Perioperative rehabilitation for autologous chondrocyte implantation: A review of two case studies

W.B. Robertson*, D.J. Wood, H.J. Gilbey, M.H. Zheng & R. Salleh The University of Western Australia

Introduction

Hyaline articular cartilage withstands high levels of mechanical stress and continuously renews its extracellular matrix. Despite this durability, hyaline articular cartilage lining the knee is essentially an avascular tissue, with limited capacity for regeneration. Lesions of the articular cartilage affect millions of people worldwide, and have a wide variety of causes, with traumatic damage and osteochondrosis dessicans (OCD) being the most frequent. Treatment is hampered by the fact that in adult life the intrinsic regenerative capacity of hyaline articular cartilage is very small. Defects, which extend down to the subchondral bone plate never heal of their own accord and ultimately lead to osteoarthrosis. In young patients this cannot be treated by joint replacement because of the risks of early loosening and premature wearing of the prosthesis (Bently et al., 2000). Increasing evidence suggests that the only technique that enables the regeneration of articular hyaline cartilage in chondral defects is autologous chondrocyte implantation (ACI). ACI in combination with periosteal grafts has been employed since 1987 with successful results particularly for those well defined defects of the medial femoral condyle (Peterson, 1998).

Materials and Methods

This clinical report outlines the experience from the Perth Orthopaedic Institute, Perth Western Australia of ACI using biodegradable type I/III collagen membrane (CACI). This report outlines two case studies (one male and one female) who had failed previous surgical treatment prior to definitive CACI. Surgery was performed at Sir Charles Gairdner Hospital or Hollywood Private Hospital. Harvesting of cartilage was performed arthroscopically as a day case. Non load bearing articular cartilage was retrieved from the lateral ridge of the femoral condyle and autologous cartilage culture was conducted at Verigen Transplantation Services in Denmark. The cartilage was enzymatically treated and cultured for two to four weeks to increase the cell count by a factor ranging from 15 to 90. Apopototic test of chondrocytes using Annexin IV before implantation showed that viability of chondrocytes was over 85% where apopototic rate of chondrocytes was less than 2%. Surgical reimplantation of the chondral defect was then performed by arthrotomy, beneath a Chondro-Guide type I collagen flap (a synthetic collagen sheet) held in place with 6/0 dexon interrupted sutures spaced 3 mm apart at the periphery and sealed with fibrin glue. The collagen flap is acellular and completely absorbed by three months.

This report outlines the progression of two interesting cases through their rehabilitation prior to and following CACI. Results from this clinical review address the impact of a presurgery exercise program on levels of pain, stiffness, physical function and muscle strength in patients with

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articular cartilage defects of the knee. Furthermore, the review outlines their postoperative recovery. The two study patients participated in an eight-week presurgery exercise program and a 12-week post-surgery rehabilitation program within Hollywood Functional Rehabilitation Clinic (HFRC), Hollywood Private Hospital, Perth Western Australia. These programs were individually tailored to the needs and capabilities of each participant. In order to be comparable with other studies we used a wide variety of scores, all performed independently of the operating surgeon. Strength and function evaluations were conducted at eight (pre-8wks) and one week (pre-1wk) preoperatively and postoperatively at three months (post+3mo), six months (post+6mo) and one year (post+1yr). Magnetic resonance imaging (MRI) scans were taken preoperatively, and postoperatively at post+3mo and post+1yr in order to determine the success of integration of implanted chondrocytes.

The presurgery program objectives are:

- to increase the strength of muscle and connective tissue of the limb in which the surgery is to be undertaken;
- to increase the active range of motion in the joints of the lower limb in order to reduce preoperative contracture;
- to improve muscular strength of the upper limbs and trunk in order to assist bed to chair transfers and ambulation during in-hospital recovery;
- to improve the level of cardiovascular fitness which may aid faster recovery from surgery;
- to prepare the patient psychologically for surgery and for the lengthy rehabilitation process.

The presurgery exercise sessions involved both presurgery and postsurgery patients working together. This gave an opportunity for the two case subjects who had not undergone CACI to observe the rate of physical and functional progress in postsurgery patients from week-1 onwards. Patients with a good outcome following surgery served as excellent role models. Exercise sessions also provided time for discussion between patients and the therapist in regard to the surgical procedure and what might be expected during the first 12-weeks of recovery. Therefore, presurgery they were both physically and mentally prepared for their operative procedure. Postsurgery rehabilitation began within two weeks of surgery and study patients were required to attend HFRC three times per week for the first 12-weeks postsurgery. The sessions were approximately 2 to 3 hours in duration and were fully supervised.

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Case #1 - Male, roof carpenter, aged 29 years, height: 163.5 cm, weight: 64.4 kg.

Medical history: 1996 right knee medial menisectomy. 1999 reinjured right knee by falling through a ceiling and was diagnosed with an anterior cruciate liagament tear with significant associated full thickness medial femoral chondylar defect. Underwent an anterior cruciate liagment reconstruction using his hamstring tendon however continued to exhibit persistent effusion and quadriceps wasting. Upon further clinical evaluation he was deemed suitable for CACI and was scheduled for surgery at the end of 1999.

Results		Pre-8wks	Pre-1wk	Post+3mo	Post+6mo	Post+1yr
Weight (kg)		65.8	66.0	65.4	65.8	64.4
6min walk distance (m)		420	547	450	670	737
Keylink Isokinetic Machine (Peak Torque Nm)						
Leg Extension	L	124.1	127.6	Contraindicated	Contraindicated	139.5
	R	107.3	107.9	Contraindicated	Contraindicated	139.5
Leg Flexion	L	123.1	173.2	Contraindicated	Contraindicated	91.7
	R	77.3	92.7	Contraindicated	Contraindicated	100.8
Three Repitition Maximum (kg)						
Straight Leg Raise	L	32.2	35.0	32.0	37.0	39.0
	R	29.5	32.2	29.0	32.0	35.0
Active Range of Motion (Degrees)						
Leg Flexion	L	124	116	140	145	150
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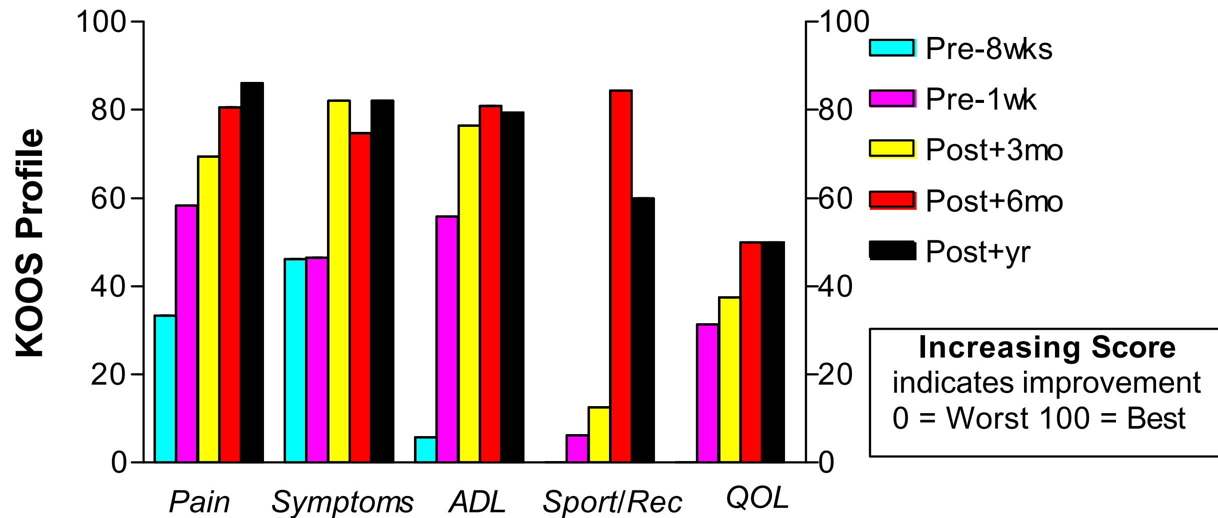
Knee Injury and Osteoarthritis Outcome Score (KOOS) profile.



ADL = Activities of Daily Living, Sport/Rec = Sport and Recreation Function, QOL = Knee Releated Quality of Life

The KOOS score, developed by Roos et al. (1998) was applied to assess five domains - pain, symptoms, activities of daily living, sport and recreation function and knee-related quality of life. It has proven to be reliable, responsive to surgery and physical therapy and evaluates the course of knee injury and treatment outcome. During his post+1yr assessment the study patient stated that he was extremely pleased with his progress to date. Whilst the patient was instructed to refrain from overloading his right knee, he stated that he had recommenced surfing and playing competitive six-a-side beach volleyball within the first postoperative year. Strength results at one year revealed a correction of presurgery muscle imbalance. AROM of both knees had improved to within the high end of normal anatomical range. MRI evaluation at the post+1yr timepoint showed full thickness infill of the defect with material that is identical in signal characteristics to adjacent hyaline cartilage.

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Case #2 - Female, bilateral OCD, aged 24 years, height: 173.4 cm, weight: 74.7 kg.

Medical history: 1997 diagnostic arthroscopy left knee. Removal of large loose fragment left knee 1998. Bilateral arthroscopy 1999, left knee small loose body removed, right knee OCD lesion stable, drilled with a K wire. Arthrotomy right knee 1999, large (4x3cm) loose fragment on medial femoral condyle, articular cartilage was intact on one margin. Fibrous tissue was curetted from below the lesion and subchondral bone was drilled and the a small amount of iliac crest graft was placed deep to the OCD lesion before fixing with five Herbert screws. Upon further clinical evaluation she was deemed suitable for to bilateral ACI and was scheduled for surgery at the end of 2000.

Results		Pre-1wk	Post+3mo	Post+6mo
Weight (kg)		75.8	-	74.7
6min walk distance (m)		462.0	473.0	537.5
Keylink Isokinetic Machine (Peak Torque Nm)				
Leg Extension	L	88.3	Contraindicated	Contraindicated
	R	44.9	Contraindicated	Contraindicated
Leg Flexion	L	53.6	Contraindicated	Contraindicated
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Straight Leg Raise	L	5.0	2.0	10.0
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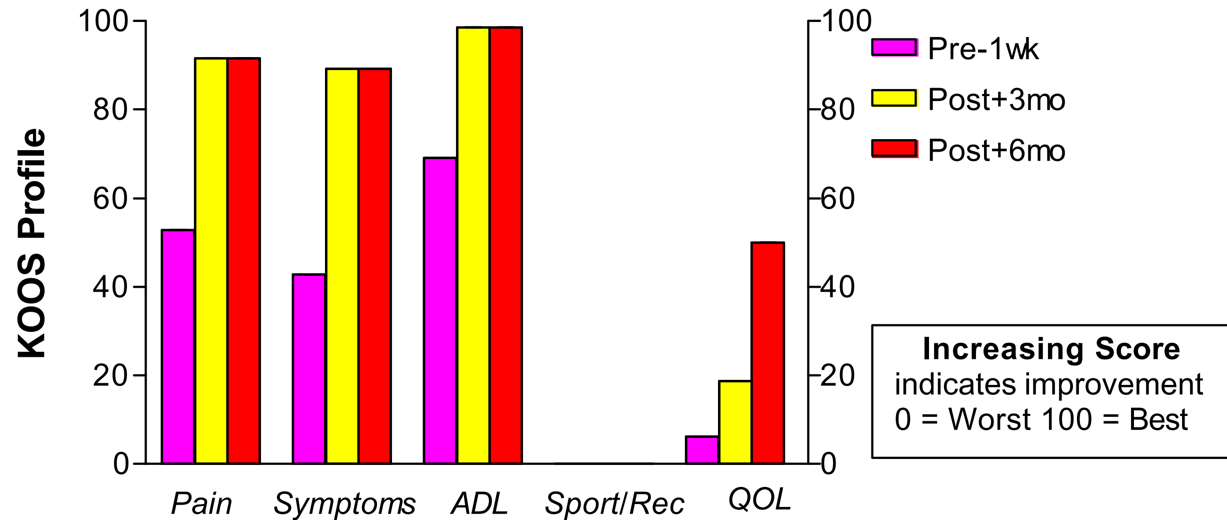

ADL = Activities of Daily Living, Sport/Rec = Sport and Recreation Function, QOL = Knee Releated Quality of Life

This patient progressed exceptionally well following bilateral CACI for osteochondritis desiccans. Her post+3mo MRI scan showed cartilage ingrowth in both knees. Pre and postoperative functional assessment results showed promising improvements up to the post+6mo timepoint. Her six-minute walk test distance had improved by 75.5m from the pre-1wk to the post+6mo timepoint. The KOOS profile also showed good improvement. For the domain of pain she improved from 52 to 92 and knee related quality of life improved from 6 to 50. Whilst the patient reported that she was anxious to begin sport and recreational activities she was strongly advised to allow her new cartilage to remodel and mature fully before she engaged in this kind of activity. At the time of this report the patient had not undergone her post+1yr review.

These case studies indicate that CACI in conjunction with an appropriately supervised rehabilitation program was successful in relieving the pain and symptoms caused by full thickness cartilage defects of the knee. Of particular interest are the KOOS and 6-minute walk results. The KOOS data illustrates improvement in outcome at the three postsurgery timepoints, with a reduction in pain and symptoms in conjunction with

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reduced difficulty performing ADL's. Ambulatory status may be one of the most important postsurgery functional outcomes (Finlay, 1993). Results show a increase in six-minute walk distance at the post+6mo and post+1yr timepoints. Hence it appears that CACI has the potential to improve the ambulatory ability and quality of life of patients with full thickness articular cartilage defects of the knee.

ACI is a relatively new technique, it was first performed in Sweden in 1987, since then over one thousand people worldwide have been treated using this procedure. However, the CACI technique has only been available in Australia since 1999 and whilst the technique itself has undergone stringent testing and development, rehabilitation following CACI is currently in it's infancy. Presently there are only a hand full of therapists in Australia who have clinical experience dealing with the perioperative management of CACI patients, this will soon change as the technique becomes more widely used. There is no definitive guide to CACI rehabilitation as there exists great individual variation between patients, and auxiliary surgical procedures (to correct instability or malalignment) also need to be considered in the treatment plan.

The rehabilitation process for CACI should begin prior to surgery as patients need to be physically and mentally prepared for their operative procedure and the lengthy rehabilitation process. In CACI patient education is essential, as the integrity of the chondrocyte repair must be protected. Postoperatively CACI patients are required to protect their repair from weightbearing stresses and are restricted to toe-touch ambulation with two crutches for the first six postoperative weeks. Over the following six-weeks a stepwise increase in weight bearing should occur so that by 12-weeks post surgery the patient should be ready to begin to fully weight bear. Postoperative knee flexion is restricted and a brace should be worn to ensure the protection of the cartilage repair. As a rough rule of thumb patients should achieve 60° knee flexion by three-weeks, 90° knee flexion by six-weeks and have returned to within normal anatomical range by 12-weeks postsurgery. At the post+3mo timepoint compressive and decompressive forces, provided by full weight bearing, further stimulate the chondrocytes to synthesise the correct matrix molecules. However, return to work and sport and recreational activities should be carefully controlled and gradually progressed. Although the cartialge defect may well have been filled with hyaline-type cartilage within the first few months, it is not advisable to undertake stressful extension or weightbearing activities, such as squats or running before twelve months. As definitive maturation and hardening of the new-formed cartilage will not be complete until 11-24 months have elapsed (VTSI).

In conclusion, recovery from CACI requires a carefully planned programme of progressive rehabilitation. The program should be conducted under the supervision of qualified physiotherapists or exercise physiologists, accredited in musculoskeletal rehabilitation. It is strongly advised that health professionals involved in the rehabilitation of ACI patients liaise closely with the patient's orthopaedic specialist throughout the course of the recovery process.

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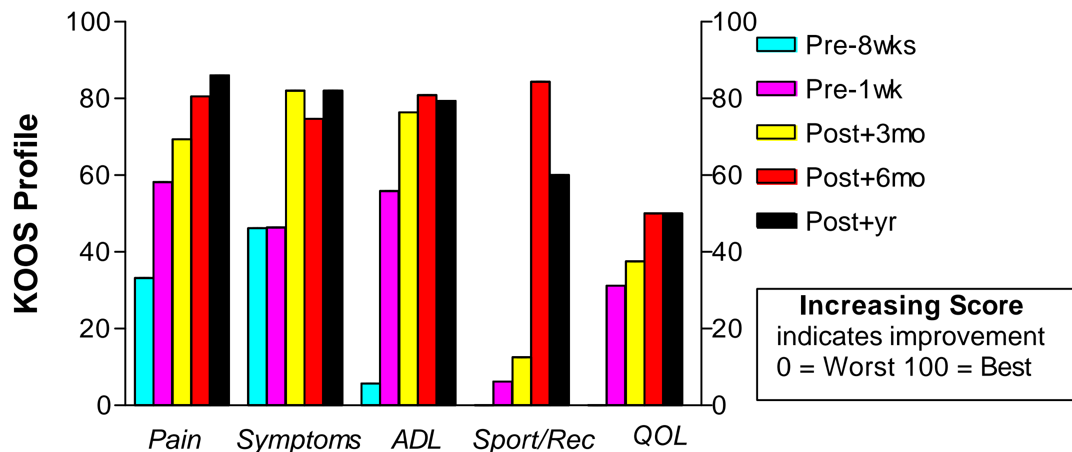

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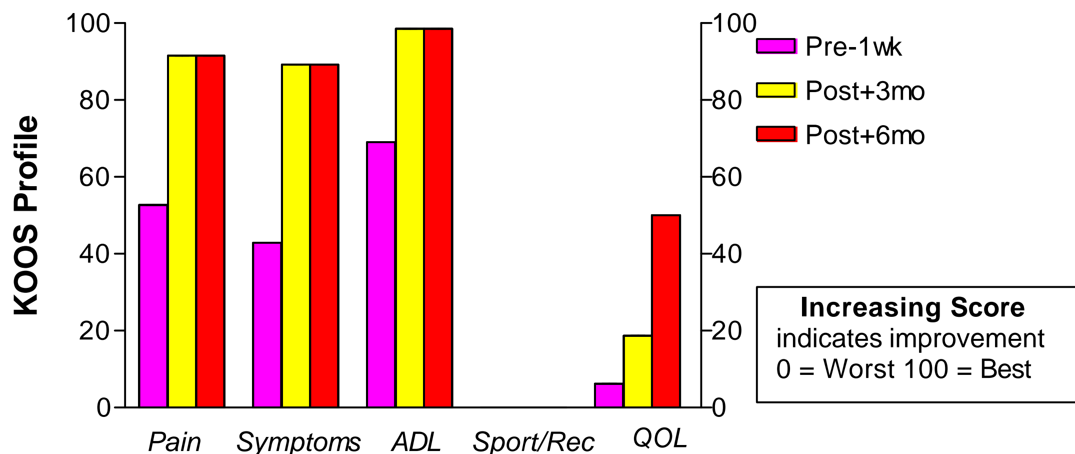

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