantation has been described as a viable treatment option for failed prior cartilage restoration. Like the OATS procedure, osteochondral allograft transplantation is a technique that essentially restores the natural cellular and molecular physiology of the articular surface, as the allograft tissue is composed of viable hyaline cartilage and bone taken from a human donor.[67] In a match-paired cohort study of 46 patients

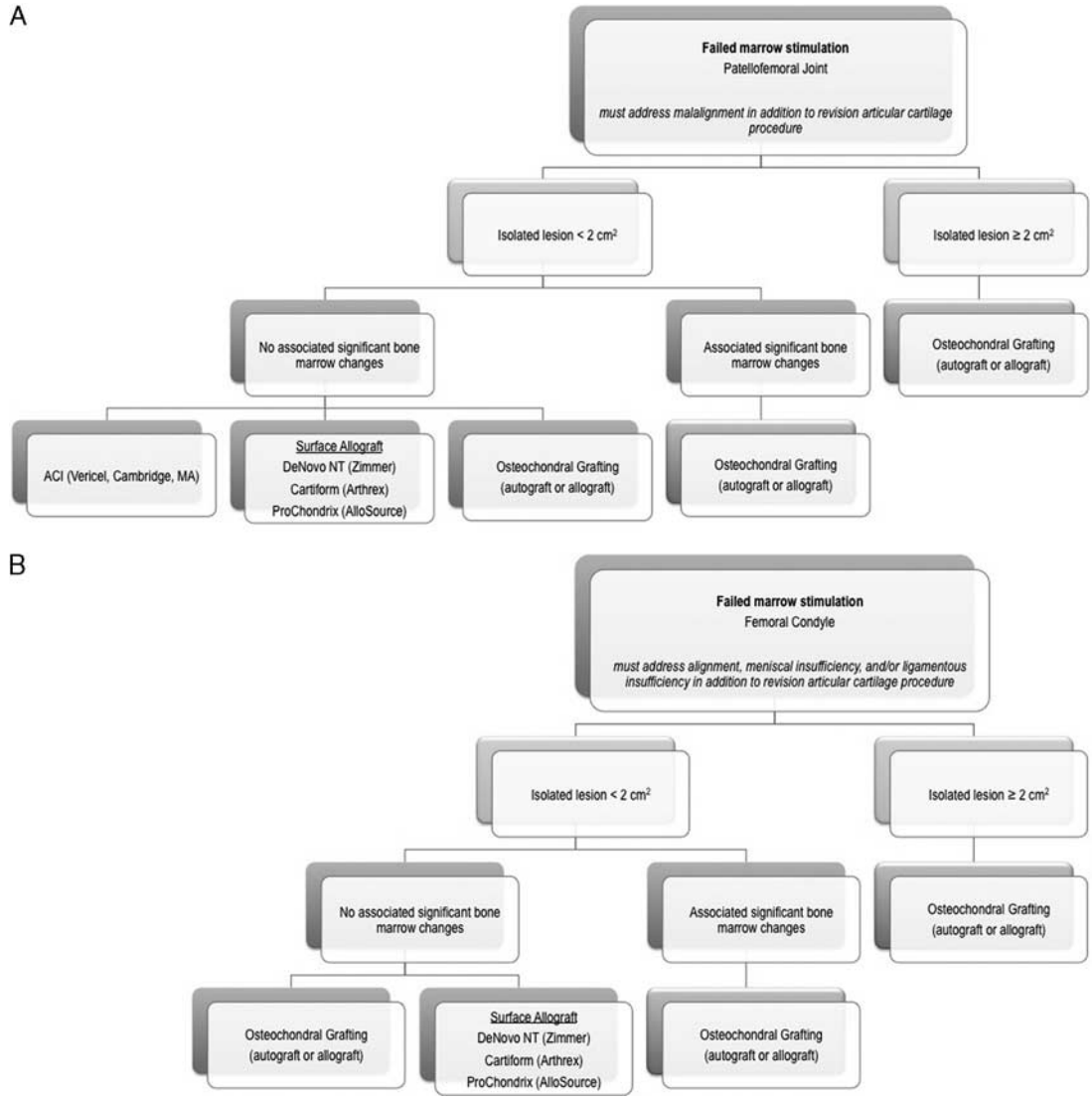

FIGURE 3. A, For lesions of the patellofemoral joint that are <2 cm^2 without significant subchondral bone changes, we recommend ACI (Vericel, Cambridge MA) or a surface allograft, including DeNovo NT (Zimmer, Warsaw, IN), Cartiform (Arthrex, Naples, FL), or ProChondrix (AlloSource, Denver, CO). Alternatively, osteochondral grafting (autograft or allograft) can be considered and should be considered for these same lesions with subchondral bone changes or for patellofemoral lesions that are > 2 cm^2. Some still prefer surface treatment for larger lesions of the patellofemoral joint when there are minimal subchondral bone changes present. B, For lesions of the femoral condyle that are < 2 cm^2 without significant subchondral bone changes, we recommend osteochondral grafting (autograft or allograft), although surface allografts can be considered. For similarly located lesions ≥ 2 cm^2 independent of the condition of the subchondral bone and smaller lesions with significant subchondral bone changes, we recommend osteochondral (autograft or allograft) transplantation. ACI indicates autologous chondrocyte implantation.

undergoing OCA as a revision procedure following failed marrow stimulation surgery, Gracitelli et al[68] reported a reoperation rate of 24% in patients undergoing primary osteochondral allograft transplantation compared with a reoperation rate of 44% in patients receiving the allograft as a secondary procedure. However, there were no significant differences in failure rates between the groups, nor in survivorship of the graft at 10 years (87% in primary allograft procedures vs. 86% in secondary allograft procedures). In addition, there were no differences in patient satisfaction, regardless of whether the surgery was a primary or a revision allograft transplantation.[68]

In stark contrast to ACI after failed microfracture, osteochondral allograft transplantation following failed microfracture has resulted in improved outcomes, approaching the results seen after primary osteochondral allograft transplantation, making it a desirable salvage procedure for focal cartilage defects of the knee. Frank et al recently reported on 180 patients undergoing osteochondral allograft transplantation at an average follow-up of 5 years. In this cohort, the presence of a prior microfracture was not associated with worse outcomes or lower allograft survival rates compared with patients without a prior microfracture.[69] The benefit of osteochondral

allograft transplantation as a salvage procedure compared with ACI is that the subchondral bone environment that was altered by the previous marrow stimulation technique becomes less relevant, as the lesion will be cored and replaced by healthy allograft bone.[70] For secondary ACI to be successful, the underlying subchondral bone environment should ideally be as close to its native environment as possible. Our recommended treatment algorithm is detailed in Figure 3.

CONCLUSIONS

Although the majority of patients experience good to excellent outcomes following microfracture, based on the current best available evidence, up to 25% or more will fail at the 10-year follow-up point,[32,35,49] requiring further treatment. Numerous technique-specific, patient-specific, and lesion-specific factors impact outcomes following microfracture, and large ($\geq 4\,cm^2$), uncontained lesions are the most likely to be associated with failure. Microfracture results in a fibrocartilage repair tissue that is molecularly different from normal hyaline articular cartilage, and may contribute to the relatively high long-term microfracture failure rate. Salvage options consistent of cell transplantation as well as osteochondral autograft or allograft transplantation, and ACI has been shown to be a relatively poor secondary treatment option compared with osteochondral allograft transplantation in patients who fail primary microfracture. Although superficial abrasion and deep drilling have shown promise as techniques that may improve outcomes, additional research in this area is needed, particularly with determining while microfracture fails in some patients, and further, gaining a better understanding as to the optimal revision strategies for lesions, taking into account defect size and location within the joint.

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