

Five-year results of arthroscopic techniques for the treatment of acetabular chondral lesions in femoroacetabular impingement

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Abstract

Purpose This study assesses and compares the clinical outcomes of the arthroscopic matrix-induced autologous chondrocyte implant (MACI) and autologous matrix-induced chondrogenesis (AMIC) techniques for the treatment of acetabular chondral defects between 2 and 4 cm² consequent to femoral acetabular impingement.

Methods Fifty-seven consecutive patients were treated with the MACI ($n=26$) or AMIC ($n=31$) technique. Patients were assessed pre-operatively and up to five years using the modified Harris Hip Score (mHHS) to compare outcomes.

Results In both the MACI and AMIC groups, significant hip score improvements were measured over baseline levels at six months post-op (81.2±8.4 for MACI, 80.3±8.3 for AMIC, both $p<0.001$). The mHHS continued to improve up to three years post-op and remained stable over time until the final five year follow-up. Statistically significant differences between the groups were not observed. The mean mHHS improvement at the five year follow-up with respect to preoperative level was 37.8±5.9 and 39.1±5.9 in patients who underwent MACI and AMIC, respectively (NS). Subgroup analysis of both MACI and AMIC treatment outcomes for patients with an initial chondral defect larger than 3 cm² yielded comparable results at each time point.

Conclusions This study suggests that both arthroscopic MACI and AMIC are valid procedures to repair medium-sized chondral defects on the acetabular side of the hip found during treatment of femoroacetabular impingement. Due to its

high sustainability and minimal invasiveness, the single-stage AMIC procedure can reduce total treatment time and minimise morbidity while providing the same beneficial effects as the two-stage MACI intervention.

Keywords Hip arthroscopy · MACI technique · AMIC technique · Acetabular chondral defects

Introduction

Femoroacetabular impingement (FAI) is a common cause of hip pain most frequently affecting athletes and active young individuals [1–4]. Although FAI is often compounded by acetabular cartilage damage and labral lesions, rapid return to health is of personal and economic importance, particularly in such patient groups [5–7]. Choice of treatment option to repair cartilage defects in the hip depends on the size and severity of the injury. Specifically, small, partial thickness defects are often treated with arthroscopic debridement [1], whereas full-thickness defects smaller than 2 cm² are generally treated with microfracture (MFX) and show good outcomes [1, 8–10]. Indeed, most patients treated with MFX realise complication-free functional improvement, are able to resume an active lifestyle and return to sport [11, 12]. Conversely, MFX is known to be less effective in patients with larger chondral lesions (2–4 cm²) or early osteoarthritis [13].

In the knee and talus, large chondral defects are successfully treated with autologous chondrocyte implantation (ACI) or matrix-associated autologous chondrocyte implantation (MACI) [14–22]. ACI has also been effectively used in the hip. Both ACI and MACI are two-stage techniques where chondrocytes are harvested from the patient, cultured and then returned to the patient in a second surgical intervention.

Autologous matrix-induced chondrogenesis (AMIC) is a single-stage procedure combining MFX with the use of a

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collagen I/III matrix (Chondro-Gide, Geistlich Pharma AG, Wolhusen, Switzerland). Through MFX, the chondrogenic blood clot formed containing cells, cytokines and growth factors is stabilised and protected by the collagen matrix. AMIC has been used to successfully repair chondral and osteochondral defects of the knee [23–25], talus [22, 26] and hip [27, 28].

The aim of this study was to evaluate and compare the long-term performance and efficacy of MACI and AMIC for the treatment of mid-sized acetabular chondral lesions (2–4 cm²) found during arthroscopic treatment of FAI in a group of selected patients.

Materials and methods

Between 2002 and 2008, 143 patients underwent arthroscopic MACI or AMIC procedures for the treatment of acetabular chondral lesions, all performed by the same senior surgeon. These techniques were used to repair grade III and IV (Outerbridge classification) [29] acetabular chondral lesions, mostly located in the superior chondral acetabulum, consequent to FAI. Of the 143 patients, this retrospective, non-randomised study includes 57 consecutive patients who satisfied the following inclusion/exclusion criteria. Patients between the age of 18 and 50 with acetabular chondral lesion size between 2 and 4 cm² with radiological Tönnis degree <2 who were followed up to five years were included. Patients with concomitant presence of femoral head chondral lesion (kissing lesion), systemic rheumatoid diseases, dysplasia, femoral neck axial deviations, coxa profunda and/or protrusio acetabuli were excluded. Among these 57 patients, 26 were treated with MACI (from November 2002 to June 2005) and 31 with AMIC (from November 2004 to June 2007) (Fig. 1). In the overlapping period during which both techniques were used, six patients were treated with MACI and 15 with AMIC. The choice to treat a patient either with AMIC or MACI was made on an economic basis.

For all patients, the primary indication for surgery was FAI diagnosed with the aid of standard anteroposterior (AP) and Dunn view radiographs and magnetic resonance imaging (MRI), in accordance with commonly accepted criteria [30–33]. For cam-type impingement, arthroscopic femoral head-neck resection arthroplasty was performed to eliminate the bony prominence that impinges the labrum and acetabular rim and to restore the anatomic offset between the femoral head and neck. In case of pincer-type impingement, arthroscopic acetabular rim trimming was performed to reduce the bony overhang and to reshape the acetabulum into its normal contour. An eventual detached labrum was reattached to the superior acetabular rim with suture anchors. Mixed cam-pincer impingements have been surgically addressed for both pathologies. Dynamic tests were performed moving the hip

along its full range of motion checking the absence of any remaining bony impingement [34, 35].

Surgical technique

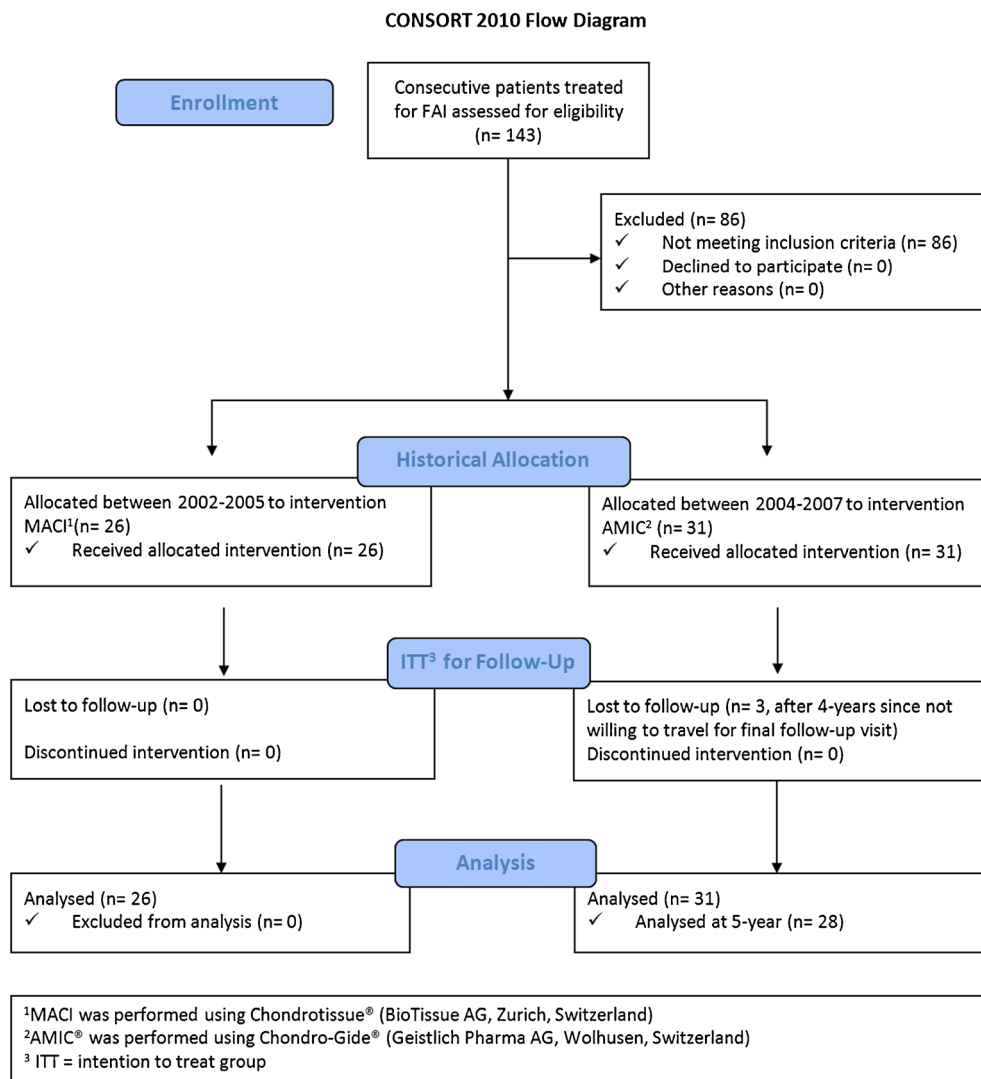
MACI Following the arthroscopic diagnosis of chondral damage, a cartilage biopsy from the area surrounding the pulvinar was taken. Chondrocytes were isolated, expanded and seeded onto a polymer scaffold composed of fibrin, polylactic/polyglycolic acid and polydioxanone (Bioseed-C, BioTissue AG, Freiburg, Germany). About three weeks thereafter, in a second intervention, graft implantation was performed arthroscopically as previously described [36]. Briefly, the chondral defect was accurately debrided and fibrous tissue removed to expose the subchondral bone. Care was taken to create clear margins between the healthy cartilage and the lesion in order to properly measure the chondral defect with an arthroscopic probe. After removing the fluids from the joint space by continuous aspiration, the cellular matrix was trimmed to the size and shape of the chondral defect area, inserted using an arthroscopic cannula and the lesion was covered (Fig. 2).

AMIC This procedure was performed arthroscopically in a single surgical stage as previously described [24]. During the procedure a resorbable collagen I/III matrix (Chondro-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) was placed to cover the acetabular chondral defect, after MFX of the subchondral bone. Briefly, the chondral defect was measured with an arthroscopic probe and standard MFX was carried out. Bone marrow bleeding from the holes was verified after removing the fluids from the joint space by continuous aspiration. Destroyed and unstable cartilage was removed using angled curettes or motorised shavers to achieve a well-contained defect. The Chondro-Gide matrix was cut to fit the size and the shape of the lesion and placed on the chondral defect with the porous layer facing the bone surface through an arthroscopic cannula (Fig. 3).

The post-operative rehabilitation programme was identical for both groups. On the first post-op day, patients began rehabilitation with isotonic and isometric quadriceps and gluteus contractions. Walking was allowed with the aid of two crutches with partial weight-bearing (30 % of body weight) on the operated leg for three weeks. Cycling exercises started from post-operative day two, whereas swimming was allowed after three weeks. At four weeks post-op, walking with the aid of one crutch opposite to the recovering leg was allowed for seven days, then normal walking thereafter. Impact sport activity could resume at three months post-op and complete return to sport activities was allowed six months after surgery.

All patients were assessed preoperatively and at follow-up after six, 12, 24, 36, 48 and 60 months using the modified

Fig. 1 CONSORT flow chart for patient enrolment



Harris Hip Score (mHHS) [37]. The mHHS assesses hip function with a maximum score of 91. Our results were rated as follows: excellent (81–91), good (71–80), fair (61–70) and poor (less than 60) [38]. Follow-up radiographic exams were only conducted in symptomatic patients. MRI assessment was

not performed due to non-coverage by the health insurances and second-look arthroscopy was not allowed by the Institutional Review Board (IRB). The study was approved by the IRB of the Institute and all patients gave their consent to the data collection and publication.

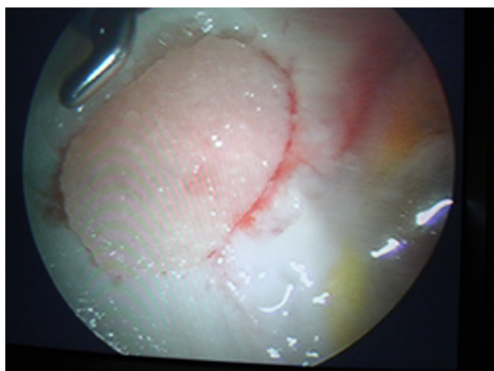


Fig. 2 Arthroscopic view of MACI procedure

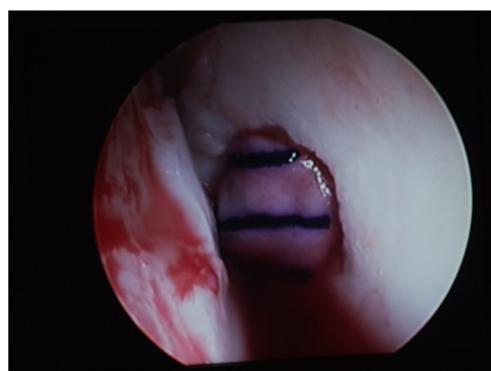


Fig. 3 Arthroscopic view of the final phase of the AMIC procedure

Statistical analysis

Comparison of the groups was performed using the two-way analysis of variance for repeated treatment time values. Variance analysis was preceded by a homogeneity of variances test (Mauchly's and Levene's) to verify the pertinence of parametric statistical methods. All analyses were done using the software package SPSS 11.0 and $p < 0.05$ was considered statistically significant. Data are reported as mean \pm standard deviation, unless otherwise indicated.

Results

A total of 57 patients, of which 26 underwent MACI and 31 AMIC, were clinically evaluated during the five year follow-up. Patient characteristics including demographics and defect assessments were comparable between the two groups (Table 1). In particular, the average age was comparable (36 ± 9.3 years for MACI and 36.4 ± 10.3 years for AMIC, NS) as well as the mean defect size (2.8 ± 0.7 cm² and 2.9 ± 0.8 cm² for MACI and AMIC, respectively, NS). Pre-operative mHHS was also similar between the groups, with mean scores of 46.5 ± 7 for the MACI group and 44.9 ± 5.9 for the AMIC group (NS). In the overlapping period during which MACI and AMIC were both performed (6 MACI and 15 AMIC), allocation into each treatment group did not affect the homogeneity of each group as the mean lesion size for these subgroups was comparable and similar to the respective whole population (2.8 ± 1 and 2.8 ± 0.8 for MACI and AMIC, respectively, NS; a lesion smaller than 3 cm² accounted for 50 % in the MACI group and 53 % in the AMIC group).

Significant improvement, as measured by the mHHS, was observed in both groups at 6 months in comparison to preoperative levels (81.2 ± 8.4 for MACI and 80.3 ± 8.3 for AMIC, both $p < 0.001$), with no significant difference between the groups. Continuous improvement with respect to each previous evaluation time point was seen, reaching the highest improvement level at the three year follow-up in both groups (85.5 ± 7.4 and 85.5 ± 7.2 for MACI and AMIC, respectively). The mHHS then remained stable over time until the final five

year follow-up, without any significant differences between the two groups. At each of the 12-, 24-, 36-, 48- and 60-month time points, the mHHS was significantly higher in comparison to the six month values in both groups (Fig. 4). The mean mHHS improvement recorded at the five year follow-up compared with preoperative scores was 37.8 ± 5.9 and 39.1 ± 5.9 for MACI and AMIC, respectively, without any significant difference between the groups (NS) (Fig. 5). No patient had a poor post-operative mHHS (all > 60). No significant differences were observed when comparing the subgroups of MACI and AMIC patients with an initial chondral defect larger than 3 cm² at all time points. In these moderately large defects, the mHHS of both subgroups significantly improved with respect to pre-operative values by six months post-op (82.8 ± 8.9 for MACI and 80.3 ± 8.9 for AMIC). In the subgroup of lesions larger than 3 cm² of both MACI and AMIC treatment groups, the improvements achieved by the three year time point were maintained at least up to the five year follow-up (85.2 ± 8.1 and 83.2 ± 8.5 for MACI and AMIC, respectively).

Second-look arthroscopy was performed incidentally in a patient treated with the AMIC technique. In this case, 13 months after surgery, the patient experienced haemorrhagic bursitis due to a fall occurring during a marathon. During the arthroscopic bursectomy, regenerated tissue with a fibrocartilage-like aspect and consistency was observed covering the whole defect (Fig. 6).

No adverse event was observed and no failure resulting in hip arthroplasty was detected in any of these patients during the five year follow-up.

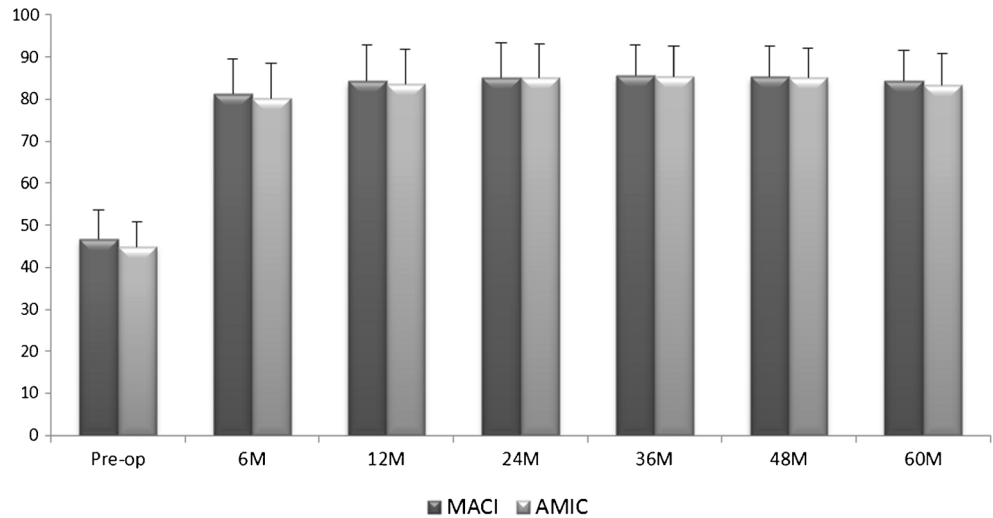
Discussion

To the best of our knowledge, this is the first study comparing long-term clinical outcomes up to five years in patients with medium-sized acetabular chondral defects resulting from FAI treated with the MACI or AMIC technique. Our results show comparable long-term clinical outcomes for repair of 2–4 cm² lesions with both MACI and AMIC, as assessed by mHHS. No impairment over time for either group could be seen. Instead, significant improvements were observed in both treatment groups up to the three year follow-up.

Table 1 Baseline characteristics of the study groups

	MACI ($n=26$)	AMIC ($n=31$)	<i>p</i>
Sex (M/F)	12/14	13/18	NS
FAI-cam (n)	16	21	NS
FAI-pincer (n)	13	16	NS
FAI-combined (n)	3	6	NS
Preoperative mean age (years)	36 ± 9.3 (19–50)	36.4 ± 10.3 (19–50)	NS
Preoperative mean defect size (cm ²)	2.8 ± 0.7 (2–4)	2.9 ± 0.8 (2–4)	NS
Preoperative mean mHHS	46.5 ± 7 (36–62)	44.9 ± 5.9 (38–60)	NS

Fig. 4 Pre-operative mHHS and up to 5 years after MACI and AMIC procedures



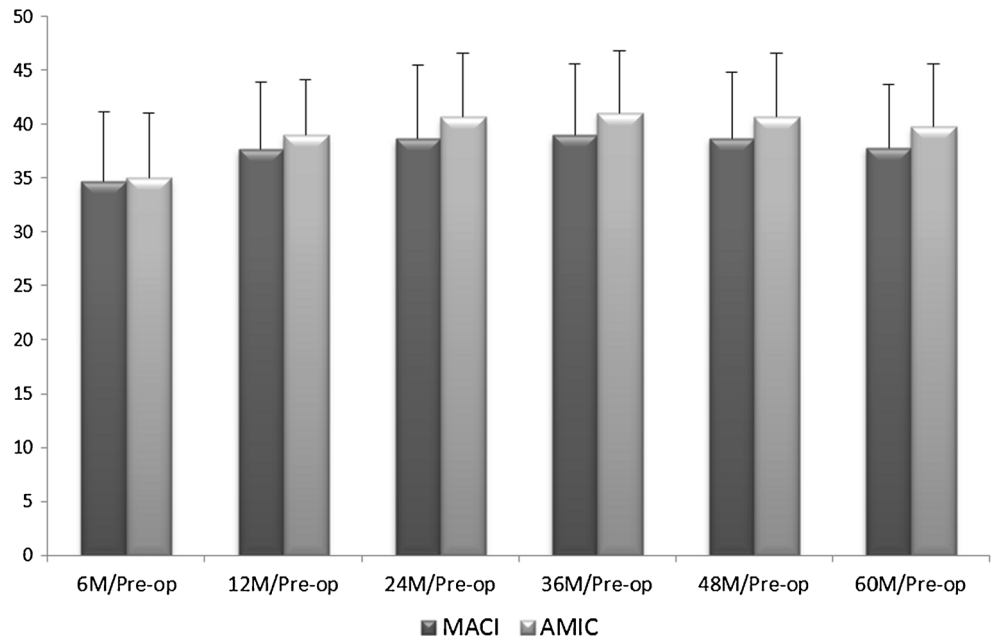
Moreover, subgroup analysis of patients presenting larger lesions (>3 cm²) yielded similar therapeutic outcomes between both treatment groups, demonstrating that AMIC can be reliably extended to 4 cm² defects. Several arthroscopic techniques have been used to treat full-thickness chondral defects of the hip in the past few decades. However, due to the more recent introduction of arthroscopy in the hip joint for FAI, published outcome studies on hip cartilage repair are scarce and comprehensive evidence-based treatment guidelines for chondral lesions of the hip remain to be defined.

MFx is still currently the first choice treatment for both acetabular and femoral head small chondral defects (≤2 cm²) as it is not invasive and very rarely has it been associated with major post-operative complications. Satisfactory clinical results after MFx of the hip [9, 13, 39–41], including athletes [10, 42], have been recently reported; however, the follow-up

reported for MFx in the hip did not exceed two years [10, 40, 43]. In comparison, knee MFx, which is also known to be effective for lesions ≤2 cm², has seen 47–80 % of cases reporting deterioration of knee function after two years [44]. Thus, clinical data relating lesion size, treatment choice and evaluation of cartilage repair procedures beyond two years are of critical importance to determine predictable and sustainable therapy for chondral cartilage defects of the hip.

Literature on the use of MACI for the treatment of medium-sized chondral defects in the hip is particularly scarce. The first case report by Akimau and colleagues [45] described the treatment of an extensive loss of cartilage and osteonecrosis in the hip treated with bone grafting and MACI using Chondro-Gide. Sixteen months after the procedure, the patient showed satisfactory clinical improvement and was able to return to daily activities. Another report described a

Fig. 5 mHHS differences between follow-up and preoperative level for MACI and AMIC procedures



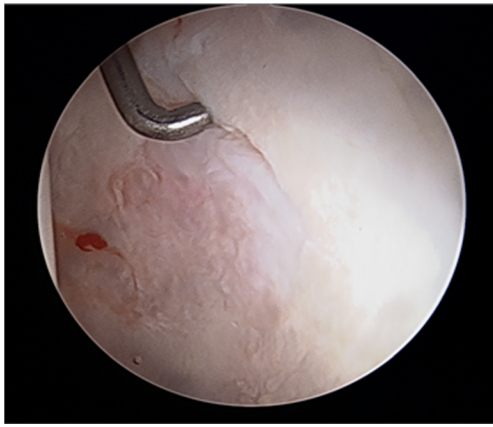


Fig. 6 Second look of an AMIC patient 13 months after surgery

patient who underwent MACI in the presence of a full-thickness loss around the osteochondral plugs consequent to autologous osteochondral mosaicplasty [46]. At the two year follow-up, the patient was pain-free and MRI showed good tissue repair with normal joint space. These limited results have been supported by a larger controlled retrospective study comparing arthroscopic MACI with debridement for the treatment of grade III/IV (according to Outerbridge) acetabular and femoral head chondral defects larger than 2 cm². A total of 30 patients were equally distributed in the two treatment groups, assessed at six months post-operatively and then yearly up to five years using the HHS. The results showed significantly better outcomes in the MACI group with respect to debridement at all evaluation time points. At the last follow-up, the HHS was 87.4 and 56.3 for the MACI and debridement groups, respectively. The best results were recorded in patients with acetabular defects treated with MACI and the positive outcomes were maintained over time. Despite these encouraging results about the use of MACI for the treatment of chondral defects of the hip, this technique is not associated with negligible donor site morbidity [47]. Further, partial chondrocyte dedifferentiation during two-dimensional in vitro expansion can result in the formation of fibrocartilage-like tissue once the graft is implanted [48]. Moreover, the MACI procedure is cost intensive because it requires two surgical interventions, and from a regulatory point of view, it is included in the so-called advanced therapy medicinal products (ATMPs) necessitating a more complex approval process.

Some of the MACI drawbacks can be overcome by AMIC, especially for the treatment of patients with medium-sized chondral defects. The AMIC technique spares donor site morbidity since effective cartilage regeneration can be stimulated in a single surgical intervention without the need for harvesting cells from a second site. AMIC exploits the regenerative potential of mesenchymal progenitor cells deriving from subchondral bone. The collagen type I/III matrix used in AMIC protects the blood clot and supplies the regenerating site with a proper microenvironment supporting cell adhesion,

growth and differentiation. Collagen matrices have previously been shown to support chondrogenic differentiation of mesenchymal stem cells [49] and to maintain chondrocyte phenotype [50], in particular when the matrix is composed of collagen types I and III [51]. The AMIC technique is further beneficial because it eliminates the need for specialised centres and laboratory support to cultivate cells, in turn reducing total therapy time and overall cost, compared to two-stage procedures such as MACI.

Our findings are in line with the results deriving from the treatment of cartilage defects of the knee and talus with the AMIC technique [23–25, 52]. Gille et al. [24] showed that patients affected by large grade IV (according to Outerbridge) chondral lesions experienced significant improvement in terms of five different evaluation scores at 12 months and up to 24 months after the AMIC procedure. Similar results were also found in a larger multicentre observational study including patients with grade III or IV chondral lesions, evaluated at the two year follow-up. Satisfactory outcomes were also reported for osteochondral lesions of the talus treated by AMIC [53] and confirmed in another study with a three year follow-up [22]. In addition, Wiewiorski and colleagues showed that, although neo-formed cartilage resulting from AMIC treatment of osteochondral lesions of the talus presents a significantly lower glycosaminoglycan content than normal hyaline cartilage, it can be considered as possessing hyaline-like properties [53].

Until now, long-term outcome data for the treatment of chondral defects of the hip utilising the MACI and AMIC methods were not available. Nevertheless, several studies in the knee showed that the MFX technique is associated with excellent short-/medium-term clinical outcomes [54, 55] which tend to decline over time. For this reason we examined the AMIC technique, which can be considered an evolution of the MFX technique, for its potential to overcome the problem of transient positive clinical outcomes. Our data demonstrate sustainable positive outcomes, reflected by high mHHS over a 5-year follow-up period, for patients who underwent AMIC or MACI procedures.

One of the limitations of our study is that it is a retrospective analysis of data collected over years of treatment. Patients were not randomised, but despite this, the patient baseline characteristics were comparable between groups. Another limitation is that clinical improvement was judged based only on the mHHS. Although this test has high validity and reliability [37], it is most suitable for assessment of functionality in elderly arthritic patients and might not be sensitive enough to assess subtle changes in function in young, otherwise healthy patients. Nevertheless, the improvement in these scores suggests that both MACI and AMIC provide clinical benefits to patients affected by a chondral lesion consequent to femoral acetabular impingement.

Finally, for ethical reasons, no biopsy of the neo-regenerated tissue was performed and thus histological data of the neo-tissue are not available. An incidental second look was however performed in a patient who underwent AMIC 13 months previously. Here, a satisfactory tissue quality with the fibrocartilage-like aspect was observed.

In conclusion, both the MACI and AMIC techniques allowed a marked clinical improvement in patients affected by chondral defects due to FAI, without significant differences between the two groups. This study suggests that both MACI and AMIC are valid procedures to repair medium-sized chondral defects on the acetabular side of the hip found during treatment of FAI and lead to long-term favourable outcomes. AMIC, due to its minimal invasiveness, single-stage procedure and proven safety, may be favoured with respect to minimising therapy time and cost. Accordingly, ongoing studies from our group intend to further investigate the clinical and economic benefits of the AMIC technique.

Conflict of interest The authors declare that they have no conflict of interest.

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