Failures, re-operations, and complications after autologous chondrocyte implantation: a systematic review

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CRD summary
The review concluded that the failure rate after all autologous chondrocyte implantation generations was low, but was highest with periosteal implantations, and lower with collagen implantations and second-generation techniques. Unplanned re-operations, hypertrophy and delamination were most commonly seen after periosteal implantations. The review had some serious flaws, meaning its conclusions should not be considered as being reliable.

Authors' objectives
To determine and compare failure, re-operation and complication rates of all generations and techniques of autologous chondrocyte implantation.

Searching
MEDLINE, CINAHL, SPORTDiscus and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched to May 2010 for studies published in English; search terms were reported. Conference abstracts were excluded. Reference lists of included studies were also searched.

Study selection
Any clinical studies that reported complications, failures and re-operations, following autologous chondrocyte implantation (any generation, open or arthroscopic) in knee joints were eligible. Definitions of first, second and third generation implantation were reported in the paper.

Mean patient age was 33.4 years and mean follow up was 3.3 years. The mean defect size was 4.8cm²; half of defects were located in the medial femoral condyle. Most studies were of first generation implantation techniques, using a collagen or periosteal autologous chondrocyte implantation technique. Very few patients underwent third generation procedures. Definitions of failure, and of various complications, varied across studies.

It was unclear how many reviewers selected studies for inclusion, although it was reported that any disagreements were resolved by the senior author, and that the review reported that it was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) guidelines.

Assessment of study quality
Study quality was assessed using the Modified Coleman Methodology Score, which evaluates 15 criteria (covering aspects of study bias, reporting and precision) which resulted in a score from 0 to 100. Studies that scored 85 to 100 were deemed excellent, 70-84 good, 55-69 fair and less than 55 poor. The authors did not state how many reviewers performed the quality assessment.

Data extraction
Number of events by outcome type was extracted. The authors did not state how many reviewers extracted data.

Methods of synthesis
It appeared that event data were summed to produce overall rates by type of implantation and across all studies. Two proportion Z-tests were used to compare rates between types of implantation.

Results of the review
Eighty-two studies were included (5,276 participants, number of knees was 5,352). Prevalence of study designs in relation to levels of evidence were presented, but the meaning of all the levels was not presented (but was referenced). The mean Modified Coleman Methodology Score was 35.4 (poor quality); 90% of studies were rated as being poor. The level one evidence (reported as being randomised trials) was rated as being fair overall (mean score 56.7).
Since only one study (of eight patients) involved a third generation implantation technique, the results were not compared with the first and second generation technique results.

The failure rate was 5.8% overall, and was highest (7.7%) for first generation periosteal autologous chondrocyte implantation. The overall rate of re-operation was 33%, and was highest for first generation collagen autologous chondrocyte implantation (40%). The unplanned re-operation rate was highest for first generation periosteal autologous chondrocyte implantation (27%). The most common complication was graft/periosteal hypertrophy, which occurred in 18% of patients who received first generation periosteal autologous chondrocyte implantation and 3% of patients who received first generation collagen autologous chondrocyte implantation.

Rates of failure, unplanned re-operations, hypertrophy, delamination and arthrofibrosis were all significantly higher after first generation procedures when compared with second generation procedures. Further results were reported.

**Authors' conclusions**

Failure rate following all autologous chondrocyte implantation generations was low, but was highest with periosteal implantations, and lower with collagen implantations and second-generation techniques. Unplanned re-operations, hypertrophy and delamination were most commonly seen after periosteal implantations.

**CRD commentary**

The review addressed a clear question and was supported by appropriate inclusion criteria. Several electronic databases were searched, but the restriction to studies published in English meant that relevant studies may have been missed (and the review may have been subject to publication or language bias). The authors stated that the PRISMA guidelines were applied, but they did not clearly report using methods (such as independent duplicate processes) which could have minimised the risk of reviewer error and bias during the quality assessment and data extraction processes.

Study quality was evaluated, but serious deficiencies highlighted in the review's discussion were not incorporated into the overall conclusions. Data were pooled using simple statistics, seemingly without use of weightings, or of sensitivity/subgroup analyses to minimise clinical or methodological heterogeneity. This meant the analyses (particularly those used to compare different techniques) were of questionable value. Individual study characteristics and results were not provided, which made it difficult for the reader to interpret the data. The review had some serious methodological and reporting flaws, meaning its conclusions should not be considered as being reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated a need for better reporting in future studies, and for high quality randomised trials that compared different autologous chondrocyte implantation generations with regard to clinical, radiographic and histologic outcomes.

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