



Title	Clinical and Cost Effectiveness of Autologous Chondrocyte Implantation for Cartilage Defects in Knee Joints: Systematic Review and Economic Evaluation
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Aim

To support a review of the guidance issued by the National Institute for Health and Clinical Excellence (NICE) in December 2000 by examining clinical and cost effectiveness evidence on autologous cartilage transplantation.

Conclusions and results

Four randomized controlled trials (RCTs) and observational data from case series were included. The trials studied 266 patients and the observational studies up to 101 patients. Two studies compared autologous chondrocyte implantation (ACI) with mosaicplasty, the third compared ACI with microfracture, and the fourth compared matrix-guided ACI (MACI®) with microfracture. Followup was 1 year in one study, and up to 3 years in the remaining three studies. The first trial of ACI versus mosaicplasty found that ACI gave better results than mosaicplasty at 1 year. Overall, 88% had excellent or good results with ACI versus 69% with mosaicplasty. About half of the biopsies after ACI showed hyaline cartilage. The second trial of ACI versus mosaicplasty found little difference in clinical outcomes at 2 years. Disappointingly, biopsies from the ACI group showed fibrocartilage rather than hyaline cartilage. The trial of ACI versus microfracture also found only small differences in outcomes at 2 years. Finally, the trial of MACI versus microfracture contained insufficient long-term results, but the study does show the feasibility of doing ACI by the MACI technique. It also suggested that after ACI, it takes 2 years for full-thickness cartilage to be produced. Reliable costs per quality-adjusted life-year (QALY) could not be calculated owing to the absence of necessary data. Simple short-term modeling suggests that the quality of life gain from ACI versus microfracture would have to be between 70% and 100% greater over 2 years for it to be more cost effective within the GBP 20 000 to 30 000 per QALY cost-effectiveness thresholds. However, if the gains in quality of life could be maintained for a decade, increments relative to microfracture would only have to be 10%–20% greater to

justify additional treatment costs within the cost-effectiveness band indicated above. Followup from the trials has been only up to 2 years, with longer term outcomes uncertain.

Recommendations

Evidence is insufficient to say that ACI is cost effective compared with microfracture or mosaicplasty. Longer term outcomes are required. Economic modeling suggests that ACI could be cost effective since it is more likely to produce hyaline cartilage, which is more likely to be durable and prevent osteoarthritis in the longer term (eg, 20 years).

Methods

Evidence on clinical effectiveness was obtained from randomized trials, supplemented by data from selected observational studies for longer term results and the natural history of chondral lesions. Because of a lack of long-term results on outcomes such as later osteoarthritis and knee replacement, only illustrative modeling was done.

Further research/reviews required

Further research is needed into earlier methods of predicting long-term results. Basic science research is also needed into factors that influence stem cells to become chondrocytes and to produce high-quality cartilage, as it may be possible to have more patients developing hyaline cartilage after microfracture. Study is also needed into cost-effective methods of rehabilitation and the effect of early mobilization on cartilage growth.