Evidence Table

Clinical Area: Autologous chondrocyte (Carticel) implantation for treatment of defects in articular cartilage of the knee

Keywords: autologous chondrocyte, osteochondral cylinder transplantation, knee


Study Type: Randomized controlled trial
Study Aim: To compare the effectiveness of autologous chondrocyte implantation (ACI) and transplantation of an autologous osteochondral cylinder for repairing defects of the articular cartilage of the knee.

Outcomes
- **Primary:** Speed of recovery, pain, knee function
- **Secondary:** Histological outcomes

Design
- **Number of subjects:** N=40 (n=20 ACI; n=20 autologous osteochondral cylinder transplantation).
- **Description of study population:** ACI group: 12 women/8 men, mean age=31.4 years. Cylinder transplantation group: 5 women/15 men, mean age=35.4 years.
- **Inclusion criteria:** 18-45 years old; clinical knee symptoms (e.g. pain with weight-bearing); history of a single traumatic event; single cartilage lesion extending to or through the articular cartilage tidemark without an osseous lesion; lesion in the weight-bearing area of the femoral condyle.
- **Exclusion criteria:** Knee joint instability, matching lesion on the opposing tibial articular surface, axial malalignment; osteochondral tumor; skeletal immaturining; degenerative or rheumatoid joint disease.
- **Power:** Not discussed.
- **Method of randomization:** Alternated assignment to each group.
- **Intervention:** Patients were assigned to receive either ACI or transplantation of autologous osteochondral cylinder. **ACI:** This was a two-part procedure. In the first procedure, a slice of healthy articular cartilage was obtained arthroscopically and chondrocytes were isolated according to the Brittberg method. Cells were cultured for 2-3 weeks. In a second operation, the chondrocyte suspension was transplanted. **Osteochondral cylinder transplantation:** A pair of carving cylinders differing 0.1 mm in diameter was used to harvest the osteochondral transplants. The defect was resurfaced with the appropriate sized cylinder. Both groups received the same rehabilitation program.
- **Blinding:** Not discussed.
- **Source of outcome data (e.g. patient self-report, doctor report, lab results):** Clinical evaluation, histological evaluation, post-operative arthroscopy on some patients.
- **Length of follow-up:** Patients were examined pre-operatively and at 3, 6, 12, and 24 months post-operative.
- **Completeness of follow-up:** Not clear.

Validity
- **Is the study type appropriate for the questions being asked?** Yes.
- **Was the study population typical of patients with this disease?** Appear to be.
- **Were the treatment/control groups comparable at baseline?** Appear to be on measured characteristics.
- **Was the intervention compared to placebo and/or best accepted intervention?** Yes.
- **Was there compliance with the intervention?** Yes.
- **Was there equal intensity of observation of study and control subjects?** Yes.
- **Was the process of observation likely to effect the outcome?** Possibly. If outcome assessment was not blinded, this could have affected the functional status measurements.
- **Intention to treat analysis?** Not discussed.

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Conclusions regarding validity of methods:
This was a small study and randomization was inadequate. Patient assignment was by alternating, which is not true randomization. The authors did not discuss power and it is likely that there was insufficient power to detect differences between groups. Blinding was also not discussed, and if the study was not double-blind, bias could be introduced. The authors did not provide descriptions of their measures, the Lysholm, Tegner and Meyers scores.

Results
Lysholm scale: Evaluates knee instability (instability is defined as “giving way” during activity)
Tegner scale: Activity grading scale (work and sport activities)
Meyers: Unclear what is measured with this scale.

Preoperative Lysholm, Tegner and Meyers scores were similar between the two treatment groups (p<0.12).

The authors did not report the exact scores for the three scales. Results were displayed in a figure and the exact scores for the three scales pre-operatively or post-operatively were not reported. The time points on the figure were pre-operative and 3,6,12 and 24 months post-operative.

- Lysholm score differed significantly (p<0.05) between groups at 6, 12 and 24 months.
- There were no significant differences between groups on the Meyers and Tegner scores at any time points.

Authors’ Conclusions
“Both treatments resulted in a decrease in symptoms. However, the improvement provided by the autologous chondrocyte implantation lagged behind that provided by the osteochondral cylinder transplantation…Limitations of our study included the small number of patients, the relatively short (two-year) follow-up and the absence of a control group.”

Reviewer’s Conclusions
In this small study with alternating assignment to groups (not random assignment), the group that was assigned to autologous chondrocyte implantation (ACI) differed significantly on the Lysholm instability scale compared to the group assigned to osteochondral cylinder transplantation. According to the authors, this difference favored osteochondral cylinder transplantation. The scores on other measures (Tegner activity scale, Meyers scale) did not differ significantly between groups. This study had weak methodology. In addition to inadequate randomization, the authors did not discuss blinding or statistical power and did not sufficiently describe their outcome measures.