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Outcomes of Autogenous Osteochondral Mosaicplasty in the treatment of very large cartilage defects of the femoral condyles in young patients

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Abstract
Cartilage defects in femoral condyles of knee joint are a menace in young patients and cause severe pain and inability to climb stairs and carry out routine activities. This type of injury occurs commonly in sports activities. Knee articular cartilage defects > 4 cm2 are considered large defects. Treatment of articular cartilage lesions in the knee remains a challenge for the practising orthopaedic surgeon. A wide range of options are currently practised, ranging from conservative measures to various types of surgeries and recently, use of growth factors and emerging gene therapy techniques. The end result of these methods is usually a fibrous repair tissue (fibro cartilage), which lacks the biomechanical characteristics of hyaline cartilage that are necessary to withstand the compressive forces distributed across the knee. The fibro cartilage generally deteriorates over time, resulting in a return of the original symptoms and occasionally reported progression to osteoarthritis. Autologous Chondrocyte Implantation (ACI) is at present considered to be the gold standard treatment for large cartilage defects (size >4 cm^2) in the femoral condyles. The purpose of this study was to find out if the single staged, cheaper and easily accessible option of Autogenous osteochondral cylinder transfer or Mosaicplasty gives equivalent functional outcomes as compared to ACI in the treatment of large cartilage defects of the femoral condyles in the young patients.

Keywords: Large cartilage defects in knee, Mosaicplasty, Autologous chondrocyte implantation (ACI)

1. Introduction
Articular cartilage lesions in weight-bearing joints often fail to heal on their own and may be associated with pain, loss of function and long-term complications such as osteoarthritis. Osteochondral injuries are both naturally and therapeutically irreversible with current treatment parameters. Inferior repair commonly occurs, but stable regeneration of hyaline cartilage has never been documented. Treatment of articular cartilage lesions in the knee remains a challenge for the practising orthopaedic surgeon. Decisions about whether and how to treat an individual lesion are problematic. A wide range of options are practised nowadays, ranging from conservative measures, simple arthroscopic interventions, marrow tapping techniques, osteochondral auto/allografting, cell-based techniques to the more recently developing growth factors and emerging gene therapy techniques. Regardless of the treatment method or the origin of repair factors, the end result is generally a fibrous repair tissue (fibrocartilage) which lacks the biomechanical characteristics necessary to withstand the compressive factors distributed across the knee during articulation. This fibrocartilage generally deteriorates over time, resulting in return of the original symptoms and occasionally reported progression to osteoarthritis.

Autologous Chondrocyte Implantation (ACI) is at present considered to be the gold standard treatment for large cartilage defects (size >4 cm^2) in the femoral condyles. The purpose of this study was to find out if the single staged, cheaper and easily accessible option of Autogenous osteochondral cylinder transfer or Mosaicplasty gives equivalent functional outcomes as compared to ACI in the treatment of large cartilage defects of the femoral condyles in the young patients.

1.1 Grading system for OSTEOCHONDRAL defects

Grade 1: Superficial lesions/softening
Grade 2: Involves <50% cartilage
Grade 3: Involves >50% cartilage
Grade 4: Involves subchondral bone involvement

1.2 Methods of operative management

1.2.1 Fragment refixation

Acute cases require careful curettage of the blood clots and any fibrous tissue, in order to avoid any damage to the subchondral bone at the base of the lesion. In chronic lesions, a more extensive curettage is required to debride the fibrous tissue covering the lesion and the sclerotic subchondral bone; then, it may be necessary to pack cancellous bone at the level of the surrounding osteochondral junction to favour the integration of the refixed fragment. The fragment can be refixed using different fixation devices (bone pegs, K-wire, pins, compression screws, biodegradable pins, sutures). The most superficial part of the fixation device should be kept 2 mm below the level of the cartilage surface in order to avoid mechanical damage on the opposite cartilage surface. In case part of the fragment is severely damaged, this part can be removed and the fragment refixed through an additional autologous osteochondral transplant. Good clinical results have been reported using these different devices. Moreover, some studies have analysed the histology of refixed fragments. Chondral fragments resulting from acute delamination showed healing into the subchondral bed, with no evidence of fibrous tissue and a normal transitional area with hyaline cartilage at 12 months after surgery. OCD cases also showed normal features of the refixed cartilage and the development of new bone trabeculae at 12 months after surgery.

1.2.2 Marrow stimulation

Even though in older patients marrow stimulation procedures (micro-fracture or drilling) are usually recommended only for small lesions, in younger patients these techniques may be indicated when a small detached fragment is severely damaged or not re-fixable. Good results can be expected, even for larger articular defects, thanks to the high intrinsic activity of resident bone marrow cells in this patient group. Moreover, these procedures represent a minimally invasive, relatively cheap and technically easy option to perform. This surgical approach can be performed arthroscopically, taking care to accurately prepare the damaged area, especially in case of chronic lesions. More generally, positive outcomes for micro-fracture have been reported to be correlated with younger age, even in high-level athletes. However, despite these satisfactory findings, there is agreement about the limitations in terms of the tissue quality produced by marrow stimulation: 90% of the biopsies after micro-fractures showed predominant fibrocartilage. Since fibrocartilage has inferior mechanical properties compared to hyaline cartilage, poor results are generally expected when treating large defects, with a rapid worsening of outcomes reported at midterm follow-up. Thus, the indication is mainly limited to small cartilage defects (<2 cm^2), with a higher chance of success in children or adolescent patients. The aetiology of articular cartilage defects in patients aged between 20 and 60 years old can be heterogeneous, ranging from traumatic to degenerative/micro-traumatic, OCD sequelae or osteonecrosis, reflecting the clinical history of the patient, different presentation, symptom modality and duration. Regenerative procedures are the preferred method in this age group, in order to maximise the body's self-regenerative potential and restore the defect with a tissue resembling as closely as possible the original one, aiming to obtain durable clinical benefits.

1.2.3 Autologus chondrocyte implantation (ACI)

ACI is the most documented regenerative method for the surgical treatment of large articular defects in young to middle aged patients. However, ACI has notable Disadvantages due to the need for two different surgeries – the first operation for the arthroscopic harvest of articular cartilage and after cell isolation and culture, the second for the implantation of cultured chondrocytes. The first generation ACI technique involved the injection of a cell suspension under an autologous periosteal flap that had been previously sutured to the edge of the surrounding cartilage to cover the defect. Beris *et al*. treated a group of 42 patients for large symptomatic chondral defects of the knee (mean size 5.3 cm^2), showing significantly improved clinical and functional scores at 8-year follow-up. Minas *et al*. reported the results of over 200 patients treated for very large lesions (mean size 8.4 cm^2) and observed durable outcomes at long-term follow-up and a 71% graft survivorship at 10 years follow up. Interestingly, the authors reported an increased risk of failure in patients with larger lesions and in those previously treated with microfracture for the same defect. Moreover, level one studies reported no clear difference in outcomes between ACI and microfractures at 60 months follow-up for the treatment of large lesions. Despite these good and durable clinical results using first generation ACI, a relatively high rate of graft hypertrophy, together with the need for an open and technically demanding surgery prompted the use of newer techniques in which the cultured cells are seeded into three-dimensional matrices (mainly type I/III collagen or hyaluronan). Some of these second generation techniques simplified the overall approach and even allowed for arthroscopic implantation. Further modifications include combination with autologous bone implants to address deeper lesions that are very frequently associated with large size defects or OCDs. These Matrix Assisted ACI (MACI) procedures have also been successfully used for the treatment of large lesions, with positive results at long term follow-up. Bigger focal defects can be treated up to 12 cm^2 in size; however, large lesions often occur in a degenerative joint environment, which is a relative contraindication for MACI procedures. Infect, MACI did not show superior mid-term results to those of microfracture when the onset of symptoms was more than 3 years before the operation. Saris *et al*. showed in a level one study that MACI produced superior results and a lower failure rate at 24 months follow-up in 137 patients treated for large lesions of the knee (mean size 4.8 cm^2). This superiority, however, was not reflected by MRI appearance of the repair tissue. Finally, some findings also highlighted poorer but still effective and durable results in patients older than 40 years, suggesting the possibility to extend the treatment indication to this age group, where the regenerative approach has traditionally been excluded. Beside some controversial findings, ACI procedures seem to produce better tissue repair quality and longer-lasting results than microfracture and currently there is an overall consensus for the treatment of large lesions with such a biological approach.

1.2.4 Osteochondral autograft transfer (OAT)

OAT techniques including mosaicplasty rely on viable osteochondral grafts to fill an articular defect through a

single-step surgery. Despite being reported to offer overall good and durable clinical results at long-term follow-up, their use for the treatment of large lesions is questionable due to technical limitations, graft availability and issues related to donor site morbidity. Thus, while OATs represent an affordable choice for the treatment of small size defects (usually not larger than 2.5 cm^2) requiring a limited number of plugs, autologous one step procedures are not indicated for large lesions. The mega-OATS technique was proposed as a salvage procedure for large osteochondral lesions of the knee. It involves the harvest of a significant part of the posterior knee condyle as a source of osteochondral graft, which is then prepared with a specific device. The few available studies show this technique has produced a significant clinical improvement at midterm follow-up, with satisfactory outcomes in terms of knee function. Paired with this, in a few cases positive MRI features were reported in terms of vitality of the graft and also partial remodelling of the posterior condyle. However, the loss of the posterior femoral condyle makes a certain degree of donor site morbidity unavoidable and the use of this procedure should be restricted to salvage procedures in young patients with large knee osteochondral defects and limited treatment alternatives.

1.2.5 Osteochondral allograft transplantation (OCA)

Osteochondral allografting allows the replacement of a damaged osteochondral unit with viable tissue, while avoiding the issues related to donor-site morbidity; thus, it is a suitable option for the treatment of a large surface area. The different storage methods (fresh, fresh frozen and cryopreserved) are important factors, since chondrocyte viability directly correlates with the clinical success of OCA transplantation and it has been shown that fresh OCAs stored at physiological temperatures have the highest chondrocyte viability. Fresh osteochondral grafts can be harvested and implanted through free hand technique or as described above for Mega-OATS implantation. This procedure is common in the United States, where the use of allografts is widespread. Excellent results have been reported in 122 patients by Levy *et al*. with 82% survivorship at 10 years, decreasing to 66% at 20 years follow-up. Patients over 30 years old who had two or more previous surgeries were associated with graft failure. On the other hand Gracit Elli *et al*. showed that, while previous bone marrow stimulation was correlated to a higher re-operation rate after osteochondral allografting, no influence was observed on graft survivorship or functional outcomes. Raz *et al*. also confirmed the benefits of OCA after up to 22 years follow up, with an acceptable survival rate of 59% at final-follow-up. Finally, limited and controversial data are available on more active patients, in terms of their return to previous sports or physical activity.

2. Materials and Methods

We carried out prospective study of 23 patients, with mean age of 27 years among them 18 were males and 5 were females. All patients selected had cartilage defect of >4cm^2 (mean 6.7cm^2) in weight-bearing zone of femoral condyle. All patients underwent proper pre-operative score assessment and clinical and radiological investigations. All patients were operated through standard parapatellar arthrotomy and mosaicplasty performed using specialised instruments (OATS instrument set-Arthrex). Ethical committee clearance was taken for this research project from the local ethics committee board.

All patients were operated by same para patellar approach, skin and subcutaneous tissue cut, knee arthrotomy was done, patella subluxated and cartilage defect exposed. Then the cartilage defect was assessed and loose unstable frayed out cartilage from the margins of the defect removed to achieve punched out margins of the stable healthy cartilage. Then osteochondral grafts of appropriate diameter were taken from the non-weight bearing portion of the lateral and medial femoral condyles (depending on the number of cylinders required) using specialised instruments and then the osteochondral cylinder graft implanted at the diseased area after removal of the exact size of cylinder from the cartilaginous defect portion in the weight bearing portion of the femoral condyle. The osteochondral cylinders were harvested and implanted in a direction exactly perpendicular to the surface of the surrounding cartilage. This is of paramount importance. Then proper joint lavage was given and wound closed layer wise after placing a negative suction drain inside the knee joint.

All patients were subjected through the same post-surgery physiotherapy protocol. Patients were allowed static quadriceps and ankle pumps as soon as effect of the spinal anaesthesia weaned off. 2nd post-operative day saw the patients doing active straight leg raising exercise and hamstring strengthening exercises. On the third post-operative day after the removal of the drain, patient was allowed to start knee bending on high sitting position by the side of the bed till 90 degrees of knee flexion. Local Cryotherapy was initiated immediately post-surgery and is continued till 3rd post-operative day. The patient was discharged on the 3rd post-operative day and was asked not to bear weight on the operated limb. He was called for stitch removal on the 15th post-operative day. Partial weight bearing on the operated lower limb with toe touch weight bearing with the use of a walker was initiated at 6 weeks post-surgery and full weight bearing started at around 3 months post-surgery.

All patients were called or follow up at 6 months and 12 months post-surgery. All patients underwent MRI scan of the operated knee on the same MRI machine which was used to do the pre-operative MRI scan at 1 year post surgery and the patient assessed using scores and MRI picture at 1 year follow up.

Ideally Autologous Chondrocyte Implantation is considered to be the gold standard treatment for such large defects in the knee but Autologous Chondrocyte Implantation is still not available for clinical use in our institute and also because of the high amount of cost involved in Autologous Chondrocyte Implantation, all these patients having large cartilage defects were treated using Mosaicplasty in our institute and the outcomes of those patients analysed and compared to the results of other international studies where Autologous Chondrocyte Implantation was done for similar defects.

2.1 Pre-operative images

Fig 1: Pre-operative MRI (A and B) and 3D CT scan (C) showing the large cartilage defect in weight bearing portion of Medial Femoral Condyle

2.2 Intra operative images

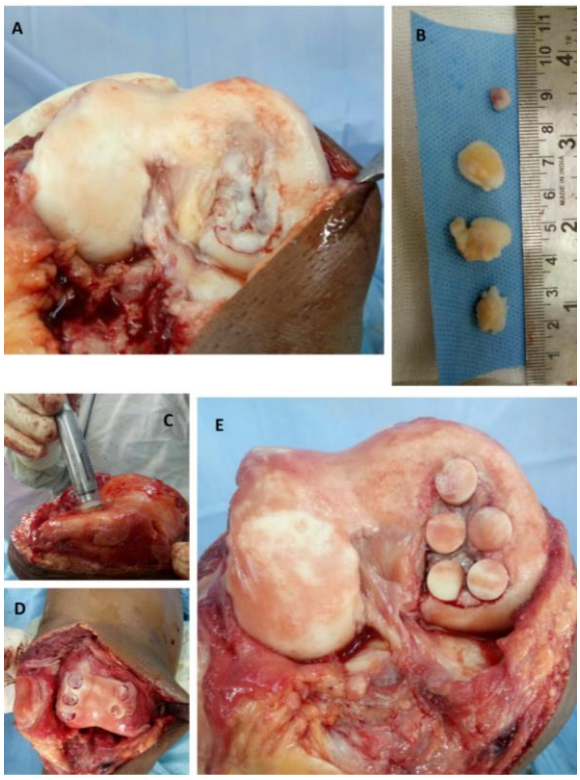

Fig 2: Show the Cartilage osteochondral cylinder

A. Cartilage defect measuring about 7 cm^2 on weight bearing portion of Medial Femoral Condyle
B. Cartilaginous loose bodies
C. Impaction of an osteochondral cylinder graft into the prepared recipient site
D. Donor site after harvesting osteochondral plugs from non-weight bearing portion of femoral condyles
E. Final construct after placement of all the osteochondral cylinders into the defect.

2.3 Post-operative images

Fig 3: Post-operative MRI full knee

A. Post-operative full knee flexion (0 to 140 degrees)
B. Post-operative ability of the patient to sit cross legged
C. Post-operative active full knee extension.
D. Post-operative MRI at 1 year follow up showing good integration of the plugs to the host bone and good cartilage regeneration and contour.

3. Results

At 1 year post-surgery, all patients were able to walk, climb stairs, even run without any assistance and had full Range of movement of the operated knee joint.

Table 1: Showing pre-operative and post-operative functional outcome scores

Scores	Mosaicplasty (current study)		ACI (LC Biant *et.al.*)	
	Pre Op	Post Op	Pre Op	Post Op
Pain VAS	8	1	7	1
Modified Cincinnati score	54	90	60	92
Knee Society Score	72	90	68	87
SF-36	58	93	56	96
Lysholm	53	89	51	80

Table 2: Showing MRI findings at 1 year follow up post-surgery

		Mosaicplasty (present study)	ACI (Ian Henderson *et al.*)
Donor site healing	Partial healing	4 (17.4%)	-
	Complete healing	19 (82.6%)	-
Recipient site healing	Partial healing	4 (17.4%)	3.6%
	Complete healing	18 (78.3%)	94.2%
	Rejection	1 (4.3%)	2.2%
Subchondral bone edema, cyst.		3 (13%)	11.6%
Cartilage continuity defects	Partial	4 (17.4%)	10.4%
	Complete continuous	18 (78.3%)	86.9%
	Totally uncovered	1 (4.3%)	2.7%
Cartilage surface counter	Irregular	7 (30.4%)	13%
	Regular	16 (69.6%)	87%
Osteo- arthritic changes	Grade-1	3 (13%)	10%
	Grade-2	2 (8.7%)	2%
	Grade-3	0%	0%
	Grade-4	0%	0%

Table 3: Showing number of patients according to the size of the defect

Size of defect	Number of patients
4-5 cm^2	7
5-7 cm^2	12
7-9 cm^2	4

Table 4: Showing number of patients according to the number of osteochondral cylinders used to fill up the defect

Number of cylinders used (10mm diameter)	Number of patients
3	3
4	6
5	10
6	4

4. Discussion

Large cartilage defects of the femoral condyles are rare but cause a lot of trouble to the patient. Autologous chondrocyte implantation (ACI) is considered to be the gold standard for management of such large defects and has stood the test of time in providing excellent outcome in such cases. But this procedure is fraught with many problems such as it is very expensive, two staged procedure and not easily available. Hence we treated such patients using the principles of Mosaicplasty.

We compared the functional and radiological outcomes of our study with other international studies which used ACI for treating these type of patients and found out that at short term follow up of 1 year post surgery, although Mosaicplasty lagged behind ACI in radiological signs of cartilage healing, but functional outcome parameters and scores of the patients in both the series were comparable.

All the patients in our series were having either excellent or good outcome at 1 year follow up both subjectively and objectively. All patients were able to walk, run, sit cross legged, squat and carry out all the activities of their daily living without any pain or discomfort at 1 year post surgery, similar to the results found in series where patients were treated with ACI.

5. Conclusion

The single-staged, cheaper and easily available option of Mosaicplasty may prove to be a boon for large cartilage defects of the femoral condyles in young patients and have excellent short term functional and radiological outcomes, almost equivalent to the results of Autogenous cartilage Implantation (ACI).

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