Effectiveness of autologous chondrocyte transplantation for hyaline cartilage defects in knees: a rapid and systematic review

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Authors' objectives
The objectives of the review were:

to describe the types of knee disease for which autologous chondrocyte transplantation (ACT) has been applied, the natural history and epidemiology of these conditions, and the alternative treatment options;

to determine the long-term clinical outcomes following ACT and other surgical procedures for knee cartilage defects; and

to examine the economic evidence and consider the economic gains resulting from ACT.

This abstract will only look at the data regarding effectiveness.

Searching
The following sources were searched: MEDLINE from 1966 to May 2000; EMBASE from 1988 to May 2000; the Science Citation Index from 1981 to May 2000; the Cochrane Library (Issue 1, 2000); and DARE, NHS EED and HTA, all accessed in March 2000. Details of the search strategy were reported in the review.

In addition, the abstracts from meetings of the Cartilage Repair Society (1998 to 1999) and the American Academy of Orthopaedic Surgeons (1997 to 1999) were searched, and leading researchers were contacted. The authors also searched the Internet using a metasearch engine, and searched for unpublished studies in industry submissions to the National Institute for Clinical Excellence. Studies reported in any language were considered. If data from the same source were available in multiple publications, the most recent or most complete report was used.

The authors also carried out a scoping search to identify data on other therapies used to treat knee cartilage defects. This search was restricted to English language publications.

Study selection
Study designs of evaluations included in the review
Any report, published or unpublished, was eligible for inclusion.

Specific interventions included in the review
Studies which described the use of ACT were eligible for inclusion.

Participants included in the review
Studies in which any patient group with knee cartilage defects had undergone ACT were eligible for inclusion. Studies focusing exclusively on patella cartilage defects were excluded. The mean age of the participants in the included studies (where reported) ranged from 27 to 38 years. There was wide variation in the site(s) and size of the lesion, the need for concomitant procedures, and the proportion of patients who had undergone prior surgeries.

Outcomes assessed in the review
Studies that reported patient outcomes were eligible for inclusion. The included studies reported a variety of clinical outcomes.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.
Assessment of study quality
Quality was not assessed using a published checklist. However, the studies were given a rating from A to D, based on whether the study outcomes included patient input and were reported before and after surgery. The authors state how the papers were assessed for quality, but not how many of the reviewers performed the quality assessment.

Data extraction
Two reviewers abstracted the data on patient outcomes using a specifically designed form. Any discrepancies were resolved by discussion, or by repeated independent checking of the extracted data, until there was consensus.

The following categories of data were extracted: mean participant age; defect size and characteristics; concomitant procedures; previous surgeries; minimum follow-up; clinical outcomes; adverse effects and the need for further surgery.

Methods of synthesis
How were the studies combined?
A narrative synthesis was undertaken.

How were differences between studies investigated?
Differences between the studies were discussed within the text of the review.

Results of the review
Seventeen reports (including at least 2,600 participants) met the inclusion criteria. The authors also included data collated by the Robert Jones and Agnes Hunt (RJAH) Orthopaedic and District Hospital NHS Trust. All of the included studies were case series without historical or concurrent controls. Eight of the included reports were available as abstracts only.

The authors also identified ten randomised controlled trials, either proposed or in progress, comparing ACT with other interventions.

The quality scores of the included studies were as follows: 4 were rated A, 11 were rated B, 1 was rated C, 1 was rated C to D, and 3 were rated D. Data from two studies were listed twice.

The outcome of ACT surgery was rated as ‘good’ or ‘excellent’ by 71 to 77% of the patients, 2 years after treatment. Approximately 16% of the patients required further arthroscopic surgical procedures during follow-up, and treatment was judged to have failed in 3 to 7% of the patients. For comparator treatments, the outcome was rated as ‘good’ or ‘excellent’ in 10 to 95% of the patients, 2 years after treatment.

The authors reported that it was evident that there were no established standard therapies for cartilage defects, against which ACT could be compared.

Cost information
Using data from two studies (based in the USA and Sweden) and other sources, it was estimated that ACT performed in the UK would cost £4,667 or £8,167 for cell culture and surgery, depending on which service provider was used for cell culture. The incremental cost over 2 years, when set against comparator treatments, was estimated to be £3,771 or £7,271 (base-case) for cell culture, surgery and rehabilitation. Using the OsCell facility for cell culture (RJAH Orthopaedic and District Hospital NHS Trust), this figure would be £3,167.

Authors’ conclusions
The reported literature on ACT and comparators is subject to bias because of the inherent weaknesses of case series. In addition, the long-term impact of conventional surgical treatment or no surgical treatment is poorly documented.
CRD commentary
Overall, the methodological quality of this review was good. The authors addressed a clear review question and provided adequate inclusion and exclusion criteria. The search strategy was wide-ranging and the authors did not apply any language restrictions. The data extraction was carried out independently by two reviewers, and details of the studies were summarised clearly in tabular format. The authors assessed the quality of the included studies, but their quality assessment scale was fairly basic and did not address issues such as adequacy of follow-up and whether a representative sample was chosen. The data were combined appropriately using a narrative synthesis and heterogeneity was discussed. The authors failed to describe how the studies were selected for inclusion in the review, or how many reviewers performed the selection or assessed quality.

The authors’ conclusions follow on from the results of the included studies.

Implications of the review for practice and research
Practice: The authors state that there is a need to (1) establish surgical standards to ensure that ACT is used only for appropriate indications and by trained specialists; and (2) ensure that patients give truly informed consent.

Research: The authors state that further studies are required:

- to provide more accurate data on the occurrence of hyaline cartilage defects, including defects that arise acutely and those that are secondary to other types of knee injury;
- to clarify the relationship of cartilage defects to clinical symptoms;
- to evaluate in detail the natural history of cartilage defects diagnosed by modern arthroscopic methods;
- to compare ACT with other treatments deemed appropriate, based on randomised trials currently in progress or planned;
- to examine issues, such as the differences in outcome in patient subgroups, in prospective randomised trials with patients followed as long as possible;
- to address the deficiencies in evaluating the clinical outcomes of knee injury and incorporate measures of general health status; and
- to consider study designs, other than randomised trials, that might be used to assess complex interventions such as those required in complex knee injuries.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.