Cost and health status analysis after autologous chondrocyte implantation and mosaicplasty: a retrospective comparison

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Autologous chondrocyte implantation (ACI) and mosaicplasty, which are surgical techniques for the treatment of symptomatic osteochondral defects in the knee, were studied.

Type of intervention
Treatment (surgical).

Economic study type
Cost-utility analysis.

Study population
Patients were eligible for inclusion in the study if they received first ACI or first mosaicplasty for chondral or osteochondral lesions of at least 1 cm diameter at the Royal National Orthopaedic Hospital (RNOH) between March 1997 and February 2001. The authors also collected and presented data from patients who were on an ACI waiting list at the RNOH between December 2002 and April 2003. Patients were ineligible if they were younger than 16 years at first referral, or were unable to complete an English-language postal health status questionnaire. They were also ineligible if they had had operations on both knees, or had both an ACI operation and a mosaicplasty on different sites of the same knee.

Setting
The setting was secondary care at the RNOH in the UK. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness evidence related to surgeries performed between March 1997 and February 2001. Resource use was collected for each patient for 2 years post-surgery. The costs related to the 2003/2004 financial year at the RNOH.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The authors used a convenience sample from their hospital setting, inviting all eligible patients (178 persons) to participate if they had presented at the RNOH between March 1997 and February 2001. Ninety-five (53%) of these
patients consented to having their records reviewed. There were 53 ACI recipients, 20 mosaicplasty recipients and 22 ACI waiting-list patients. The authors did not find any statistically significant differences in patient characteristics among groups, as measured at the time of surgery or postal questionnaire.

Study design
The study was a cross-sectional, retrospective cohort study that was conducted in a single centre. Given the design, there was variable length of follow-up in the surgical groups because patients did not complete the postal questionnaire at a consistent time-point postoperatively. Postal questionnaires were completed by 44 ACI, 12 mosaicplasty and 20 waiting-list patients.

Analysis of effectiveness
The patients evaluated their health status via a questionnaire using several instruments:

- the Modified Cincinnati Knee Rating System;
- the Pain Disability Index (PDI);
- a global condition-related life satisfaction scale; and
- the EQ-5D.

The analysis of the clinical study was based on available patient data. The mean EQ-5D scores for those patients who supplied data was assumed to equate to the mean in that treatment group. There was no investigation into the characteristics of patients who refused to participate or failed to supply completed questionnaires, or into how differences might have affected the effectiveness results.

Effectiveness results
The authors reported results for the waiting-list group and combined the results for the two postoperative surgery groups.

The mean Cincinnati Knee Score was 42 (standard deviation, SD=23) in the waiting-list group and 55 (SD=25) in the combined ACI/mosaicplasty group, (p = 0.04).

The mean PDI was 30 (SD=15.5) in the waiting-list group and 23 (SD=16) in the combined ACI and mosaicplasty group, (p=0.09).

The distribution of life satisfaction scores was 9% satisfied, 5% equally satisfied/dissatisfied and 86% dissatisfied in the waiting-list group, and 33% satisfied, 12% equally satisfied/dissatisfied and 54% dissatisfied in the combined ACI and mosaicplasty group, (p=0.01).

The mean EQ-5D score was 0.41 (SD=0.35) in the waiting-list group and 0.61 (SD=0.31) in the combined ACI and mosaicplasty group, (p=0.03).

The authors reported that no statistically significant differences between the ACI and mosaicplasty groups were found for any of the health status outcomes.

The EQ-5D mean social tariff score was 0.64 for the ACI group (n=41) and 0.47 for the mosaicplasty group (n=11), (p=0.22).

No other results were reported separately for the surgery groups.

Clinical conclusions
The authors concluded that, postoperatively, ACI and mosaicplasty patients experienced better health status than patients waiting for ACI, according to the Cincinnati Knee Score, Life Satisfaction scores, PDI and EQ-5D social tariff. They also found a trend towards improved health status with ACI when compared with mosaicplasty, though none of their results reached significance.

**Measure of benefits used in the economic analysis**
Quality-adjusted life-years (QALYs) were used in the economic analysis. These were derived from EQ-5D scores collected during the study and the UK tariff. The EQ-5D scores of the waiting list group were used as proxy for the pre-operative scores for the ACI/mosaicplasty groups. Forty-one ACI, 11 mosaicplasty and 20 waiting-list patients completed the EQ-5D for the study. This outcome was measured at various time points postoperatively in the surgery groups. It was assumed that, for the surgery groups, the estimated improvement in EQ-5D health status occurred immediately after surgery and was stable for 2 years (corresponding to the resource use data collection period).

**Direct costs**
Discounting was not carried out because "costs tended to occur in the first year". The quantities and the costs for the National Health Service secondary care resources used were reported. Information was collected for presurgery arthroscopy, surgery, inpatient ward stays, day case admissions, outpatient consultations, unanticipated postoperative events and their associated consultations, treatments and admissions, and investigations and interventions relating to the original knee surgery (e.g. echocardiograms, histology, X-rays, magnetic resonance imaging and ultrasound). Resource use was drawn from RNOH patient records from the first preoperative outpatient appointment for the original ACI or mosaicplasty up to 2 years following surgery (patients received surgery between March 1997 and February 2001). The costs for resource use were obtained from the RNOH financial services department for 2003 to 2004. Where patients received several interventions concurrently, the cost of the most expensive procedure was included together with half of the cost of the secondary intervention.

**Statistical analysis of costs**
The cost data were skewed and formed a small sample. Therefore, a non-parametric bootstrap method was used to calculate a confidence interval around the arithmetic mean.

**Indirect Costs**
No indirect costs were included.

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
The authors conducted a sensitivity analysis to investigate the effect of substituting a different published cost for ACI. They also reported the results assuming recovery from surgery meant 6 months would pass before an improvement in health status occurred.

**Estimated benefits used in the economic analysis**
The estimated incremental utility benefit following surgery was 0.23 for ACI patients and 0.06 for mosaicplasty patients. This was assumed to apply directly after surgery and constantly for a period of 2 years. The utility effects of adverse events or re-operations were not considered.

**Cost results**
The mean total cost of immediate preoperative care, surgery and follow-up to 2 years was 10,600 (95% confidence
interval, CI: 10,036 - 11,214) for ACI patients and 7,948 (95% CI: 6,957 - 9,243) for mosaicplasty patients. The costs of adverse effects or knock on costs were dealt with in the costing.

**Synthesis of costs and benefits**
The costs and benefits were combined as average cost-utility ratios for the surgery groups (equating to incremental ratios compared with waiting-list patients).

These were 23,043 per QALY for ACI and 66,233 for mosaicplasty.

The incremental cost per QALY for ACI compared with mosaicplasty was 16,349.

When the lower cost of ACI was substituted, the average cost per QALY became 20,361, while the incremental cost per QALY over mosaicplasty became 13,694.

If recovery took 6 months before improvement, the average cost per QALY was 30,725 for ACI and 88,311 for mosaicplasty.

**Authors' conclusions**
Autologous chondrocyte implantation (ACI) resulted in cost-effective improvements in health status. ACI was associated with higher health care costs than mosaicplasty, but showed a trend towards improved health outcomes over mosaicplasty. The authors stated that the incremental cost of additional health improvement fell below the implicit 30,000 per quality-adjusted life-year (QALY) threshold in the UK.

**CRD COMMENTARY - Selection of comparators**
A justification was given for comparing ACI and mosaicplasty. Both were relatively new surgical techniques in the authors' setting. However, it was unclear why the authors also compared these to waiting-list patients (i.e. patients who had not received any treatment). Standard practice would suggest that best alternative care would have been the most appropriate comparator. You should decide if the comparators represent current practice in your own setting.

Note: since this abstract was written the authors have provided clarification of the reasoning behind the selection of comparators. Specifically they stated that this "was a retrospective study, and therefore it was not possible to obtain pre-operative outcome valuations for the ACI/mosaicplasty groups. Therefore the waiting list group were approached for pre-operative outcome valuations, and these were used as a proxy for pre-operative scores for the ACI/mosaicplasty groups. Waiting list patients were therefore only involved on the outcome side, and not to obtain cost information".

**Validity of estimate of measure of effectiveness**
The analysis was based on a cross-sectional cohort study. A randomised controlled study might have addressed the study question with less bias and confounding, but a reason was not given for the authors' choice of design. Indeed, some enrolled patients had already taken part in a randomised controlled trial. It was unclear whether the sample was representative of the intended population, as the reasons for the patients' initial non-participation or failure to complete the questionnaire were not investigated for systematic bias. Also, the patients were chosen from a single site in London offering specialist care. It is possible that patients attending this hospital differ from the “average” patient in the UK. The patient groups were shown to be comparable at baseline. In the analysis of effectiveness, the authors did not control for incomplete data or account for potential biases or systematic factors. The mean response of completers was applied to the group as a whole.

**Validity of estimate of measure of benefit**
The estimate of benefits was modelled. Essentially, however, it was obtained directly from the effectiveness analysis because it was assumed that effects on quality of life were immediate after surgery and applied constantly over a 2-year period. Thus, the estimates of benefit equated to the estimate of effectiveness using EQ-5D utilities multiplied by 2
years. The choice of QALYs was justified as they permit the cost of treatment to be compared with the benefit afforded to the patient, considering both health status magnitude and duration of effect.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included. For each category, all relevant costs were included. The costs and the quantities were reported separately. No statistical analysis of the quantities or prices was performed. It was unclear whether the costs from the financial department of the hospital were charges or true costs. Although patients attended the hospital for surgery at various times over a 4-year period, with follow-up of 2 years, the costs from a single financial year (2003 to 2004) were applied to all resource use.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was not addressed. The authors presented some results selectively. For example, they combined the health outcome results for ACI and mosaicplasty and did not present separate results. The authors’ conclusions reflected the scope and limitations of their study. Limitations, recommended for further research, included the absence of primary care costs or direct patient costs in the model and the lack of detailed utility data for this patient group.

Implications of the study
The authors’ recommendations for further research included the incorporation of primary care costs and direct patient costs. Also, the estimation of utility values, both to confirm the small-sample results in their study and to allow assessment over the longer term. The authors noted that postoperative recovery is not immediate and the effects of rehabilitation should be integrated into the analysis.

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