Original Article

Outcome of combined autologous chondrocyte implantation and anterior cruciate ligament reconstruction

Baljinder S Dhinsa, Syed Z Nawaz, Kieran R Gallagher, John Skinner, Tim Briggs, George Bentley

Abstract

Background: Instability of the knee joint, after anterior cruciate ligament (ACL) injury, is contraindication to osteochondral defect repair. This prospective study is to investigate the role of combined autologous chondrocyte implantation (ACI) with ACL reconstruction.
Materials and Methods: Three independent groups of patients with previous ACL injuries undergoing ACI were identified and prospectively followed up. The first group had ACI in combination with ACL reconstruction (combined group); the 2nd group consisted of individuals who had an ACI procedure having had a previously successful ACL reconstruction (ACL first group); and the third group included patients who had an ACI procedure to a clinically stable knee with documented nonreconstructed ACL disruption (No ACL group). Their outcomes were assessed using the modified cincinnati rating system, the Bentley functional (BF) rating system (BF) and a visual analog scale (VAS).
Results: At a mean followup of 64.24 months for the ACL first group, 63 months for combined group and 78.33 months for the No ACL group; 60% of ACL first patients, 72.73% of combined group and 83.33% of the No ACL group felt their outcome was better following surgery. There was no significant difference demonstrated in BF and VAS between the combined and ACL first groups. Results revealed a significant affect of osteochondral defect size on outcome measures.
Conclusion: The study confirms that ACI in combination with ACL reconstruction is a viable option with similar outcomes as those patients who have had the procedures staged.

Key words: Anterior cruciate ligament, autologous chondrocyte, chondrocyte, knee, osteochondral defect
MeSH terms: Anterior cruciate ligament, chondrocytes, autologous, knee

Introduction

Anterior cruciate ligament (ACL) injuries commonly affect the athletic patient, resulting in instability and impaired function. Articular cartilage injury to the knee may occur with ACL injuries in the acute setting, with incidence of 16–46%,[1,2] and in chronic ACL deficient knees.[3] The presence of articular cartilage damage can impact on the outcome from ACL reconstruction, with the suggestion that it is a predictor of failure.[4,5] Inadequately managed osteochondral defects predispose individuals to pain and early onset osteoarthritis of the joint.[6,7]

Patients with ACL deficient knees have an altered region of load bearing on the articular surface due to a shift in the tibiofemoral biomechanics.[8] The transmitted axial load through the articular cartilage and subchondral bone can culminate in the formation of chondral lesions.[9-11] At present, instability of the knee joint, after ACL injury, is a contraindication to osteochondral lesion repair.

Areas of articular cartilage damaged will repair without intervention, forming fibrocartilage rather than the original hyaline cartilage, with its inherent inferior mechanical properties.[12] Reported management options for osteochondral defects include physiotherapy, fibrocartilage forming (marrow stimulating) techniques such as debridement and curettage; bone drilling; abrasion chondroplasty; and microfracture. Articular cartilage autografting (such as mosaicplasty), and autologous chondrocyte implantation (ACI) are techniques aimed at hyaline cartilage repair.[12-16] Bentley *et al*.[17] have reported favorable outcomes of ACI over mosaicplasty for the

Joint Reconstruction Unit, Royal National Orthopaedic Hospital NHS Trust, Stanmore, Middlesex, HA7 4LP, United Kingdom

Address for correspondence: Mr. Baljinder S Dhinsa, Royal National Orthopaedic Hospital NHS Trust, Brockley Hill, Stanmore, Middlesex, HA7 4LP, United Kingdom.
E-mail: bsd14@hotmail.com

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repair of osteochondral lesions. Evolution of ACI techniques has led to the use of an inert porcine type I/III collagen membrane sutured to the chondral defect (ACI-C), with the cultured chondrocyte cells injected below the seal.[17-21] With matrix assisted autologous chondrocyte implantation (MACI), a porcine type I/III collagen bilayer is seeded with the cultured chondrocyte cells, which is then glued to the chondral defect using a fibrin sealant.[22,23]

This prospective study is to investigate the affect of correction of instability (ACL injury) on outcome of ACI procedures and to evaluate the results of a combined ACL reconstruction with ACI procedure.

Materials and Methods

Three independent groups of patients with previous ACL injuries who underwent ACI-C or MACI at our institution were identified and prospectively followed up. The first group had ACI in combination with ACL reconstruction (combined group); the 2nd group had an ACI procedure having previously had a successful ACL reconstruction (ACL first group); and the third group included had an ACI procedure for a chondral or osteochondral lesion to a clinically stable knee with documented ACL injury in the past, but had no reconstruction (no ACL group).

Combined group

Twenty two patients (14 male and eight female) who had combined ACL reconstruction with ACI, with an average age at the time of surgery of 32.2 years (range 20–45 years). Hamstring autograft[15] or bone-patella tendon-bone autograft (BPB) (seven) was used for the ACL reconstruction and MACI (19) or ACI-C (three) for ACI. Previous surgical procedures to these knees included medial menisectomy;[10] lateral menisectomy (three); screw fixation for osteochondral fragments (two); drilling of chondral lesions (two); previous ACL reconstruction (two) and osteochondral allograft to a chondral lesion (one). The mean area of defect was 300 mm^2 (range 225–600 mm^2) involving the medial femoral condyle,[16] lateral femoral condyle (three), patella (two) and with one patient having no documentation of site or defect size. Followup was for an average of 63 months (range 8–112 months).

Anterior cruciate ligament first group

Twenty five patients (20 males and 5 females) who had previous ACL reconstruction using hamstring autograft,[16] BPB (six) and synthetic graft (three) that underwent ACI for a chondral lesion. The average time from ACL reconstruction to the 2nd stage of ACI was 74.04 months (range 12–156 months). Mean age at time of 2nd stage procedure was 35.94 years (range 27–48 years), with 14 patients undergoing MACI and 11 had ACI-C. One patient had no documentation for the site and size of chondral defect. The average area of defect was 300 mm^2 (range 212–465 mm^2) involving the medial femoral condyle,[15] trochlea (four), patella (three), lateral femoral condyle (one) and multi site defect (one). Previous surgical procedures in the knees included medial menisectomy (eight); lateral menisectomy (three); drilling of chondral defect (three); microfracture (two); ACI (two) and open reduction with internal fixation of medial femoral condyle fracture (one). Followup was an average of 64.24 months (range 11–102 months).

No anterior cruciate ligament group

Twelve patients (10 male and two female) who underwent an ACI procedure to a knee that was felt to be stable, although there had been a previous nonreconstructed ACL injury. Eight of these patients had partial disruption and four of these had no laxity of the ACL. These patients presented with pain however their knee was felt stable on clinical examination and assessed further at first stage arthroscopy.

The Lachman test was utilized to assess the ACL in all 12, with three knees being graded as 0, seven as 1 and two as 2. Previous surgical procedures to these knees included; medial menisectomy (four); drilling to chondral defect (two); open reduction and internal fixation for proximal tibia and fibula fracture (one); lateral soft tissue release (one) and osteochondral allograft to a chondral lesion (one). The average age at time of 2nd stage procedure was 33.45 years (range 20–47 years), with seven patients undergoing MACI and five having ACI-C. The mean defect size was 225 mm^2 (range 150–500 mm^2), involving the medial femoral condyle (five), trochlea (three), lateral femoral condyle (two), patella (one) and multi site defects (one). There was one patient for whom we had no documentation for the size of the defect. Followup was for an average of 78.33 months (range 12–139 months).

There was another subset (complete rupture) within this group that was investigated separately; these patients were clinically stable although there was documented evidence of complete ACL rupture. There were four patients (three male and one female) with a mean age of 37.45 years, with two undergoing ACI-C and two having a MACI procedure. Three patients had a Lachman grade of 1+ and one was assessed as grade 2+, with average defect size of 524 mm^2 (range 300–660 mm^2) and the medial femoral condyle and patella were affected equally.

The diagnosis and treatment plan was formulated following clinical review, plain radiographs, MRI and arthroscopy. The Kellegren–Lawrence grading system was used[24] to assess degenerative changes on plain radiographs and the MRI findings were used to confirm this assessment. Prior

to surgery the patients completed the modified Cincinnati (MC) rating system questionnaire,[25] the Meister *et al*. functional rating (BF) system[26] and a visual analog scale (VAS).

Operative procedure

Each patient underwent a two stage procedure; an initial arthroscopy to assess the chondral lesion for suitability for ACI and if suitable a biopsy of nonweight bearing articular cartilage was harvested from the trochlea margin and sent for cell culturing. All the patients in the ACL first and No ACL group had stable knees on examination under anaesthesia. Postoperative management was routine for arthroscopy.

The 2nd stage was performed 4–6 weeks later, after satisfactory cell culture, in all patients. In patients in the combined group, the ACL reconstruction was performed prior to ACI. The ACI procedure was performed through either a medial or lateral arthrotomy incision, depending on site of lesion and the defect prepared before implantation. With ACI-C a template sized piece of porcine type I/III collagen membrane was sutured (using 6/0 vicryl) to the margins of the defect and a watertight seal ensured with the use of fibrin glue to the margins. This seal was checked by injecting a saline solution below the membrane, looking for leaks, prior to the cultured cells being injected below the membrane, and the final suture and glue applied to the membrane cartilage junction.[19] With MACI the chondrocyte cell seeded type I/III collagen bilayer membrane was cut to size to fit the defect and secured with fibrin glue.[22,27] The wound was closed in layers using nonabsorbable sutures, with wool and crepe pressure bandaging applied.

Rehabilitation

The patients in the ACL first and No ACL groups were placed in plaster-of-Paris backslab for 24 h, with rest and elevation advice, as well as foot and ankle exercise encouragement. After 24 h full weight bearing was allowed. The knee was placed in a lightweight cylinder cast in full extension at 48 h, which was removed on the 10th day postoperatively. The patients were progressively mobilized with daily physiotherapy for 2 weeks, after which more strenuous, low-impact activities were permitted. By 6 months light jogging was allowed and strenuous sports at 12 months if the knee was painless.

For patients undergoing the combined procedures, no range of movement exercises were permitted and the patients were placed in a hinged knee brace at 48 h postoperatively, for up to 4 weeks. From 28 h, they were progressively mobilized with regular physiotherapy to work on strength, core stability, proprioception and mobility. Closed channel active range of movement exercises were commenced after 1-week as symptoms allowed, but no open kinetic quadriceps work was started until 12 weeks. From 6 weeks controlled active range of movement, strengthening of muscles stabilizing the knee and core stability work was started. At 12 weeks, a full range of movement was achieved and exercises progressed from static to dynamic as tolerated. By 9 months patients returned to sport-specific activities, such as low-impact jogging in the gym and swimming and return to normal sports were achieved after 1-year.

Patients were reviewed at 6 weeks, 6 months, 1-year and then annually to assess them clinically. At these times, they were also asked to complete the MC questionnaire, BF and VAS score systems for postoperative evaluation. The patients also graded their outcome as better, same or worse.

Results

Patients in the three groups had varying baseline characteristics and scores for BF, VAS and MC preoperatively [Table 1]. Analysis was adjusted for these known variables.

Table 1: Clinical details of three groups

Variable	Procedure (%)		
	ACL first (*n*=25)	Combined (*n*=22)	No ACL (*n*=12)
Age at 2nd operation (in years)	35.9±5.3	32.2±6.6	33.5±10.4
Followup (months)	64.2±29.9	63±31.8	78.3±45.2
Baseline bentley score	3 (2, 3)	3 (2, 3)	3 (2.5, 3)
Baseline VAS score	5.2±1.8	5.3±2.2	5.8±2.1
Baseline cincinnati	56.2±13.5	46.2+/10.2	44.0±14.0
OA			
Grade 0	9, 36	12, 55	8, 67
Grade 1	6, 24	4, 19	2, 17
Grade 2	7, 28	4, 19	2, 17
Grade 3	3, 12	2, 9	-
	n=24	*n*=21	*n*=12
Site			
LFC	1, 4	3, 14	2, 17
MFC	15, 63	16, 76	5, 42
Patella	3, 13	2, 10	1, 8
Trochlea	4, 17	-	3, 25
Multisite	1, 4	-	1, 8
	n=24	*n*=21	*n*=11
Size	300 (212, 465)	300 (225, 600)	225 (150, 500)
ACI/MACI			
ACI	11, 44	3, 14	5, 42
MACI	14, 56	19, 86	7, 58
ACL recon			
Allograft	3, 12	-	-
BPB	6, 24	7, 32	-
Hamstring	16, 64	15, 68	-

ACL=Anterior cruciate ligament, VAS=Visual analogue scale, OA=Osteoarthritis, ACI=Autologous chondrocyte implantation, MACI=Matrix-assisted autologous chondrocyte implantation, BPB=Bone-patella tendon-bone autograft, LFC=Lateral femoral condyle, MFC=Medial femoral condyle

At final followup, 16 (72.73%) patients in the combined group reported their outcome as better, with six patients (27.27%) reporting the symptoms as the same as the preoperative level. All the knees in this group were found to be clinically stable on examination at final followup. In the ACL first group the outcome was better in 15 cases (60%), the same in six cases (24%) and worse in four (16%). The 12 patients in the No ACL group reported the outcome as better in 10 instances (83.33%) and the same in two patients (16.67%). This is in contrast to the complete rupture group; with 2 (50%) reporting a worse outcome and 2 (50%) reporting the outcome to be the same [Table 2].

The mean change in BF from baseline was largest for the No ACL group [Figure 1]. There was a significant association between the procedure and BF ($P = 0.004$) [Table 3]. In comparison to the ACL first group, the No ACL group had significantly lower postoperative BF ($P = 0.001$), while comparison with the combined group was not significantly different ($P = 0.251$). Multiple linear regression analysis of procedure demonstrated similar association [Table 4].

When considering the MC score, the largest change from baseline was observed in the No ACL group, while the least change was in the ACL first group [Figure 2]. A significant association between the procedure and MC score was observed ($P = 0.036$), with the No ACL group having significantly higher postoperative MC scores ($P = 0.018$) compared with the ACL first group [Table 3]. Patients in the combined group also had significantly better MC in comparison with the ACL first group ($P = 0.049$). With multiple linear regression analysis, comparison of the postoperative MC in the combined and ACL first groups were found not to be significant ($P = 0.113$) [Table 5].

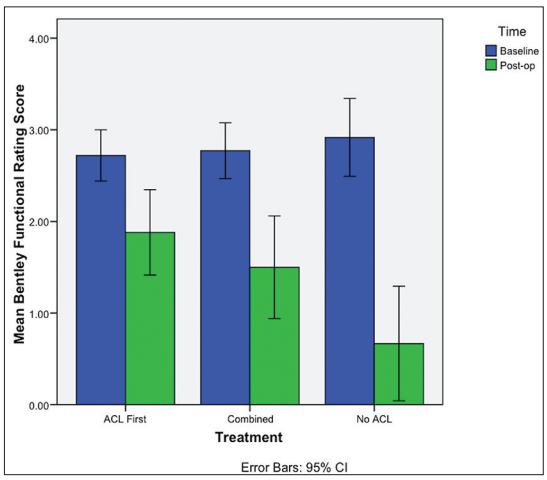

Figure 1: Bar diagram demonstrating mean change in Bentley functional score

Table 2: Functional scores and subjective outcome

Patient	Preoperative scores			Updated 2010 scores			Patient self-rating
	BF rating	VAS	MC rating system	BF rating	VAS	MC rating system	
Staged group							
1	3	9	46	0	0	96	Better
2	3	4.5	64	1	1	86	Better
3	3	2	56	0	0	99	Better
4	2	5.5	66	1	1	76	Better
5	3	7	25	3	3	29	Better
6	3	6	60	3	8	24	Worse
7	3	6	46	3	8	38	Worse
8	3	6	46	3	8	38	Worse
9	2	5	70	4	9	40	Same
10	3	3	33	2	4	54	Better
11	2	6	53	3	4	48	Same
12	2	2	63	2	3	68	Same
13	1	4	80	1	0	75	Same
14	3	6	61	1	2	67	Better
15	3	4	61	2	4	65	Better
16	3	4	61	2	4	65	Better
17	2	6	63	0	0	100	Better
18	2	6	59	1	4	77	Better
19	3	4	30	1	1	79	Better
20	3	7	52	2	1.5	66	Better
21	4	6	48	2	4	68	Better
22	3	5	53	1	1	84	Better
23	4	8	61	3	5	70	Same
24	2	2	78	3	4.5	49	Worse
25	3	6	70	3	5	76	Same
Combined group							
26	2	3	41	0	0	100	Better
27	3	7	54	1	3	76	Better
28	3	7	44	0	0	100	Better
29	3	1.5	56	0	0	95	Better
30	3	4	50	0	0	87	Better
31	1	1	64	0	0	95	Better
32	3	4	38	3	6	46	Same
33	2	4	41	3	3	54	Same
34	3	7	34	3	2	48	Better
35	3	6	49	3	4	61	Same
36	3	6.5	56	3	7	56	Same
37	3	7	41	3	5	34	Same
38	2	3	51	1	4	62	Better
39	3	5.5	64	1	3	96	Better
40	3	6	26	1	1	89	Better
41	3	7	35	2	3	78	Better
42	4	9	50	2	6	83	Better
43	3	6	52	2	2	58	Better
44	4	9	32	3	7	71	Better
45	2	3	56	2	4	77	Same
46	2	3	38	0	0	98	Better
47	3	6	45	0	2	85	Better
ACI only group							
52	3	3	34	0	0	97	Better
53	3	7	47	1	3	81	Better

Contd...

Table 2: Contd...

Patient	Preoperative scores			Updated 2010 scores			Patient self-rating
	BF rating	VAS	MC rating system	BF rating	VAS	MC rating system	
55	2	4	62	0	1	94	Better
56	3	6	42	0	0	98	Better
57	3	6	50	1	2	82	Better
58	2	5.5	36	2	6	41	Same
59	4	10	22	3	8	28	Same
60	2	6	71	0	0	84	Better
61	3	4.5	34	1	1	78	Better
62	3	4	56	0	0	72	Better
63	3	5	43	0	0	83	Better
Complete rupture group							
48	2	4	10	3	8	12	Same
49	2	7	73	1	2	70	Same
50	4	9	18	4	10	8	Worse
51	4	7	33	4	9	39	Worse

VAS=Visual analogue scale, MC=Modified cincinnati, ACI=Autologous chondrocyte implantation, BF=Bentley functional

Table 3: Linear regression model

Variable	Coefficient	Robust SE	95% CI	*P*
Univariate analysis for BF rating score (*n*=59)				
Procedure				0.004
ACL first	0			
Combined	−0.407	0.351	−1.109-0.295	0.251
No ACL	−1.246	0.354	−1.955-0.537	0.001
Univariate analysis for MC clinical rating (*n*=59)				
Procedure				0.036
ACL first	0			
Combined	13.404	6.663	0.057-26.752	0.049
No ACL	17.413	7.144	3.102-31.723	0.018
Univariate analysis for VAS (*n*=59)				
Procedure				0.143
ACL first	0			
Combined	−0.620	0.746	−2.115-0.874	0.409
No ACL	−1.787	0.898	−3.585-0.012	0.051

SE=Standard error, CI=Confidence interval, BF=Bentley functional, VAS=Visual analogue scale, MC=Modified cincinnati, ACL=Anterior cruciate ligament

The ACL first group also demonstrated the smallest mean change in VAS from baseline, with the largest change seen in the No ACL group [Figure 3]. The No ACL group had marginally significant lower VAS than the ACL first patients ($P = 0.051$) [Table 3]. Comparing the combined group with the ACL first group failed to show a significant difference in VAS ($P = 0.409$). This was confirmed by multiple linear regression analysis of procedure [Table 6].

In the combined group, there was no significant difference in clinical outcome scores, nor mean change in outcome scores, between individuals treated with ACI-C and those treated with MACI. Multiple linear regression analysis demonstrated that whether ACI-C or MACI had been performed had no significant affect on BF ($P = 0.197$), and neither was the use of hamstring or BPB graft ($P = 0.088$), as

Table 4: Multiple linear regression analysis of procedure, with the postoperative Bentley score as the dependent variable

Variable	Multivariate analysis (*n*=56)			*P*
	Coefficient	Robust SE	95% CI	
Baseline bentley score	0.529	0.238	0.051-1.006	0.031
Followup time	−0.008	0.007	−0.021-0.005	0.243
Age	0.002	0.020	−0.038-0.041	0.929
Procedure				0.022
ACL first	0	-	-	-
Combined	−0.327	0.396	−1.122-0.468	0.413
No ACL	−1.239	0.438	−2.119-0.360	0.007
ACI/MACI				
ACI	0	-	-	-
MACI	0.131	0.466	−0.804-1.066	0.780
Site				0.924
LFC	0	-	-	-
MFC	0.310	0.547	−0.787-1.408	0.573
Multisite	0.409	1.084	−1.764-2.583	0.707
Patella	0.519	0.687	−0.859-1.896	0.453
Trochlea	0.545	0.654	−0.766-1.857	0.408
Size	0.001	0.001	0.000-0.003	0.062
OA				0.709
Grade 0	0	-	-	-
Grade 1	0.180	0.510	−0.843-1.202	0.726
Grade 2	0.085	0.563	−1.044-1.214	0.880
Grade 3	0.669	0.587	−0.508-1.845	0.260

ACI=Autologous chondrocyte implantation, MACI=Matrix-assisted autologous chondrocyte implantation, OA=Osteoarthritis, SE=Standard error, CI=Confidence interval, ACL=Anterior cruciate ligament, LFC=Lateral femoral condyle, MFC=Medial femoral condyle

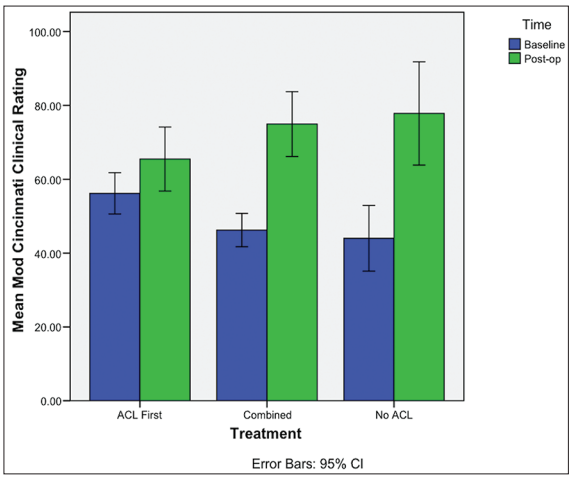

Figure 2: Bar diagram demonstrating mean change in modified Cincinnati score

well as reporting the significance of OA grade ($P = 0.038$), followup time ($P = 0.025$) and size of defect ($P < 0.001$) in the combined group [Table 7].

The size of defect ($P = 0.004$) and patella site ($P = 0.048$) was found to significantly affect MC [Table 7], and using multiple linear regression analysis, the size of the defect ($P = 0.038$) was found to significantly affect the VAS in the combined group [Table 7].

Table 5: Multiple linear regression analysis of procedure, with postoperative MC rating score as the dependent variable

Variable	Multivariate analysis (*n*=56)			*P*
	Coefficient	Robust SE	95% CI	
Baseline cincinnati rating	0.503	0.253	−0.006-1.011	0.053
Followup time	0.064	0.102	−0.141-0.268	0.535
Age	−0.097	0.349	−0.797-0.602	0.781
Procedure				0.087
ACL first	0	-	-	-
Combined	11.446	11.446	−2.816-25.709	0.113
No ACL	19.708	8.868	1.921-37.494	0.031
ACI/MACI				
ACI	0	-	-	-
MACI	−2.871	8.606	−20.132-14.390	0.740
Site				0.459
LFC	0	-	-	
MFC	−5.415	9.105	−23.677-12.847	0.555
Multisite	−24.060	14.607	−53.359-5.239	0.105
Patella	−17.201	11.685	−40.637-6.236	0.147
Trochlea	−11.387	12.278	−36.014-13.239	0.358
Size	−0.022	0.013	−0.048-0.004	0.101
OA				0.950
Grade 0	0	-	-	-
Grade 1	−2.499	9.363	−21.279-16.281	0.791
Grade 2	−5.302	10.272	−25.906-15.301	0.608
Grade 3	0.443	8.932	−17.472-18.357	0.961

ACI=Autologous chondrocyte implantation, MACI=Matrix-assisted autologous chondrocyte implantation, OA=Osteoarthritis, SE=Standard error, CI=Confidence interval, ACL=Anterior cruciate ligament, LFC=Lateral femoral condyle, MFC=Medial femoral condyle, MC=Modified cincinnati

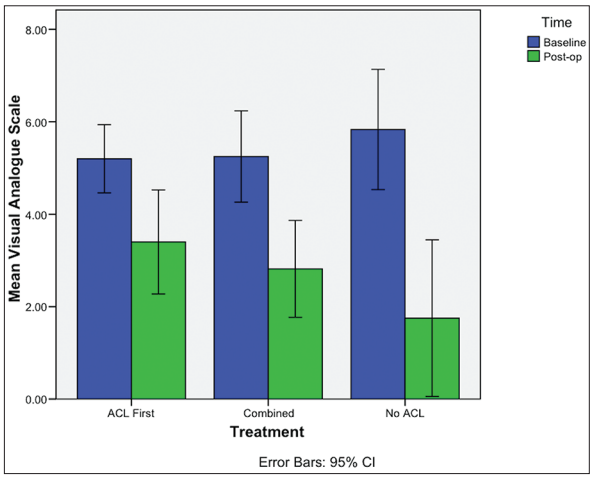

Figure 3: Bar diagram demonstrating mean change in visual analogue scale

In the No ACL group, the baseline characteristics of the twelve patients against the four with documented evidence of complete ACL rupture (complete rupture group) [Table 8]. On average, there was a much bigger change in BF, MC and VAS outcomes for the cases that did not have complete ACL ruptures, in comparison to those who had complete ACL ruptures. Independent

Table 6: Multiple linear regression analysis of procedure, with postoperative VAS as the dependent variable

Variable	Multivariate analysis (*n*=56)			*P*
	Coefficient	Robust SE	95% CI	
Baseline VAS score	0.455	0.182	0.089-0.821	0.016
Followup time	−0.017	0.015	−0.047-0.012	0.245
Age	−0.020	0.043	−0.106-0.065	0.637
Procedure				0.108
ACL first	0	-	-	-
Combined	−0.411	0.735	−1.885-1.064	0.579
No ACL	−2.253	1.052	−4.363-0.142	0.037
ACI/MACI				
ACI	0	-	-	-
MACI	−0.535	1.080	−2.702-1.631	0.622
Site				0.978
LFC	0	-	-	-
MFC	−0.426	1.239	−2.909-2.058	0.732
Multisite	0.962	2.385	−3.821-5.745	0.688
Patella	−0.330	1.536	−3.410-2.750	0.831
Trochlea	0.449	1.607	−2.775-3.673	0.781
Size	0.002	0.002	−0.001-0.006	0.189
OA				0.776
Grade 0	0	-	-	-
Grade 1	0.168	1.007	−1.853-2.188	0.869
Grade 2	0.139	1.250	−2.368-2.646	0.912
Grade 3	0.992	1.053	−1.119-3.104	0.350

ACI=Autologous chondrocyte implantation, MACI=Matrix-assisted autologous chondrocyte implantation, OA=Osteoarthritis, SE=Standard error, CI=Confidence interval, ACL=Anterior cruciate ligament, LFC=Lateral femoral condyle, MFC=Medial femoral condyle, VAS=Visual analogue scale

t-tests confirmed a significant difference in the mean change in BF ($P = 0.002$), MC ($P = 0.006$) and VAS score ($P = 0.012$) by rupture status.

Discussion

An ACL injury results in functional instability that can lead to osteoarthritis.[10,27,28] ACI is contraindicated in those patients with instability from ACL injury, due to potential damage to the repair tissue from shearing forces and damage from abnormal biomechanical stresses across the knee joint.[8,29] ACL reconstruction should be performed if ACL rupture is clinically evident to provide stability followed by any osteochondral defect can be addressed.

In our series, the patients who underwent combined ACI with ACL reconstruction reported their outcome to be better in 72.73% and the same in 27.27%. The patients who were ACL deficient, but thought to be clinically stable and underwent ACI only reported the outcome to be worse in 50%. There were four patients in the ACL first group that felt their outcome was worse. This can be multifactorial. An explanation may be the number of previous surgeries performed; as these patients had the most procedures prior to referral to our institution.

Table 7: Multiple linear regression analysis was conducted to derive the independent effects of ACI versus MACI and hamstring versus BPB on the outcome scores while additionally controlling for the other measured determinants of outcome in the combined group

Variable	Coefficient	SE	95% CI	P
Multivariate analysis for BF rating score (*n*=21)				
Baseline bentley	0.544	0.325	−0.191-1.279	0.128
Age at 2nd operation (in years)	0.031	0.025	−0.026 -0.089	0.247
Followup	0.013	0.005	0.002-0.024	0.025
OA				0.038
Grade 0	0			
Grade 1	0.406	0.581	−0.908-1.721	0.502
Grade 2	1.782	0.543	0.552-3.011	0.010
Grade 3	1.765	0.680	0.227-3.304	0.029
Site				0.131
LFC	0			
MFC	1.122	0.666	−0.383-2.628	0.126
Patella	1.527	0.686	−0.024-3.078	0.053
Multisite	-	-	-	-
Trochlea	-	-	-	-
Size	0.004	0.001	0.003-0.006	<0.001
ACI/MACI				
ACI	0			
MACI	0.718	0.515	−0.447-1.883	0.197
ACL recon				
Hamstring	0			
BPB	0.778	0.406	−0.140-1.696	0.088
Multivariate analysis for MC rating (*n*=21)				
Baseline cincinnati rating	−0.234	0.376	−1.086-0.617	0.549
Age at 2nd operation (in years)	−0.775	0.612	−2.16-0.609	0.237
Followup (months)	−0.333	0.127	−2.159-0.609	0.237
OA				0.255
Grade 0	0	-	-	-
Grade 1	−2.325	11.216	−27.697-23.047	0.840
Grade 2	−29.097	14.722	−62.400-4.206	0.080
Grade 3	−16.936	19.486	−61.017-27.145	0.407
Site				0.125
LFC	0	-	-	-
MFC	−18.246	15.327	−52.919-16.427	0.264
Patella	−35.586	15.549	−70.761-0.412	0.048
Multisite	-	-	-	-
Trochlea	-	-	-	-
Size	−0.059	0.016	−0.094-0.024	0.004
ACI/MACI				
ACI	0	-	-	-
MACI	−22.430	12.693	−51.143-6.283	0.111
ACL recon			-	
Hamstring	0	-	−43.743-4.714	-
BPB	−19.514	10.710		0.102
Multivariate analysis for VAS (*n*=21)				
Baseline VAS	0.102	0.298	−0.572-0.776	0.741
Age at 2nd operation (in years)	0.067	0.086	−0.129-0.263	0.458
Followup	0.020	0.017	−0.018-0.058	0.257
OA				0.713
Grade 0	0	-	-	-
Grade 1	−0.680	1.701	−4.529-3.168	0.699
Grade 2	1.630	1.928	−2.732-5.992	0.420
Grade 3	1.800	2.375	−3.574-7.174	0.468
Site				0.753
LFC	0	-	-	-
MFC	−1.154	1.989	−5.654-3.347	0.576
Patella	−1.536	2.145	−6.389-3.316	0.492
Trochlea	-	-	-	-
Multisite	-	-	-	-
Size	0.005	0.002	0.000-0.010	0.038
ACI/MACI				
ACI	0	-	-	-
MACI	1.387	1.720	−2.505-5.278	0.441
ACL recon				
Hamstring	0	-	-	-
BPB	1.362	1.421	−1.852-4.576	0.363

ACI=Autologous chondrocyte implantation, MACI=Matrix-assisted autologous chondrocyte implantation, OA=Osteoarthritis SE=Standard error, CI=Confidence interval, ACL=Anterior cruciate ligament, LFC=Lateral femoral condyle, MFC=Medial femoral condyle, VAS=Visual analogue scale, BPB=Bone-patella tendon-bone autograft, BF=Bentley functional, MC=Modified cincinnati

Table 8: Baseline summary data table for no ACL group and complete rupture group

Variable	No ACL with incomplete rupture (*n*=12) %	Complete rupture (*n*=4) %
Age at 2nd operation (in years)	33.5±10.4	37.5±8.3
Followup	78.3±45.2	107.3±23.9
Baseline bentley score	3 (2, 3)	3 (2, 4)
Baseline VAS score	5.8±2.1	6.8±2.1
Baseline Cincinnati	44.0±14.0	33.5±28.0
OA		
Grade 0	8, 67	2, 50
Grade 1	2, 17	-
Grade 2	2, 17	2, 50
Grade 3	-	-
Site		
LFC	2, 17	-
MFC	5, 42	2, 50
Patella	1, 8	2, 50
Trochlea	3, 25	-
Multisite	1, 8	-
	***n*=11**	
Size	225 (150, 500)	524 (300, 660)
ACI/MACI	***n*=12**	
ACI	5, 42	2, 50
MACI	7, 58	2, 50

VAS=Visual analogue scale, ACL=Anterior cruciate ligament, OA=Osteoarthritis, LFC=Lateral femoral condyle, MFC=Medial femoral condyle, ACI=Autologous chondrocyte implantation, MACI=Matrix assisted autologous chondrocyte implantation

The role of combined repair of osteochondral defects and ACL reconstruction has been reported using osteochondral autograft,[9,10,30-32] autologous periosteum transplantation[1] and ACI.[12,21] The use of osteochondral transfer and periosteum transplantation for the repair of osteochondral

defects has raised concern regarding the long term stability of the repair tissue and its integration with surrounding articular cartilage.[15,31]

The use of ACI in osteochondral defect repair has produced encouraging clinical outcomes;[18,20,21,33] however, the use of a periosteum cover is associated with periosteal hypertrophy and donor site morbidity among after complications. The use of the MACI technique avoids these complications, as well as providing greater stability[22,34] and reduces operative time, as suturing of the membrane is not usually required. Good outcomes have been reported with the use of the MACI technique for osteochondral defect repair.[22,34,35]

Peterson *et al*.[21] demonstrated encouraging results with the use of ACI, with a periosteum cover, in combination with ACL reconstruction. Amin *et al*.,[12] reported good to excellent results in eight patients in a nine patient series, using ACI-C or MACI, in combination with ACL reconstruction (both hamstring and bone-patellar tendon-bone autograft).

As separate procedures, ACL reconstruction and ACI are costly to health care providers as well as the patient, as they must undergo a long rehabilitation period with restriction in function.[29] Thus the benefit of performing the procedures in combination applies to both the patient and health care provider. Further work is required to determine whether this procedure is effective in preventing osteoarthritis in the joint, as well as to define specific factors that impact on outcome and thus can be used to select ideal patients as well as predict outcome in the future.

Conclusion

The similar outcomes of the combined and ACL first groups suggest that in specific indications the combined procedure will produce good to excellent outcomes with reduced cost and impact on the individuals. The poor outcome in the complete rupture group emphasize that ACL deficient knees, whether clinically stable or not, are a contraindication to osteochondral defect repair. The outcome of the remaining patients in the ACI only group suggest that it is safe to perform ACI in those patients with a clinically stable knee after partial ACL injury. The results have been encouraging in this study and demonstrate that ACI in combination with ACL reconstruction is a possible option in the management of the young and active patient who wishes to return to their preinjury activity level. The role of this procedure in acute ACL rupture requires further investigation.

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