Systematic Review

Failures and Reoperations After Matrix-Assisted Cartilage Repair of the Knee: A Systematic Review

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Purpose: To quantify the reported failures and reoperations for the emerging technique of matrix-assisted cartilage repair at short-term and midterm follow-up. **Methods:** We conducted a systematic review of 3 databases from March 2004 to February 2014 using keywords important for articular cartilage repair. Two authors reviewed the articles, the study exclusion criteria were applied, and articles were determined to be relevant (or not) to the research question. All studies with a minimum of 2 years' clinical follow-up were reviewed for all reported reoperations. The reasons for reoperations were recorded. **Results:** We reviewed 66 articles from the 301 articles identified in the original systematic search. There were 60 articles on matrix-assisted cartilage transplantation and 6 articles on matrix-induced chondrogenesis. The matrix-assisted cartilage transplantation studies reported on a total of 1,380 patients at 2 to 5 years' follow-up. Among these, there were 72 reoperations (5%) including 46 treatment failures (3%). These numbers increased to an 11% reoperation rate and 9% treatment failure rate at minimum 5-year follow-up of 961 patients. The most common procedures performed other than revision cartilage surgery or arthroplasty were manipulation under anesthesia for arthrofibrosis (0.7%) and debridement for graft hypertrophy (1.2%). The matrix-induced chondrogenesis studies reported on 163 patients. Among these, there were 15 reoperations (9%) that included 4 treatment failures (2%), 9 manipulations under anesthesia (6%), and 2 debridements for graft hypertrophy (1%). **Conclusions:** Treatment failure rates for matrix-assisted cartilage repair increase from short-term to midterm follow-up, with 11% of patients having undergone further surgery at a minimum of 5 years' follow-up. These data can be used to counsel patients on the potential need for further operative intervention after this emerging cartilage repair technique. **Level of Evidence:** Level IV, systematic review of Level I through IV studies.

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The repair of isolated chondral defects of the knee has evolved over the past 20 years.[1] Microfracture has been the mainstay for treatment of chondral defects measuring less than 2 square centimeters.[2] Larger defects can be treated by many other methods including osteochondral transplantation or autologous chondrocyte transplantation.[1,3] Microfracture creates fibrocartilaginous "scar" cartilage that is histologically and biomechanically inferior to hyaline cartilage.[4] Similarly, standard autologous chondrocyte transplantation does not restore normal hyaline cartilage.

The autologous chondrocyte transplantation technique has evolved since it was originally described in 1994 with the use of a periosteal flap over transplanted chondrocytes.[5] The periosteal membrane was replaced by a collagen bilayer membrane, which reduced the incidence of graft hypertrophy.[4,6] The newest techniques use a variety of matrices as scaffolds to support chondrogenesis and tissue ingrowth.[7] Studies comparing matrix-assisted chondrocyte transplantation versus microfracture consistently report improved clinical outcomes with matrix-assisted chondrocyte implantation.[8]

The microfracture technique has evolved as well. Similar to chondrocyte transplantation, newer microfracture techniques use matrix scaffolds to support cartilage regeneration.[4] This technique is referred to as "autologous matrix-induced chondrogenesis" or "autologous collagen-induced chondrogenesis." The matrix is

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The authors report the following potential conflict of interest or source of funding: S.K.A. receives support from Pivot Medical/Stryker. Paid educational consultant. T.G.M. receives support from Arthrex. Paid presenter/speaker.

Received June 7, 2015; accepted July 24, 2015.

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0749-8063/15517/$36.00

http://dx.doi.org/10.1016/j.arthro.2015.07.025

used to capture the marrow elements that infiltrate the defect through the microfracture holes in the cartilage defect site to promote improved repair tissue.[9] However, currently, there are no comparative clinical studies showing improved outcomes compared with the traditional microfracture technique.

These evolving techniques that use matrices to augment cartilage repair are currently in clinical practice outside the United States but have not been approved by the US Food and Drug Administration (FDA). There are 2 products that are approved as minimally processed allografts: DeNovo Natural Tissue (NT) (Zimmer, Warsaw, IN) and BioCartilage (Arthrex, Naples, FL).[10,11] However, many of the remaining products are in clinical trials in the United States, making their use a likely clinical option for cartilage repair in the United States in coming years. The rate of treatment failure or reoperation for any reason reported after these procedures ranges from 0% to 36%, with most studies consisting of uncontrolled, small case series.[12,13] This creates difficulty in counseling patients on the potential need for further surgery at short-term to midterm follow-up. Therefore our objective was to systematically review the literature on matrix-assisted cartilage repair to determine the incidence of reoperation for any reason and the incidence of treatment failure, defined as the need for revision cartilage surgery or joint arthroplasty. We hypothesized that the incidence of reoperation would increase from short-term to midterm follow-up and that treatment failure would be the most common reason for reoperation.

Methods

Search Strategy

Two authors (M.K.H. and A.L.K.) independently conducted a comprehensive review of the citation databases PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Medline to confirm that each search was comprehensive and reproducible. Search terms included "cartilage," "chondral," "cell source," "chondrocyte," "matrix," "augment," "articular," "joint," "repair," "treatment," "regeneration," and "restoration." All searches were performed with the last letter replaced by an asterisk to capture further articles. The final search term entered in the search fields included a combination of 2 searches: (1) "articular" OR "joint" AND "repair" OR "treatment" OR "regeneration" OR "restoration" and (2) "cartilage" OR "chondral" AND "cell source" OR "chondrocyte" OR "matrix" OR "augment." The search date range was March 1, 2004, to February 28, 2014. For all 3 search engines, filters for English language and human subjects were applied. The PubMed and Medline searches included an additional filter for clinical trials, which was not available in CINAHL.

Study Screening

The PubMed search yielded 137 articles, the CINAHL search yielded 190 articles, and the Medline search yielded 48 articles. The searches were then combined into 1 database to remove duplicate articles, and we were left with 301 articles to consider. The abstracts were then reviewed for relevance to the proposed research question. Only articles relating to matrix-assisted articular cartilage repair of the knee were considered. A minimum clinical follow-up of 2 years was required. Articles pertaining to osteochondral autograft or allograft transplantation were excluded. In addition, all unpublished studies, proceedings/abstracts, and non−English-language studies were excluded from our analysis. The reference lists of selected articles were then searched to identify relevant articles that may have been missed by the initial search process. Available matrices for matrix-assisted chondrocyte transplantation or matrix-induced chondrogenesis identified in our systematic search were then searched by name in PubMed to ensure comprehensive inclusion of available articles for each product. Given the limited availability of prospective comparative studies for matrix-assisted chondrocyte transplantation, all levels of evidence (I through IV) were considered. If multiple articles that reported on the same patient cohort were reviewed, then only the article with the longest reported follow-up was used to quantify treatment failures and reoperations.

Data Abstraction

A systematic review of the selected articles was performed to extract the number of patients, level of evidence, length of follow-up, size of defect treated, matrix used, and type and number of reoperations and treatment failures reported. The Methodological Index for Non-Randomized Studies (MINORS) scale was used to quantify the quality of the literature for nonrandomized studies.[14] The MINORS score is reported as a percentage of the available points.

Statistical Analysis

Most of the included studies were retrospective case series, that is, Level IV studies. Heterogeneity among included studies prevented a meta-analysis. Therefore a qualitative assessment is presented.

Results

Search Results

The systematic search identified 66 articles, consisting of 2,341 patients, on the following 11 matrices: Chondro-Gide (Geistlich Pharma, Wolhusen, Switzerland), 21 articles (599 patients [25%]); Hyalograft C (Anika Therapeutics, Bedford, MA), 19 articles (944 patients [40%]); Bioseed C (BioTissues Technology, Freiburg, Germany),