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Biological Augments for Acetabular Chondral Defects in Hip Arthroscopy—A Scoping Review of the Current Clinical Evidence

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Abstract

Purpose of Review A wide array of joint-preserving surgical techniques exists in the management of acetabular chondral defects (ACDs). The purpose of this review is to summarize the clinical outcomes of the recent biologics used to treat ACDs during hip arthroscopy.

Recent Findings Increasing evidence is available for different biological solutions used in the hip. Studies have shown promising outcomes with minimal complications when using biologics as augmentation to microfracture (MF), including different scaffolds or stem cells, or to enhance autologous chondrocyte implantation (ACI). However, data so far is scarce, and more trials and longer follow-ups are needed to better delineate the appropriate indications and benefits for each technique.

Summary Presently, the level of evidence is low, but in general, biologics appear safe and trend toward beneficial compared to standard surgical techniques. Augmented MF is recommended for small to medium ACDs, and matrix-assisted ACI or three-dimensional ACI is recommended for medium to large defects.

Keywords Hip biologics · Hip arthroscopy · Acetabular chondral defects · Augmented microfracture · Stem cell therapy · Matrix-assisted autologous chondrocyte implantation

Introduction

Management of chondral injuries around the hip is more challenging than that of other joints, given the weight-bearing nature and the importance of coxofemoral congruency in stability [1, 2]. Acetabular or femoral head lesions can cause significant dysfunction and chronic pain given that the cartilage has a limited healing capacity [3, 4]. If left untreated, chondral defects can lead to a higher risk of progression to osteoarthritis (OA) [5]. Many factors have been implicated in the occurrence of acetabular chondral defects (ACDs) including trauma [6], dysplasia [7], OA [8], and femoroacetabular impingement (FAI) [9]. However, they are more commonly found and treated in the setting of FAI given that FAI is the most common indication for hip arthroscopy [8].

Hip arthroscopy is rapidly evolving and shows recent trends toward joint-preserving surgical techniques, which are the preferred treatment for young and active patients with ACDs, not only to treat the defect but also to delay progression to OA [10]. Many of the techniques used to treat hip chondral defects have been adopted from those previously used in the knee, including microfracture (MF) [11], mosaicplasty [12], and autologous chondrocyte implantation (ACI) [13]. However, different biological treatment options are emerging [10, 14]. These are typically used to enhance the primary treatment and promote healing [14]. There is a paucity of data with regard to clinical outcomes for combining these therapies with various surgical techniques; however, this review has summarized the clinical outcomes for the use of hip biologics during hip arthroscopy.

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Prevalence of Cartilage Lesions

Acetabular chondral lesions in the hip are underestimated. ACDs were found in 14% of asymptomatic volunteers compared to 47% in a matched population of patients with FAI using 1.5-T magnetic resonance imaging (MRI) [15]. Advancements in MRI, as well as a rise in surgical indications for hip arthroscopy, have shown higher numbers of chondral lesions in people with hip pain [8, 16]. McCarthy and Lee reported on 457 hip arthroscopies performed over 6 years and showed that chondral injuries were found in 59% (269 cases) in the anterior acetabulum, 25% (114 cases) in the posterior acetabulum, and 24% (110 cases) in the superior acetabulum [8]. Using an MRI arthrogram (MRA), chondral lesions were found in 76% of patients presenting with hip mechanical symptoms, with 53% demonstrating involvement in more than one compartment [16]. Despite MRA having a high positive predictive value for diagnosing chondral lesions, it has limited accuracy and sensitivity in the detection of small lesions [17, 18].

Effect of Chondral Defects on Hip Biomechanics

The coxofemoral articular congruency is the main stabilizer of the hip joint [2]. Any abnormality in the acetabular chondral surface, the chondrolabral junction, or the labrum has severe implications on hip biomechanics [19]. Acetabular under coverage, or hip dysplasia, has also been correlated with higher incidence of full-thickness chondral defects secondary to the chronic shear stress [19, 20].

The location of chondral lesions can vary, but given the predominance of FAI among the causative factors, it is more commonly found in the anterosuperior area of the acetabulum due to the resulting shear forces associated with cam morphology [2]. Klennert et al. used finite element analysis to study the effect of focal ACDs on the contact mechanics of the hip during gait and found that they increased maximum shear stress of the acetabular cartilage [19]. This was further increased in the presence of labral delamination, which could lead to further chondral damage and progression of OA. Successful surgical treatment of chondral defects is therefore a priority in patients undergoing hip arthroscopy, regardless of etiology.

ACDs as Poor Prognostic Factors After Hip Arthroscopy

ACDs have been associated with worse outcomes in patients undergoing hip arthroscopy, with larger lesions correlating with worse outcomes [4, 21]. A full-thickness acetabular chondral lesion was established as an independent risk factor for treatment failure and conversion to total hip arthroplasty (THA) [22]. If left untreated, chondral defects can lead to higher risk of progression of OA [5]. This is well established with chondral defects in the knee joint due to the availability of long-term data [23, 24]. However, as FAI is becoming an increasingly recognized cause of hip pain, it seems that it does contribute to progression of OA as we better understand the impact of the severity of bony abnormalities, mainly the cam-type impingement that can predispose patients to chondral lesions and eventually OA [9]. However, well-designed prospective cohorts and randomized trials are still lacking.

Biomaterials and Outcomes in ACDs

The use of biologics for treatment of chondral lesions is becoming increasingly prevalent worldwide. There are many treatment options, with many relying on the formation of blood clots following MF, which releases bone marrow stem cells (BMSC). Biomaterials augment this typical treatment by improving cell proliferation and differentiation of BMSC through the chondrogenic effect. The mechanical aspect of biomaterials increases the stability of blood clots to help retain BMSC and to enhance the potential for healing [10, 14]. There are numerous products with variable results in different joints, but this review will focus on the recent clinical outcomes of biomaterials used to treat ACDs during hip arthroscopy.

Solution-Based Approach

Solution-based biological techniques are mainly used to augment MF to promote chondral healing in small- to medium-sized ACDs [1]. These include scaffolds used to enhance cartilage repair and can be grouped under autologous matrix-induced chondrogenesis (AMIC). Other solutions like fibrin adhesive, hyaluronic acid (HA), platelet-rich plasma (PRP), and different types of growth factors can be injected into the MF site or into the joint following the procedure [14].

1. AMIC

AMIC is a one-step procedure that combines MF with a scaffold that aids in blood clot stabilization and enhances healing. Scaffolds can be injectable solutions or solid hydrogel matrices. These allow easy application on all surfaces, even large or irregular defects. Different products are described including collagen-based [25], chitosan-based [26•, 27], and HA-based [28] scaffolds. However, only collagen- and chitosan-based scaffolds have clinical outcomes in the treatment of ACDs so far [26•].

A. Collagen-Based Scaffolds

AMIC was originally developed as a type I/III collagen membrane used in chondral defects treated with MF [29]. Despite lacking evidence of chondrogenicity when used alone, this technique continues to be frequently used [29]. In vivo evidence does not show improved histological structure or biomechanical function of the repair tissue with the use of these matrices [30]. Moreover, the combination of solid scaffolds with MF could compromise subchondral bone integrity. Beck et al. demonstrated the development of subchondral bone cysts in 42% and 92% of sheep femoral condyle defects treated with MF + type I/III collagen scaffold implantation at 13 and 26 weeks, respectively [31]. This result was attributed to elevated subchondral pressure. Given that both the knee and hip are weight-bearing joints, cyst development may be a potential complication when treating ACDs with this technique.

Chondro-Gide® (Geistlich Pharma AG) is a resorbable bilayer collagen I/III membrane frequently used in AMIC. AMIC with Chondro-Gide is a safe and valid procedure for medium-sized ACDs [25] with good short-to-mid-term functional outcomes [32, 33•]. Fontana and De Girolamo reported on acetabular grade III and IV lesions in 147 patients (77 treated with MF alone and 70 treated with AMIC) over a period of 5 years [32]. They showed significantly improved modified Harris hip scores (mHHS) at 6 months and 1 year post-operatively in both groups, but outcomes in the MF group slowly deteriorated over the subsequent 4 years, particularly in patients with large (> 4 cm^2) defects. Their outcomes were maintained for 8 years in the AMIC group without any reported failure, compared to 22% of patients in the MF group who underwent conversion to THA [33•].

B. Chitosan-Based Scaffold

Chitosan-based scaffolds are more recent types of scaffolds used in AMIC. BST-CarGel® (CarGel) (Smith and Nephew) is a chitosan-based scaffold that is mixed with autologous blood to make a gel-forming solution that can be injected into MF sites to stabilize blood clots and enhance healing [34]. Chitosan is primarily composed of polyglucosamine with a thrombogenic effect. It has demonstrated better healing capacity and improved histological quality with more pronounced fibrocartilage when compared with bone marrow stimulation alone in animal models [35, 36]. The safety and efficacy of treating ACDs with CarGel have been well documented [26•, 27, 37–39]. Rhee et al. evaluated 37 patients with ACDs during hip arthroscopy and showed improved International Hip Outcome Tool (iHOT) scores with the use of CarGel even in large defect sizes (> 6 cm^2) [38]. A prospective trial used CarGel in conjunction with MF for ACDs in 23 patients over an average of 24 months and showed improved Hip Outcome Scores (HOS) for both daily activities and sports subscales [39]. This technique also showed good radiological outcomes with homogenous healing of the chondral defect with MRI quantitative T2 mapping [37]. Promising outcomes can therefore be expected with complete restoration of the cartilage defect [39].

Randomized controlled trials have demonstrated that CarGel has superior functional outcomes when compared to MF alone in treating cartilage defects in the knee [40, 41]. Recent evidence suggests similar outcomes in the hip [26•]. A comparative case series reported on 80 patients with ACDs (54 treated with MF + CarGel; 26 treated with MF) and found a significant improvement in functional outcomes in both groups, despite larger defect sizes in the CarGel group (p = 0.002). The authors also showed significantly lower conversion to THA in the CarGel group with only 5.9% of cases undergoing THA, compared to 43.6% of the MF cases. While MF is the most performed treatment for defects < 2 cm^2 [1, 42••], CarGel-augmented MF seems to be an effective alternative even in medium to large defects (> 2 cm^2). However, clinical outcomes have only short-term follow-ups in the hip and more trials with longer follow-ups are needed.

2. Fibrin Adhesive

Fibrin is a natural biopolymer formed by thrombin and fibrinogen in the blood-clotting cascade. Fibrin is known for its viscoelastic behavior, which has led to the widespread surgical application of fibrin glues [43]. It can be used alone or as an adjuvant to arthroscopic repair of delaminated cartilage flaps [44]. In the hip, success rates between 74 and 93% were seen with the use of fibrin for treatment of acetabular flaps in patients undergoing arthroscopy for FAI [45, 46]. In patients who had revision hip arthroscopy and were previously treated with repair for acetabular flaps, it was found that the wave sign was absent in 85% of the cases, suggesting that the technique was successful [47]. Recent evidence questioned the benefit of refixation of delaminated chondral flaps in FAI, with histology revealing that delaminated cartilage has a smaller proportion of viable chondrocytes, a disrupted extracellular matrix, and lower chondrogenic potential compared to non-delaminated control cartilage samples [48]. In addition, fibrin glue did not provide sufficient fixation to repair chondral flaps on the acetabular surface when used alone in human cadaveric models [49]. Unless a suture repair was added, all glued flaps were detached early after gait cycle loading. Due to the sparse and inconsistent data available, more studies are needed to determine the benefit of the use of fibrin in acetabular chondral repair.

3. Biological Injections

A variety of biological injections exist to treat chondral injuries of the hip. These mainly include HA or PRP, in addition to other types of injections including corticosteroids (CS) and growth factors [3]. However, many of the published trials evaluated the benefit of these injections in the treatment of OA or as nonoperative treatment in FAI, as opposed to ACDs in the setting of hip arthroscopy [50, 51]. Moreover, there is still controversy over the superiority and indications among different types of injections [52].

A. Hyaluronic Acid (HA)

HA is a naturally produced glycosaminoglycan mainly found in the extracellular matrix of most human tissues and in the synovial fluid of the joints. HA has lubricating, viscoelastic, and anti-inflammatory properties that are important to the structural integrity of the chondral surface [53]. The use of viscosupplementation in OA is widespread in clinical practice despite its controversial benefit and high cost [54, 55]. Although the application of HA after MF has shown improved healing capacity and anti-inflammatory effect in animal models [56, 57], there are still no human trials reporting on the benefit of augmenting MF or the use of HA as injection during hip arthroscopy.

B. Platelet-Rich Plasma (PRP)

PRP has been commonly used in a variety of surgical indications including tendinopathy, OA, and chondral defects [58]. PRP is derived from autologous blood centrifugation which separates the plasma component with a high concentration of platelets and platelet-derived growth factors implicated in tissue healing [58]. It can be used as direct injection or in conjunction with fibrin to form a membrane [59]. PRP was found to have the highest rank for pain relief for up to 6 months among different intra-articular injections as therapy for hip OA [52]. PRP augmentation is commonly reported following surgery; however, intra-operative injections are emerging [60, 61••]. Biologic augmentation to MF with PRP has also been suggested to improve clinical outcomes in the treatment of cartilage lesions [60, 62]. The clinical benefits of intra-operative PRP in the knee and ankle showed improvement at short-term follow-up [60]. However, the benefit was not perceived by the patients since the difference did not reach the minimal clinically important difference (MCID) for the reported scores.

PRP use in hip arthroscopy has only targeted FAI and labral tears with controversial outcomes [61••, 63, 64]. LaFrance et al. evaluated the effect of PRP versus placebo in 35 patients treated for labral repair and femoral neck osteoplasty [65]. There were no significant differences in outcomes in both groups although the PRP group included more patients with acetabular chondral injuries. A similar randomized controlled trial showed that PRP injection did not have additional benefits with regard to labral integration and healing, but had less acute postoperative pain and decreased joint effusion on MRI at 6 months [64]. However, the authors did not report on the presence of ACDs or their healing capacity on MRI. A case series of patients who received hip arthroscopy for labral tears included 308 patients, with 104 receiving PRP at the end of the procedure and 202 receiving local anesthetic. All patients had a minimum 2-year follow-up and had similar chondral injuries at baseline. There were no significant differences in functional outcomes or conversion to THA [66]. These results suggest that PRP is not beneficial for patients undergoing hip arthroscopy for FAI; however, there are limited studies and variability in PRP preparation [61••].

Cell-Based Approach

The cell-based approach encompasses all techniques involving the transfer of chondrocytes or mesenchymal stem cells (MSCs). Different scaffolds can be used as matrices to enhance ACI; hence, these techniques are called matrix-assisted ACI (MACI) which are typically used for medium to large ACDs [10]. Similar to the first category, different solutions including different types of MSCs can be used as adjuncts to MF or as separate injections as well.

1. ACI

ACI is a two-step procedure that helps with hyaline cartilage regeneration and is recommended for the treatment of medium to large chondral defects (> 2 cm^2) [10]. Chondrocytes are first harvested from a donor site, expanded through in vitro culture, and then are reintroduced in the joint [67]. In the hip, chondrocytes can be harvested from the femoral head neck junction or areas surrounding the pulvinar [68, 69] with baseline chondrocyte viability exceeding 50%, with the ability to reach above 90% after culture [70, 71]. More importantly, immunohistochemistry for collagen and aggrecan showed a pattern resembling that of hyaline cartilage. ACI was first described using a periosteal flap to support the implantation of chondrocytes for treatment of chondral knee defects [72], but the first generation of this technique has not been performed in the hip.

A. MACI

MACI is a second-generation ACI that relies on absorbable scaffolds to support the implanted chondrocytes. Similar to AMIC, different matrices have been described including collagen-, hyaluronan-, and fibrin-based matrices, or mixed

polymers [13, 73]. The patch can be fixed with fibrin glue or sutures. A recent systematic review of MACI showed favorable mid- to long-term clinical outcomes in the knee, with a 9.7% failure rate [13]. However, few of these products have been documented in the hip due to difficulty of fixation.

BioSeed-C® (BioSeed) (BioTissue AG, Freiburg, Germany) is a polymer scaffold composed of fibrin, polylactic/polyglycolic acid, and polydioxanone [74]. BioSeed has demonstrated improved short- to mid-term functional outcomes for ACDs between 2 and 4 cm^2 consequent to FAI [75]. No adverse events or clinical failures were observed over 5 years. MACI with BioSeed was also compared to debridement in the treatment of combined acetabular and femoral head chondral defects with a mean follow-up of 74 months [69]. Significantly better outcomes were observed in the MACI group over the whole duration of follow-up. MACI using BioSeed seems to be safe and effective for the treatment of medium-sized ACDs, but the level of evidence is low.

NOVOCART® Inject (Novocart) (TETEC AG, Germany) is an injectable scaffold introduced to overcome the difficulty of solid scaffold fixation. Novocart, a hydrogel formed by a combination of human albumin and HA, produces in situ polymerization when combined with autologous chondrocytes, allowing the solution to bond to the defect without additional fixation [76]. The feasibility of injectable ACI for full-thickness cartilage defects in the hip was demonstrated in recent studies [68, 76, 77]. The first case series reported on the use of Novocart in the hip for full-thickness ACDs with a mean defect size of 1.91 cm^2 [77]. All patients showed significant improvement regardless of the size of the defect at 12 months post-treatment. Unfortunately, the follow-up was short with no MRI or second-look surgery evaluating the quality of repair. Similar short-term studies evaluated MACI with Novocart [68, 76]. Only one study used MRI to assess the defect filling at 12 months post-operatively, and it showed complete filling of the defect in 55% of patients, with total integration at the borders of the defect in 80% of patients [76]. Unexpectedly, the authors showed better functional improvement with larger defect sizes, which could relate to the importance of the effect of large ACDs on the shear stress during the gait as previously mentioned. Only two adverse events were reported so far, including septic arthritis and persistent pain, which could be related to the scaffold [76]. Novocart seems to be an easy and safe way to administer ACI with promising outcomes; however, more trials with longer follow-ups are still needed.

B.Three-Dimensional (3D) ACI

The evolution of ACI entailed the development of 3D matrices introducing the third generation of ACI [74]. The culture process generates redifferentiated autologous chondrocytes with their derived extracellular matrix and produces scaffold-free 3D spheroids of neocartilage [74, 78••]. These are injectable solutions, and therefore, the second step of chondrocyte implantation is similar to injecting scaffolds into the defect site. Similar to Novocart, the ease of application of this technique, the adhesive properties of the solution, and the absent risk of scaffold fixation failure have led to numerous reports evaluating the efficacy of 3D-ACI in the treatment of chondral defects with promising results both in the knee and the hip [68, 78••, 79–82].

Chondrosphere® (Co.don AG, Germany) is the hallmark of this generation. The longest series of patients showed improved mHHS and iHOT scores, irrespective of defect size (average: 4.9 cm^2), at 3-year follow-up [82]. This series found two cases of failed cell cultivation with no other major complications. Others reported on a similar patient population and found that Chondrosphere was easy to apply and had favorable results, even in patients with large defects [80]. A prospective evaluation of 16 patients found a significant clinical improvement 6 weeks after surgery that persisted at the last follow-up (average: 16 months), with two patients reporting decreased range of motion resulting in revision arthroscopy [81]. The second look of the chondral defects showed complete healing and restoration of hyaline cartilage in the two cases. 3D-ACI appears to be a safe and effective treatment for medium to large ACDs; however, further studies are required to determine whether the benefits outweigh the risks of the longer culture time and complexity of preparation which may lead to failure [74].

2. Osteochondral Allograft Transplantation (OAT)

OAT is recommended for treatment of large chondral defects with good survival rates in the knee and ankle [83, 84]. However, only few studies reported on the use of this technique in the hip. Most of these cases involved treatment of femoral head lesions with open surgical dislocation of the hip [85–87]. Krych et al. were the only ones to report on two patients with focal ACDs treated by OAT [88]. Both patients were young adults and showed improved HOS outcomes with no progression of OA at 2+ years post-operatively. MRIs at 18 months post-operatively demonstrated the incorporation of the allograft bone into the host acetabulum. Thus, the authors believed that OAT for ACDs is a feasible option to restore joint congruity.

3. Augmented MF with Stem Cell Therapy

With MF being the most common technique used worldwide for chondral defects [42••], augmenting MF with biologics is rapidly evolving as more favorable outcomes can be expected when compared to MF alone, especially in medium to large defect sizes [26•, 38, 41, 89••]. MF alone yields fibrocartilage that is softer and more prone to shear stress than hyaline cartilage, which may explain the poor outcomes in large defects and at long-term follow-up [74]. As previously mentioned, many biologics can be used to augment MF;

however, this part of the review will focus on augments involving transfer of stem cells in the defect area, which are believed to restore hyaline-like cartilage. Mesenchymal stem cells (MSCs) can be harvested from different sources of the body and, hence, named after their sources. These include bone marrow (bone marrow–derived MSCs (BM-MSCs)), fat tissue (adipose tissue–derived stromal cells (ADSCs)), synovium (synovial-derived MSCs), and many other tissues. A recent systematic review included 28 studies that investigated the use of intra-articular MSC therapy for OA and chondral defects and found strong evidence that MSCs are safe and can yield positive outcomes [90].

A. BM-SMCs and bone marrow aspirate concentrate (BMAC)

MSCs in bone marrow aspirates represent only 0.001–0.01% of mononuclear cells, even when harvested from the iliac crest, which has the highest percentage of MSCs [91, 92]. BMAC is the concentration of the whole marrow aspirate in order to concentrate nucleated cells and growth factors that potentially can enhance the amount of MSCs [93]. Despite the lack of strong evidence, BMAC has been commonly used to treat chondral defects around the knee [92, 94]. In the hip, BM-MSCs are commonly used to treat avascular necrosis of the femoral head with promising outcomes [95], and it has recently translated for arthritic hips with chondral defects in isolation or after hip arthroscopy with promising outcomes as well [96–98]. A single BMAC injection can improve pain and function up to 6 months in patients with symptomatic hip OA [99].

More recently, studies have evaluated the use of BMAC during hip arthroscopy [89••, 100••]. Stelzer and Martin were the first to introduce their technique that combines BMAC with PRP to augment labral repairs and to coat the chondrolabral junction [101]. Rivera et al. compared the results of 40 patients treated with hip arthroscopy for FAI with BMAC injected at the end of the procedure, to a control group without injection, and found improved mHHS and iHOT at 1 and 2 years post-operatively [100••]. More than 50% of the patients in each group had high-grade chondral lesions. One study evaluated the use of BMAC with AMIC and Chondro-Gide in the arthroscopic treatment for ACDs, showing improved function and better recovery compared to patients who just received MF [89••]. Moreover, the MF group had 32.6% failure rate at 18 months and the BMAC + Chondro-Gide had none. Augmented MF with BMAC therapy during hip arthroscopy is a feasible option for the treatment of ACDs. However, these observations are only derived from few retrospective series with short-term follow-up and prospective/randomized trials are necessary to validate its efficacy on the mid- to long-term follow-up.

B. ADSCs and Microfragmented Adipose Tissue Transplantation (MATT)

ADSCs can differentiate into different types of cells including bone and cartilage [102]. Unlike bone marrow, ADSCs are easy to isolate in large quantities with minimal donor site morbidity. Compared to BM-MSCs, ADSCs have a higher proliferation rate [102]. Similar to BM-MSCs, data on ADSCs is more robust with regard to knee OA and focal chondral defects, with good to excellent results. More importantly, it has a good safety profile with a low rate of minor complications and absence of major complications [103, 104]. Different formulation protocols are available for ADSCs, but isolation of MSCs from fat can be done either through a mechanical or an enzymatic process [105].

MATT through Lipogems® (Lipogems) (Lipogems International SpA, Milan, Italy) is one of the described mechanical methods used to isolate ADSCs [105]. Lipogems is a fat-processing device that isolates the cellular component of the harvested autologous fat, producing micronized fat that can be injected into the joint at the end of the procedure [73]. This technique has been shown to generate higher amounts of progenitor cells and MSCs compared to the normal lipoaspirate [93]. Few studies reported on the use of Lipogems in the hip. ADSCs were used in six patients with low-grade OA and showed functional improvement in their preliminary results at 6 months [106]. A comparative study evaluated Lipogems during hip arthroscopy for the treatment of ACDs (1–2 cm^2 in size) in patients with Tonnïs grade of 0 or 1 [107]. They compared 18 patients treated with MF with 17 undergoing MF + MATT, and showed improved clinical outcomes at 2 years with significantly higher mHHS scores in the MATT group. Neither study reported any complications and or difficulty with liposuction. ADSCs may be a safer and easier alternative to BM-MSCs for the treatment of small ACDs during hip arthroscopy. Both techniques can be done in a single-step procedure, but more studies are required to better delineate the indications for each technique.

Comparative Studies Evaluating Biological Augments in ACDs

To date, there are still no robust comparative studies assessing the superiority of one technique over another in different joints [29, 108]. This is partly related to the high number of surgical armamentaria performed by surgeons to treat chondral injuries. In the hip, data is more scarce and even comparison of standard techniques failed to show differences in outcomes [109]. One of the main reasons explaining the difficulty of comparison of these techniques was the influence of the lesion size on the surgical indication, as small defects were typically treated with debridement and MF, and larger defects with ACI. To date, there are no randomized trials comparing biological treatments for ACDs in hip arthroscopy, but some

observations can be noticed from some comparative series or when pooling data together from systematic reviews.

It is evident that augmented MF whether using a scaffold solution or MSCs is superior to standard MF [26•, 100••, 107], but there are no reports comparing two different augmented MF techniques. Similarly, the use of ACI or AMIC for medium-sized ACDs showed superior functional outcomes at short- and mid-term follow-up versus standard MF [110••]. However, no difference could be observed between ACI and AMIC. Only one retrospective series compared clinical outcomes between MACI with BioSeed (n = 26) and AMIC with Chondro-Gide (n = 31) for the treatment of medium-sized ACDs [75]. Both groups showed significant functional improvements that remained stable for 5 years without any significant differences. The authors concluded that AMIC is preferred as a single-stage procedure that can reduce total treatment time and minimize morbidity while providing the same beneficial effects as the two-stage MACI intervention. The work of Thier et al. might be the only one so far comparing two methods of MACI in the hip [68]. Nineteen patients treated with Novocart were compared to 10 patients treated with Chondrosphere. Both groups showed clinical improvement without significant differences in short-term outcomes or complications. The authors mentioned one possible advantage of Novocart related to its remarkable bonding capacity.

New Directions

Regenerative medicine and the use of biologics are rapidly evolving. Newer scaffolds are being manufactured with the aim of regenerating hyaline or hyaline-like cartilage. Biocartilage® (Arthrex) is a dehydrated allograft cartilage extracellular matrix composed of type II collagen, proteoglycans, and cartilaginous growth factors [111]. The use of scaffolds made from dehydrated cartilage has shown to stimulate stem cells in a chondrogenic pathway, generating cells similar to articular cartilage cells [112]. Biocartilage has been used in combination with PRP in different joints [111, 113, 114], and was recently described in ACDs [115]. The use of Biocartilage + PRP was found to generate improved cartilage repair in an equine model when compared to MF alone [116]. More trials are necessary to validate its safety and benefits in the treatment of ACDs. In addition, as research is focusing more on bioactive scaffolds, enhanced scaffolds are emerging as well.

There are many biological treatment options that surgeons can choose from to treat chondral defects. Surgeons tend to prefer single-step procedures that combine biologics to enhance chondral healing while reducing cost and morbidity [75, 115, 117]. Autologous harvest of chondrocytes from the femoral head neck junction showed viable chondrocytes that could be combined with an enhanced extracellular matrix, and the mixture is reinjected in the defect area [71, 117]. This avoids the two-step procedure required for a standard ACI or a MACI, and may be an area of interest.

Stem cell therapy is witnessing a surge in innovations as well, with different formulations and solutions available. Synovial MSCs are an alternative that can be harvested from the synovial tissue to be used in a single arthroscopic procedure and to avoid donor site morbidity [118]. In the hip, synovium derived from the cotyloid fossa proved a potential source of MSCs [119]. The use of BM-MSCs differentiated to chondrocytes prior to implantation is a recent alternative to MACI. Application of these pre-differentiated chondrocytes combined with Chondro-Gide in treating full-thickness chondral defects showed promising outcomes in the knee [120]. The use of BMAC combined to scaffolds is recently emerging, with promising outcomes in the knee and hip. The use of BMAC with an HA-based scaffold showed good to excellent outcomes in the treatment of knee chondral defects in a series of 28 patients (mean follow-up: 8 years) [28]. Similarly, the use of PRP in combination with ADSCs has superior fat graft survival. One disadvantage of using fat has been the high resorption rate, but the combination with PRP has shown greater adipocyte proliferation, higher neovascularization, and less vacuolization [121]. The addition of HA to BM-MSCs has also shown improved chondral repair in chondral defects in animal models compared to BM-MSCs or HA alone [122]. Thus, the combination of different biological solutions could prove beneficial in the treatment of ACDs.

Conclusions

As arthroscopic hip preservative procedures remain the preferred treatment for patients with ACDs and early OA, the use of biologics holds high promise for improving functional and radiological outcomes in cartilage repair. Presently, the level of evidence is low, but in general, biologics appear safe and trend toward being beneficial compared to standard surgical techniques. Augmented MF is recommended for small to medium ACDs, and MACI or 3D ACI are recommended for medium to large defects.

Declarations

Conflict of Interest Dr. Johnny Rayes declares that he has no conflict of interest.

Ms. Sara Sparavalo declares that she has no conflict of interest.

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Human and Animal Rights and Informed Consent This article does not contain human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

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