Collagen-covered autologous chondrocyte implantation for osteochondritis dissecans of the knee

TWO- TO SEVEN-YEAR RESULTS

We prospectively studied the clinical, arthroscopic and histological results of collagen-covered autologous chondrocyte implantation (ACI-C) in patients with symptomatic osteochondritis dissecans of the knee. The study included 37 patients who were evaluated at a mean follow-up of 4.08 years.

Clinical results showed a mean improvement in the modified Cincinnati score from 46.1 to 68.4. Excellent and good clinical results were seen in 82.1% of those with juvenile-onset osteochondritis dissecans but in only 44.4% of those with adult-onset disease.

Arthroscopy at one year revealed International Cartilage Repair Society grades of 1 or 2 in 21 of 24 patients (87.5%). Of 23 biopsies, 11 (47.8%) showed either a hyaline-like or a mixture of hyaline-like and fibrocartilage, 12 (52.2%) showed fibrocartilage.

The age at the time of ACI-C determined the clinical outcome for juvenile-onset disease (p = 0.05), whereas the size of the defect was the major determinant of outcome in adult-onset disease (p = 0.01).

Operations for patients with symptomatic osteochondritis dissecans include drilling, fixation or removal of the fragment. More recently, autologous chondrocyte implantation using periosteum as a covering membrane (ACI-P) has shown promising results. Since 1998 we have used chondrogide, a porcine type I/III collagen membrane (ACI-C), which avoids the need to harvest periosteum and shortens the operation.

In line with national guidelines, we perform ACI-C only when symptoms have persisted after removal of the loose fragment or previous attempts to heal the osteochondritis dissecans.

It is not known whether the outcome of ACI is affected by skeletal maturity. As it is considered essential to obtain healing of a symptomatic juvenile-onset osteochondritis dissecans before skeletal maturity because its potential for healing is reduced afterwards, we attempted to compare those who were skeletally mature at the time of ACI-C with those who had open physes. We also compared the outcome after ACI-C between patients with juvenile- and those with adult-onset osteochondritis dissecans. Our mid-term results, presented here, are to our knowledge, the first report of ACI-C in osteochondritis dissecans.

Patients and Method
This study was approved by the Joint Research and Ethics Committee of our hospital where, between 1998 and 2003, 356 patients underwent ACI-C for symptomatic osteochondral defects of the knee. Of these, 37 had radiographically documented osteochondritis dissecans with a minimum of two years of follow-up. Those who developed symptoms before 21 years of age were classified as juvenile-onset, and those whose symptoms came later as adult-onset osteochondritis dissecans.

Radiographs at the time of ACI-C were examined to document skeletal maturity in the former.

The mean age at the onset of symptoms was 18.6 years (6 to 42). The mean duration of symptoms was 9.98 years (SD 5.7, 1.5 to 23). The mean number of previous operations was 2 (SD = 1.2, 1 to 6).

The technique of ACI-C is described elsewhere. Rehabilitation was the same for all patients. A plaster-reinforced compression bandage was applied, the limb rested and elevated for 12 hours, with the patient encouraged to move the foot and ankle and to perform static quadriceps exercises. Full weight-bearing was encouraged at 24 hours post-operatively to stimulate the circulation in the limb and fluid exchange in the articular cartilage. At 48 hours a light cylinder cast was applied with the knee in full extension and the patient was discharged, fully weight-bearing and using crutches for support. After removal of the plaster at ten days the patients under-
went daily physiotherapy for two weeks to achieve full movement. Crutches were used as protection for six weeks. Then, if the wound was satisfactory, swimming, gentle cycling and rowing exercises were encouraged but impact loading and twisting strains were avoided. At six weeks the patient could return to light work; at six months careful jogging could begin but contact sports were avoided until 12 months post-operatively.

Patients were assessed at six weeks, three, six and nine months, and then annually. Clinical assessment was by the modified Cincinnati rating system,8 the Stanmore functional rating system9 and a visual analogue pain score. The functional results on the modified Cincinnati rating system are graded as excellent (> 80), good (55 to 79), fair (30 to 54) or poor (< 30). In clinical terms, patients with excellent and good results were improved, those with fair results were unchanged and those with poor results were worse.

Arthroscopy and a biopsy using a 2.5-mm diameter Jamshidi needle was performed at one year whenever possible. Cartilage repair was observed and assessed using the International Cartilage Repair Society grading system. Grading of repair was absolute: no progression of the lesions was made. The quality of repair in the biopsies was assessed by a second pathologist (AMF), who was blinded to the symptoms of individual patients. The neo-cartilage was graded as hyaline-like (H), mixed fibrohyaline (FH), fibrocartilaginous (FC) or fibrous (F).

Statistical analysis used the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois), version 11, under the supervision of the hospital statistician. Linear regression analysis investigated the relationship between numerical variables. Single-factor analysis of variance (ANOVA) compared non-numerical variables between groups, and chi-squared tests were used for categorical variables. The level of significance was set at p < 0.05.

Results

The 37 patients included 23 men and 14 women. The mean age at operation was 23.8 years (15 to 36) for those with juvenile-onset and 40 years (36 to 44) for those with adult-onset osteochondritis dissecans. Follow-up ranged from two to seven years (mean 4.08, SD ± 1.2). The defects were on the medial femoral condyle in 27 patients (73%), the lateral condyle in six (16%) and the patella in four (11%). Their average area was 593.26 mm² (SD = 356.5, 100 to 1500 mm²) and their depth was 8 mm or less in all but one case, for which bone grafting was performed. The mean number of chondrocytes injected was 9.8 million (5 to 15 million).

Clinical examination showed that 27 (72.3%) of patients had excellent or good results. Their modified Cincinnati rating system improved from a mean pre-operative value of 46.2 to 68.0 (p = 0.001). The Stanmore functional rating and visual analogue scores improved from a mean pre-operative score of 2.85 and 5.3 to 1.51 and 2.88, respectively (p < 0.05).

Arthroscopy at one year revealed International Cartilage Repair Society grades of 1 (excellent) or 2 (good) in 21 of 24 patients (87.5%) who consented to the procedure. Of the remaining three patients, two scored grade 3 (fair) and one had grade 4 (poor) repair. Of the 23 biopsies taken at one year, 11 (47.8%) showed either hyaline-like or a mixture of hyaline-like and fibrocartilage, and 12 demonstrated fibrocartilage (52.2%).

Juvenile-onset osteochondritis dissecans. There were 28 patients in this group (76%). The mean age at the onset of symptoms was 13.7 years (6 to 19), the mean duration of symptoms was 10.1 years (2 to 23) and the mean size of the defect was 602.7 mm² (120 to 1225 mm²). The proportion of patients with excellent and good results was 82.1% at a mean follow-up 4.3 years with a mean age at surgery of 23.8 years. Eleven had ACI-C before skeletal maturity (group 1) and 17 afterwards (group 2). The proportion of patients with excellent and good results was 90.9% in group 1 and 76.5% in group 2. This difference was not statistically significant (p = 0.52). The mean modified Cincinnati rating system scores were 75.5 for group 1 and 70.6 for group 2. However, linear regression analysis comparing age at the time of surgery and clinical results showed that a younger age predicted a better clinical outcome (p = 0.05). The duration of symptoms showed a weak relationship with clinical outcome (p = 0.06), and the size of defect did not influence the outcome (p = 0.99). The mean modified Cincinnati rating system for those with a defect > 600 mm² was 72.9 and for those with a defect < 600 mm² was 72.0 (p = 0.92).

Adult-onset osteochondritis dissecans. There were nine patients with adult-onset osteochondritis dissecans (24%). The mean age at the onset of symptoms was 33 years (26 to 42), the mean duration of symptoms was 7.2 years (2.5 to 12) and the mean size of the defect was 583 mm² (100 to 1500 mm²). The proportion of patients with excellent and good results was 44.4% with a mean follow-up of 3.3 years and a mean age at surgery of 40 years. The only important variable influencing clinical outcome was the size of the defect (p = 0.01). Those with a defect > 600 mm² showed a significantly inferior clinical outcome to those with a defect < 600 mm². Their mean modified Cincinnati rating system scores were 27.5 and 76.2, respectively (p = 0.003).

Complications included one patient with knee stiffness, which improved after manipulation under anaesthesia. Another with juvenile-onset osteochondritis dissecans had unexplained graft failure at four years, which was treated by revision ACI-C and is currently under review.

Discussion

Various authors have reported successful outcomes by fixing or removing the fragments when treating symptomatic osteochondritis dissecans of the knee.9-13 However, the management of such patients with persisting/recurring symptoms remains controversial.8,14 Our study describes the results of ACI-C in the salvage of symptomatic osteo-
chondritis dissecans, and shows that it gives favourable clinical results in patients with symptomatic juvenile-onset disease at a mean follow-up of 4.3 years, but inferior results in adults at a mean follow-up of 3.3 years (82.1% and 44.4% excellent and good results, respectively).

We previously reported that an older age at ACI would compromise the clinical outcome.\textsuperscript{15} The mean age at surgery in adult-onset osteochondritis dissecans in our study was 40 years, which alone might explain the inferior results.

Peterson et al\textsuperscript{2} reported 91% excellent and good results at a mean follow-up of 5.6 years in patients with symptomatic osteochondritis dissecans who underwent ACI-P. Our study showed only 72.3% such results at a mean follow-up of 4.08 years. However, only 83% of Peterson’s patients had had previous operations. National guidelines in Great Britain\textsuperscript{4} restrict ACI to patients in whom other surgical options have failed. In our cohort the mean duration of symptoms before ACI-C was 9.9 years, compared to 7.8 years in Peterson’s study. ACI-P may give better results, although earlier studies from our centre reported comparable or superior results for ACI-C.\textsuperscript{2}

Magnetic resonance imaging (MRI) is useful in pre-operative delineation of the osteochondral lesion\textsuperscript{16,17} and post-operative evaluation of the morphology of ACI grafts.\textsuperscript{18} None of our patients had ACI as the first operation, and all underwent at least arthroscopy for diagnosis. As our post-operative assessment used arthroscopy and biopsy the value of MRI would have been limited. Nevertheless, almost 50% of these patients had pre- and post-operative MR scans, which are the subject of on-going studies in relation to clinical, histological and radiological outcome.

In 2002 the International Cartilage repair score Historical Endpoint Committee recommended a visual histological score to evaluate cartilage repair tissue,\textsuperscript{19} based on an expandable web-based catalogue of images rather than on verbal descriptions. As our study was set up in 1998, this scoring system was not used.

Among juvenile-onset cases our results suggest that age rather than the state of the physis is more important in determining the outcome. There were, however, small numbers in each group (11 and 17, respectively) and a larger sample would be necessary for confirmation.

It is interesting that a larger defect (> 600 mm\textsuperscript{2}) is related to an inferior clinical outcome for adult-onset disease, whereas a similar size in juvenile disease did not influence the outcome. This suggests either a greater healing potential for ACI-C at a younger age or that the healing potential of larger defects in adult-onset disease is inferior. The inferior outcome of ACI-C for patients with adult-onset osteochondritis and a large defect indicates the need to test procedures such as ACI-C combined with high tibial osteotomy.

Our study shows that the medium-term results of ACI-C for symptomatic juvenile-onset disease are promising.

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References