Patient-Oriented And Performance-Based Outcomes After Knee Autologous Chondrocyte Implantation: A Timeline For The First Year Of Recovery

By: Jennifer S. Howard, Carl G. Mattacola, David R. Mullineaux, Robert A. English, and Christian Lattermann

Abstract

Context: It is well established that autologous chondrocyte implantation (ACI) can require extended recovery postoperatively; however, little information exists to provide clinicians and patients with a timeline for anticipated function during the first year after ACI. Objective: To document the recovery of functional performance of activities of daily living after ACI. Patients: ACI patients (n = 48, 29 male; 35.1 ± 8.0 y). Intervention: All patients completed functional tests (weight-bearing squat, walk-across, sit-to-stand, step-up/over, and forward lunge) using the NeuroCom long force plate (Clackamas, OR) and completed patient-reported outcome measures (International Knee Documentation Committee Subjective Knee Evaluation Form, Lysholm, Western Ontario and McMaster Osteoarthritis Index [WOMAC], and 36-Item Short-Form Health Survey) preoperatively and 3, 6, and 12 mo postoperatively. Main Outcome Measures: A covariance pattern model was used to compare performance and self-reported outcome across time and provide a timeline for functional recovery after ACI. Results: Participants demonstrated significant improvement in walk-across stride length from baseline (42.0% ± 8.9% height) at 6 (46.8% ± 8.1%) and 12 mo (46.6% ± 7.6%). Weight bearing on the involved limb during squatting at 30°, 60°, and 90° was significantly less at 3 mo than presurgery. Step-up/over time was significantly slower at 3 mo (1.67 ± 0.69 s) than at baseline (1.49 ± 0.33 s), 6 mo (1.51 ± 0.36 s), and 12 mo (1.40 ± 0.26 s). Step-up/over lift-up index was increased from baseline (41.0% ± 11.3% body weight [BW]) at 3 (45.0% ± 11.7% BW), 6 (47.0% ± 11.3% BW), and 12 mo (47.3% ± 11.6% BW). Forward-lunge time was decreased at 3 mo (1.51 ± 0.44 s) compared with baseline (1.39 ± 0.43 s), 6 mo (1.32 ± 0.05 s), and 12 mo (1.27 ± 0.06). Similarly, forward-lunge impact force was decreased at 3 mo (22.2% ± 1.4% BW) compared with baseline (25.4% ± 1.5% BW). The WOMAC demonstrated significant improvements at 3 mo. All patient-reported outcomes were improved from baseline at 6 and 12 mo postsurgery. Conclusions: Patients’ perceptions of improvements may outpace physical changes in function. Decreased function for at least the first 3 mo after ACI should be anticipated, and improvement in performance of tasks requiring weight-bearing knee flexion, such as squatting, going down stairs, or lunging, may not occur for a year or more after surgery.

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Context: It is well established that autologous chondrocyte implantation (ACI) can require extended recovery postoperatively; however, little information exists to provide clinicians and patients with a timeline for anticipated function during the first year after ACI. Objective: To document the recovery of functional performance of activities of daily living after ACI. Patients: ACI patients (n = 48, 29 male; 35.1 ± 8.0 y). Intervention: All patients completed functional tests (weight-bearing squat, walk-across, sit-to-stand, step-up/over, and forward lunge) using the NeuroCom long force plate (Clackamas, OR) and completed patient-reported outcome measures (International Knee Documentation Committee Subjective Knee Evaluation Form, Lysholm, Western Ontario and McMaster Osteoarthritis Index [WOMAC], and 36-Item Short-Form Health Survey) preoperatively and 3, 6, and 12 mo postoperatively. Main Outcome Measures: A covariance pattern model was used to compare performance and self-reported outcome across time and provide a timeline for functional recovery after ACI. Results: Participants demonstrated significant improvement in walk-across stride length from baseline (42.0% ± 8.9% height) at 6 (46.8% ± 8.1%) and 12 mo (46.6% ± 7.6%). Weight bearing on the involved limb during squatting at 30°, 60°, and 90° was significantly less at 3 mo than presurgery. Step-up/over time was significantly slower at 3 mo (1.67 ± 0.69 s) than at baseline (1.49 ± 0.33 s), 6 mo (1.51 ± 0.36 s), and 12 mo (1.40 ± 0.26 s). Step-up/over lift-up index was increased from baseline (41.0% ± 11.3% body weight [BW]) at 3 (45.0% ± 11.7% BW), 6 (47.0% ± 11.3% BW), and 12 mo (47.3% ± 11.6% BW). Forward-lunge time was decreased at 3 mo (1.5 ± 0.44 s) compared with baseline (1.39 ± 0.43 s), 6 mo (1.32 ± 0.05 s), and 12 mo (1.27 ± 0.06). Similarly, forward-lunge impact force was decreased at 3 mo (22.2% ± 1.4% BW) compared with baseline (25.4% ± 1.5% BW). The WOMAC demonstrated significant improvements at 3 mo. All patient-reported outcomes were improved from baseline at 6 and 12 mo postsurgery. Conclusions: Patients’ perceptions of improvements may outpace physical changes in function. Decreased function for at least the first 3 mo after ACI should be anticipated, and improvement in performance of tasks requiring weight-bearing knee flexion, such as squatting, going down stairs, or lunging, may not occur for a year or more after surgery.

Keywords: cartilage, chondral repair, functional assessment, functional testing
total-joint arthroplasty patients has provided further support for the inclusion of PBAs as part of a detailed outcomes-assessment protocol. Combining PROs with PBAs may provide a more complete picture of clinical outcomes after ACI than the use of either type of outcome in isolation.

Few studies have used PBAs to document the return of function after ACI. Most of those that have examined either very low-demand activity such as the 6-minute-walk test or very high-demand activity via the single-limb hop. No known studies have examined the timeline for return to function after ACI using low- to moderate-demand PBAs that recreate the demands and stresses of common activities of daily living such as squatting, rising from sitting, or going up and down stairs, in addition to walking. A description of functional recovery during the first year after ACI is imperative to provide evidence for prescription of appropriate patient education, rehabilitation protocols, and understanding of the recovery process. Therefore, the purpose of this study was to document serial changes in knee function over 1 year after ACI using both PROs and PBAs. We hypothesized that PROs would demonstrate significant improvement from baseline at all postoperative time points. We also hypothesized that PBA measures for walking, rising from sitting, stepping up and over, and lunging would demonstrate no improvements at the 3-month time point followed, by progressive improvement at 6 months and 12 months compared with baseline measures of function.

Methods

Patients

Between July 2008 and July 2011 patients were prospectively recruited from an active cartilage center. Inclusion criteria were planned ACI surgery to the medial or lateral femoral condyle, trochlea, or patella; willingness to participate; no uncorrectable contraindications to ACI such as extensive degenerative joint disease, insufficient meniscus, or unstable knee; and ability to ambulate without use of assistive devices. There were no exclusions based on limb malalignment if the malalignment was corrected before or at the time of surgery via high tibial osteotomy or tibial tubercle transfer. Similarly, patients undergoing concomitant or staged ligament reconstruction to correct joint instability were also eligible for study participation.

A total of 50 patients (31 male, 19 female; 35.0 ± 7.9 y; 180.34 ± 30.7 cm; 92.0 ± 20.6 kg) agreed to participate. During the enrollment period 4 patients were invited to take part in the study but declined to participate, resulting in an enrollment rate of 93% of eligible patients. Of the enrolled patients, 24 underwent ACI to the patellofemoral joint with a tibial tubercle transfer and the remaining 26 underwent ACI to the femoral condyle, of whom 4 also had a concomitant high tibial osteotomy and 2 underwent concomitant meniscus transplantation. Mean number of defects treated per patient was 1.5 ± 0.6 with an average treatment area of 8.7 ± 6.8 cm² (range 1.96–39.0 cm²). All participants signed a university-approved institutional review board consent form at the time of enrollment.

Procedures

Surgical Procedures and Rehabilitation. All patients underwent a 2-step ACI procedure performed by the same surgeon (C.L.). During the first procedure a limited chondroplasty was performed and the lesion was evaluated arthroscopically. At this time a biopsy was obtained from the intracondylar notch (100–200 mg cartilage). This sample was sent to a commercial laboratory, where it was cultured and expanded (Carticel, Genzyme Corp, Cambridge, MA). In a second surgical procedure, chondrocyte implantation was performed using a miniatthroatomy. First the defect or defects were prepared using a curette to debride down to the subchondral plate with stable edges. A type I/III collagen membrane (Bio-Gide®, Geistlich Biomaterials, Wohlen, Switzerland) was shaped to match the defect. Sutures and fibrin glue (Tisseel, Baxter Healthcare Corp, Deerfield, IL) were used to adhere the membrane over the defect to form a watertight seal. The chondrocytes in suspension were then injected beneath the membrane into the defect through a small portal remaining at the edge of the collagen membrane. The portal was then closed and sealed with sutures and additional fibrin glue.

All patients followed standardized rehabilitation protocols after surgery with considerations for defect location and concomitant procedures. All patients were braced in full extension and were non-weight bearing for 2 weeks postoperatively. Toe-touch weight bearing was permitted from 2 to 4 weeks, with partial weight bearing from 4 to 6 weeks and progression to full weight bearing between weeks 6 and 12. Continuous passive motion was prescribed for all patients for 6 to 8 h/d for 6 weeks. For defects in the tibiofemoral joint, knee braces were gradually unlocked between 2 and 4 weeks as quadriceps control was gained. For defects to the patellofemoral joint, knees were braced in full extension for weight bearing through 4 weeks postoperative and then were gradually unlocked as quadriceps control was gained between weeks 4 and 6. Once good quadriceps control was gained, all patients were transitioned to a hinged knee sleeve. All patients were advised to abstain from high-intensity cutting or pivoting activity until at least 12 months post-ACI.

Patient-Reported Outcomes. The PROs used in this study were the Medical Outcomes Study–36 Item Short Form Health Survey Physical Component Scales (SF-36 PCS), the Western Ontario and McMaster Osteoarthritis Index (WOMAC), the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, and the Lysholm Scale. The SF-36, IKDC, Lysholm, and WOMAC have all been evaluated for reliability among cartilage patients. A researcher independent of the treating physician reviewed each instrument with the patients and was available to
answer any questions they may have had. All PROs were completed at the following time points: before implantation (preoperation) and 3 months, 6 months, and 12 months postsurgery.

**Performance-Based Assessments.** At each time point after completing PROs each participant completed a series of 5 PBAs in a musculoskeletal-laboratory setting. All PBAs were completed using the NeuroCom Balance Master and long force plate (NeuroCom International, Clackamas, OR). This is a commercially available system designed as both a training and an evaluation tool for function and balance tasks, and it has the ability to provide immediate feedback to clinicians and patients regarding quality of task performance for a variety of activities of daily living. The only exposure study participants had with the long force plate was for research testing purposes, and they were not provided feedback during testing.

The long force plate consists of a 45.72 × 152.40-cm force plate with data sampled at 100 Hz and a personal computer equipped with data-capture software (Balance Master version 8.1). These functional tasks were selected because of their direct relationship to activities of daily living and the feasibility of patients’ being able to complete the task at each testing time point (Table 1). Tests were completed in the order presented at all time points. This order was subjectively determined during pilot testing to be from least to most demanding. All testing was administered by the same investigator (J.S.H.). For all single-limb tests the uninvolved limb was tested first. Three successful trials of each task were performed (except for the weight-bearing squat, which consisted of a single trial at each joint angle). Approximately 15 seconds of rest were permitted between trials and 30 seconds of rest between tasks. For the purposes of this article, all outcome variables are identified using the names assigned to them by the software used. Definitions for these variables are presented in Table 1. The 5 tasks were as follows:

- **Walk-Across** (Figure 1): Patients walked across the long force plate using their freely chosen standard gait speed and pattern.

### Table 1 Functional Tasks Evaluated on the NeuroCom Balance Master Long Force Plate

<table>
<thead>
<tr>
<th>Task</th>
<th>Parameters assessed</th>
<th>NeuroCom outcome variable</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walk-across</td>
<td>Characterization of gait</td>
<td>Stride length (cm)</td>
<td>Distance between contralateral heel strikes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stride width (cm)</td>
<td>Lateral distance between center of pressure (COP) of left and right foot strikes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walking speed (cm/s)</td>
<td>Speed of forward progression of the center of gravity</td>
</tr>
<tr>
<td>Weight-bearing squat</td>
<td>Strength, weight distribution</td>
<td>% body weight (BW) at 0° (full extension), 30°, 60°, and 90° of knee flexion</td>
<td>% BW on the involved limb at each position (test duration 0.01 s)</td>
</tr>
<tr>
<td>Sit-to-stand</td>
<td>Strength, weight distribution, performance time, double limb balance</td>
<td>Weight-transfer time (s)</td>
<td>Time required from start of motion while sitting (ie, increase in COP forward velocity by 5% from resting velocity) to achieve full weight-bearing standing (ie, forward velocity drops to within 5% of standing resting velocity)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rising index (%BW)</td>
<td>Peak vertical force exerted through the legs when rising to full standing relative to stationary vertical standing force</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight symmetry</td>
<td>% difference in weight supported by each limb during the weight-transfer phase</td>
</tr>
<tr>
<td>Step-up/over</td>
<td>Concentric strength, eccentric control, performance time</td>
<td>Lift-up index (%BW)</td>
<td>Peak vertical force occurring while stepping up onto the box as a percentage of BW</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impact index (%BW)</td>
<td>Peak vertical force occurring while stepping down off the box as a percentage of BW</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Movement time (s)</td>
<td>Time between initial weight shift (ie, change in COP velocity by 5%) and contact with force plate on opposite side of box (determined by COP velocity dropping to within 5% of posttest resting velocity)</td>
</tr>
<tr>
<td>Lunge</td>
<td>Concentric and eccentric control, functional range of motion, performance time</td>
<td>Distance (% subject height)</td>
<td>Length of lunge step as a percentage of subject height</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Movement time (s)</td>
<td>Duration of lunge phase during which lead leg is in contact with the force plate, start and stop of a trial determined by 5% change in COP velocity from pretest and posttest resting velocity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impact index (%BW)</td>
<td>Peak vertical force occurring during lunge maneuver as a percentage of BW</td>
</tr>
</tbody>
</table>

Note: All tasks were performed in the order presented by patients treated for articular cartilage defects to the knee.
• **Weight-Bearing Squat (Figure 2):** Patients stood still on the force plate and force was recorded with knee-flexion angles of 0°, 30°, 60°, and 90°. The percentage of body weight on the involved limb was measured during a single trial with a duration of 0.01 second for each position. A standard goniometer was used to verify knee-joint angle at each position.

• **Sit-to-Stand (Figure 3):** Patients were seated on a 50-cm box. On both visual and audio signal from the computer, they rose to full standing as quickly as possible without using their hands and then maintained a steady stance for the remainder of the 10-second trial.

• **Step-Up/Over (Figure 4):** Participants stood behind a 29-cm-high box and stepped up onto the box with their test leg, then brought their nontest leg up and over the box, and then stepped down with their test leg. Patients were instructed to complete this task as quickly as possible while still maintaining control.

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**Figure 1** — Walk-across. Outcome variables included stride width, stride length, and speed.

**Figure 2** — Weight-bearing squat. Percentage of body weight on the involved limb was evaluated at 0° (not pictured), 30°, 60°, and 90° of knee flexion.

**Figure 3** — Sit-to-stand. Beginning from a sitting position, participants were instructed, on receiving a visual and audio cue, to rise from sitting as quickly as possible without using hands to push off the box. Outcome measures included weight-transfer time, rising index, and weight symmetry.
Step-up/over. Beginning with both feet behind the box (not pictured), participants were instructed to step up and over the box and return to stationary standing as quickly as they could do so while still maintaining control. Outcome variables were lift-up index, impact index, and movement time.
• **Forward Lunge:** Patients in a standing position stepped forward on 1 leg, squatted down as far as possible, and then returned to the initial standing position as quickly as possible.

Previous research has investigated the global components of function assessed by the long force plate. Using factor-analysis methods, Chong identified the latent functional variables assessed in several of the included tasks. He concluded that the sit-to-stand assessed the underlying factors of both agility and weight transfer, the step-up/over assessed force control, and the forward lunge assessed the underlying factor of agility. In addition, walk-across stride width and stride length evaluated walking factors not well represented in the other functional tasks. Outcomes using the long force plate have also previously been reported for postoperative recovery after total knee replacement. Finally, the long force plate has been reported to be sensitive to functional deficits after anterior cruciate ligament reconstruction. This existing literature supports the use of the long force plate as a useful tool for the assessment of lower extremity function, particularly among postoperative knee patients.

**Statistical Analysis**

A mixed-model analysis using a covariance pattern model with an autoregressive covariance matrix was used to compare changes in PROs and PBAs between preoperative and 3-month, 6-month, and 12-month postoperative evaluations. Significance level was set at \( P \leq .05 \) a priori, and when a main effect was significant, protected least-significant-difference pairwise comparisons were used to identify differences between individual time points.

**Results**

Six participants were declared clinical failures at or before the 1-year time point and were not medically cleared to complete functional testing at all follow-up time points; however, PRO scores were available for 4 of these patients, who had yet to undergo reoperation at the 1-year time point. An additional 5 participants were lost to follow-up. All available data for all participants at all time points were incorporated into the statistical analysis.

**Patient-Reported Outcomes**

There was a main effect \( (P < .001) \) for time for all 4 PRO instruments (Figure 5). The WOMAC \( (P = .050) \) was the only instrument to show significant changes between preoperation and the 3-month time point. There were significant improvements from preoperation to the 6- and 12-month follow-ups for the IKDC \( (P < .001, P < .001, \text{ respectively}) \), SF36-PCS \( (P = .002, P = .001) \), Lysholm \( (P < .001, P < .001) \), and WOMAC \( (P < .001, P < .001) \).

**Performance-Based Assessments**

All PBAs demonstrated changes over time (Table 2). For the walk-across task there was a significant increase in stride length observed at both the 6- and 12-month time points compared with preoperation (6-month, \( P = .002; \text{ 12-month, } P = .001 \)).

![Figure 5 — Patient-reported outcome scores. Abbreviations: IKDC, International Knee Documentation Committee Subjective Knee Evaluation Form; SF-35 PCS, 36-Item Short-Form Health Survey Physical Component Scales; WOMAC, Western Ontario and McMaster Osteoarthritis Index. IKDC and Lysholm are scored from 0 to 100, with 100 representing an ideal score. SF-36 PCS uses a norm-based scoring system where 50 represents a mean score with a standard deviation of 10 and higher scores represent higher levels of function. The WOMAC is scored from 96 to 0, with 0 representing no disability. Error bars represent standard deviations. \( *P \leq .05 \) compared with preoperative time point.](image-url)
12-month, \(P = .005\) and when compared with 3-month values (6-month, \(P < .001\); 12-month, \(P = .001\)). There was no main effect for time for stride width \((P = .663)\) or walking speed \((P = .051)\).

For the weight-bearing squat, a main effect for time was observed for squatting at 30° \((P < .001)\), 60°, and 90°. Post hoc analyses revealed decreases in weight distribution on the surgical limb between preoperation (48% body weight) and 3 months (43% body weight, \(P = .020\)) and 6 months (45% body weight, \(P = .020\)) for squatting at 30°. Decreased weight bearing was also observed between preoperation and 3 months \((P = .020)\) and preoperation and 6 months \((P = .048)\) for squatting at 60°. Similarly, squatting weight-distribution asymmetries were observed at 90° relative to baseline at 3 months \((P < .001)\). Although not statistically different from preoperative values, at the 12-month time point mean weight distributions remained below preoperative values at 30°, 60°, and 90°.

The sit-to-stand demonstrated the earliest positive effects of surgery, with decreased weight-transfer time at 12 months \((P = 0.016)\) compared with preoperation. Weight-transfer time continued to improve at 6 months \((P = .05)\) and 12 months \((P = .002)\).

For the step-up/over, there were significant increases in lift-up force between preoperation and the 3- \((P = .003)\), 6- \((P = .005)\), and 12-month \((P = .010)\) follow-up time points. Time required to complete the step-up/over was also increased at 3 months \((P = .009)\) but returned to baseline at later time points. Similarly, step-up/over impact index was increased over preoperation values at 3 months \((P = .001)\) and 6 months \((P = .034)\), possibly demonstrating a loss of eccentric control when stepping down from the box.

Finally, results for the forward lunge showed a significant decrease in impact index (peak vertical ground-reaction force) at 3 months \((P = .007)\) but returned to preoperative levels and began to increase at the 6- and 12-month time points. Similar to the step-up/over, forward-lunge time was slower at the 3-month time point \((P = .006)\) but gradually became faster at subsequent evaluations.

### Table 2  Patient-Reported and Performance-Based Assessments Over 12 Months After Autologous Chondrocyte Implantation, Mean (SD)

<table>
<thead>
<tr>
<th>Test</th>
<th>Preoperative</th>
<th>3 mo</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walk-across width (%)</td>
<td>10.1 (2.8)</td>
<td>9.7 (2.5)</td>
<td>9.7 (2.1)</td>
<td>9.5 (2.5)</td>
</tr>
<tr>
<td>length (%)</td>
<td>42.0 (8.9)</td>
<td>42.1 (10.5)</td>
<td>46.8 (8.1)**†</td>
<td>46.9 (7.6)**†</td>
</tr>
<tr>
<td>speed (cm/s)</td>
<td>82.6 (16.8)</td>
<td>87.7 (24.6)</td>
<td>88.2 (19.3)</td>
<td>94.5 (18.2)</td>
</tr>
<tr>
<td>Double-limb squat (% BW)</td>
<td>48 (5)</td>
<td>48 (3)</td>
<td>49 (3)</td>
<td>49 (5)</td>
</tr>
<tr>
<td>0°</td>
<td>48 (8)</td>
<td>43 (6)*</td>
<td>45 (6)*</td>
<td>46 (5) *</td>
</tr>
<tr>
<td>30°</td>
<td>47 (8)</td>
<td>42 (7)*</td>
<td>44 (6)*</td>
<td>45 (6)*</td>
</tr>
<tr>
<td>60°</td>
<td>48 (6)</td>
<td>44 (5)*</td>
<td>46 (6)†</td>
<td>46 (6)†</td>
</tr>
<tr>
<td>Sit-to-stand weight-transfer time (s)</td>
<td>0.51 (0.26)</td>
<td>0.39 (0.32)*</td>
<td>0.36 (0.19)*</td>
<td>0.33 (0.20)*</td>
</tr>
<tr>
<td>rise index (% BW &gt; 100%)</td>
<td>23.3 (9.4)</td>
<td>22.0 (8.5)</td>
<td>24.0 (8.4)</td>
<td>24.6 (8.8)</td>
</tr>
<tr>
<td>involved/uninvolved symmetry (toward uninvolved)</td>
<td>–6.2 (17.6)</td>
<td>–13.7 (15.2)*</td>
<td>–9.9 (9.8)</td>
<td>–8.37 (12.3)</td>
</tr>
<tr>
<td>Step-up/over lift-up index (% BW &gt; 100%)</td>
<td>41.0 (11.3)</td>
<td>45.0 (11.7)*</td>
<td>47.0 (11.3)*</td>
<td>47.3 (11.6)*</td>
</tr>
<tr>
<td>time (s)</td>
<td>1.49 (0.33)†</td>
<td>1.67 (0.69)*</td>
<td>1.51 (0.36)†</td>
<td>1.40 (0.26)†</td>
</tr>
<tr>
<td>impact (% BW)</td>
<td>47.6 (17.0)†</td>
<td>54.9 (18.2)*</td>
<td>54.1 (19.3)*</td>
<td>50.7 (16.9)*</td>
</tr>
<tr>
<td>Forward lunge distance (%)</td>
<td>44.9 (7.1)</td>
<td>46.8 (19.1)</td>
<td>50.5 (19.0)</td>
<td>51.3 (23.8)</td>
</tr>
<tr>
<td>impact index (% BW)</td>
<td>24.4 (7.0)†</td>
<td>21.8 (6.7)*</td>
<td>24.4 (7.4)†</td>
<td>27.2 (10.4)†</td>
</tr>
<tr>
<td>time (s)</td>
<td>1.39 (0.43)†</td>
<td>1.51 (0.44)*</td>
<td>1.34 (0.28)†</td>
<td>1.29 (0.39)†</td>
</tr>
<tr>
<td>Patient-reported outcomes</td>
<td>IKDC</td>
<td>SF-36 PCS</td>
<td>Lysholm</td>
<td>WOMAC</td>
</tr>
<tr>
<td>IKDC</td>
<td>38.43 (12.50)</td>
<td>37.39 (8.79)</td>
<td>47 (18)</td>
<td>33 (17)†</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>41.62 (15.68)</td>
<td>37.98 (9.83)</td>
<td>54 (21)</td>
<td>28 (17)*</td>
</tr>
<tr>
<td>Lysholm</td>
<td>51.10 (18.34)**†</td>
<td>43.50 (9.16)**†</td>
<td>61 (23)**†</td>
<td>22 (19) **†</td>
</tr>
<tr>
<td>WOMAC</td>
<td>56.21 (20.64) **†</td>
<td>44.22 (11.28)**†</td>
<td>65 (24) **†</td>
<td>20 (19) **†</td>
</tr>
</tbody>
</table>

*Significantly different from preoperative time point. †Significantly different from 3-month time point.
Discussion

The primary purpose of this study was to provide a timeline for recovery that could be used by both patients and clinicians in managing expectations regarding postoperative recovery of function. A summary timeline of the functional recovery observed in the first year after ACI can be seen in Figure 6. Overall, these results suggest that patients may experience physical benefits such as decreased pain and symptoms as early as 3 months after ACI, but some facets of functional performance may initially decline after surgery, with significant improvements in functional performance of complex tasks such as squatting and stepping not occurring until 12 months, or perhaps longer.

Patient-Reported Outcomes

PROs have frequently been used to document functional outcomes after ACI. The observed results suggest that patients may experience functional improvements for simple activities of daily living such as those evaluated by the WOMAC as early as 3 months after ACI. However, data from the other self-reported outcome instruments used suggest that patients should not expect significant improvement before the 6-month time point. The lack of significant improvement in most PRO scores at the 3-month time point is in agreement with previous research by Henderson and Levigne and Ebert et al. However, those authors observed decreases in self-reported function using the IKDC and SF-36 PCS at the 3-month time point, while we observed slight but nonsignificant increases. In contrast, Tohyama et al reported significant improvements in Lysholm scores as early as 3 months after treatment with adiocollagen-associated ACI.

The improvements observed among patients in IKDC, Lysholm, and SF-36 PCS scores at 6 months were similar to the outcomes observed by Niemeyer et al for the IKDC and both Niemeyer et al and Kreuz et al for the Lysholm. Other authors have observed even larger improvements in IKDC and Lysholm scores as early as 6 months after ACI.

Across all PROs we observed improvements when preoperative scores were compared with scores 12 months after ACI surgery. These results are in agreement with the findings of others when using IKDC, Lysholm, SF-36 PCS, and WOMAC scores 1 year after ACI. Regardless of which outcome instrument is used, the IKDC, Lysholm, SF-36 PCS, or the WOMAC, both clinicians and patients can anticipate improvements in self-perceived function during the first year after ACI.

Performance-Based Assessments

Limited improvements in PBAs were observed 1 year after ACI (Table 2.). In general, a decrease in physical performance was observed at 3 and 6 months postoperatively, followed by a return toward baseline at 12 months after ACI. This pattern of decreased function followed by gradual return/improvement of function was particularly true for the weight-bearing squat, step-up/over, and lunge. The only measures to show positive improvements from preoperative levels at or within the 12-month time period were walk-across stride length, sit-to-stand weight-shift time, and step-up/over lift-up index. These results suggest that improvements for simpler, less demanding
tasks such as walking or going up steps can be seen as early as 6 to 12 months after ACI. However, for more complex tasks, particularly those that require eccentric quadriceps control—such as squatting, going down steps, or lunging—meaningful changes in function may not be observed within the first year after ACI.

Decreases in physical performance at the 3-month time point have been previously observed with the 6-minute-walk test after matrix-induced autologous chondrocyte implantation (MACI) and characterized chondrocyte implantation (CCI). Similar to our results, other researchers have observed slight improvements in walking performances at the 6-month and 12-month time points that continued to improve at 24-month follow-up. During laboratory gait analysis, improvements in gait speed and stride length, without significant changes in stride width, were observed over 12 months after MACI. These results support our observation that, after an initial decrease in function, patients and physicians can anticipate improvements in gait beginning around the 6-month time point after ACI.

In examining more-dynamic tasks, Van Assche et al observed deceased functional performance for a series of hopping and strength tasks (single-limb hop, crossover hop, 6-m timed hop, and isometric knee-extension strength) at 6 months after CCI and no significant improvements as late as 24 months after CCI. For example, those authors observed a 9% decrease in the single-limb-hopping limb-symmetry index through 24 months after surgery. These results are in agreement with our observations demonstrating an initial decrease in function for more dynamic tasks such as squatting and stepping, with few or no significant or measurable improvements in functional performance at the 12-month time point after ACI.

In comparison with normative data, it can be observed that some long-force-plate variables are below preoperative levels at baseline but approach or achieve age-group normative values during the first year of postoperative recovery. These include the step-up/over lift-up index and forward-lunge distance. However, other variables such as step-up/over and forward-lunge times are below normal at baseline, become more abnormal at the 3-month time point, and despite some improvement continue to be below normative levels at the 1-year mark. These results suggest that although patients may have improvements in the ability to successfully perform the task, they continue to do so at a slower pace.

Across the literature and within our study sample, improvements in gait relative to presurgery have been observed as early as 6 months after ACI. However, improvements in more-dynamic activities such as squatting, lunging, stepping, and hopping have not been observed within the first 12 months after ACI in the current study or elsewhere. These results support existing theory that although improvements in self-report measures may occur early postoperatively, maximal defect healing and functional improvement continue beyond 12 months after ACI.

The occurrence of changes in self-report measures of function before changes in performance-based measures of function may be a result of the large influence that pain levels have been observed to have on PRO scores. The observed improvement in PRO scores in the absence of improved physical performance supports the importance of incorporating both types of outcome measures when documenting patient outcomes. The importance of a patient’s own rating of function and subjective feelings toward joint health cannot be ignored. However, when considering decisions such as ability to return to work or physical activity, or to evaluate postoperative changes in biomechanics, performance-based measures provide unique information that cannot be fully and accurately captured by PROs alone.

**Limitations**

A limitation of this study is the inclusion of a diverse ACI patient population. The study sample included individuals undergoing treatment for lesions to the patella, trochlea, and/or femoral condyle, many of whom also underwent concomitant realignment procedures. In addition, rehabilitation compliance was not tracked, and all patients were free to work with a physical therapist of their choice. Because of this variability, the presented timeline for recovery is not specific or precise for any 1 defect location and/or realignment procedure. Instead, a broad pattern of recovery has been presented that can be generalized to a variety of defect patterns and sizes.

An additional limitation of this study is the lack of outcomes beyond 12 months post-ACI. However, the purpose of this study was to provide a descriptive timeline for changes in self-perceived function and functional recovery in the first year after ACI. This timeline is intended to describe when patients can expect improvements in activities of daily living and when they will perceive a benefit from the surgery, 2 key pieces of information that may be valuable to patients and physicians when deciding if and when to undergo ACI. Future examination of these outcome variables for a longer period (>1 y) will provide more information regarding the long-term course of recovery after ACI.

**Conclusions**

This study presents a descriptive timeline for changes in both PROs and PBAs during the first 12 months after ACI. Self-perceived changes in function were observed as early as 3 months after ACI, while performance-based measures of function demonstrated functional deficits compared with preoperative levels at both the 3- and 6-month time points. Specifically, patients demonstrated increased asymmetry of weight distribution when squatting and rising from sitting, decreased vertical ground-reaction-force production during lunging, and longer performance times for lunging and stepping activities. At the 12-month time point, performance improvements were seen for walking speed, sit-to-stand weight-transfer
time, and step-up/over lift-up index; however, step-up/over time and forward-lunge impact index and time remained below previously reported norms. Overall, it was observed that patients’ perceptions of functional improvements may outpace true physical changes in function. The present results, combined with those in the literature, provide important information for both physicians and rehabilitation specialists to consider when working with cartilage patients who desire to return to high-level physical activity. Clearly, recovery can be lengthy, and intense rehabilitation (beyond the existing standard of care) may be necessary to improve beyond or even restore to preoperative levels of dynamic function.

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Conflict of Interest: Independent of the presented research, co-author C.L. serves as a consultant for Sanofi/Genzyme Corp and Zimmer Inc.

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