Editorial Commentary: The Search for the Cartilage "Holy Grail": Are We There Yet?

Abstract: A study by Zhang et al. provided a Level IV systematic review of 23 studies (13 clinical and 10 basic science) that examined the current state of single-stage procedures for cartilage repair. The results of this review suggested that in the short-term (minimum 2-year follow-up), single-stage cell-based cartilage procedures significantly improve pain and function from the preoperative state and provide comparable defect fill and tissue quality as compared with their predecessor 2-stage procedures. The authors should be commended for summarizing the current state of single-stage cartilage repair techniques; however, further work must be done to find the cartilage restoration "holy grail."

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Focal cartilage defects remain one of the most challenging clinical entities for the treating orthopaedic surgeon. Recapitulating hyaline cartilage following a full-thickness cartilage injury in the knee in a cost-effective, single-stage, and reproducible manner is the "holy grail" for cartilage restoration surgeons. Recent advances in the biologic applications of cell-based technologies have renewed interest in this quest.[1] In pursuit of this goal, Zhang et al.[2] published their systematic review "One-Step Cartilage Repair Technique as a Next Generation of Cell Therapy for Cartilage Defects: Biological Characteristics, Preclinical Application, Surgical Techniques, and Clinical Developments." In this systematic review, the authors provided a synthesis of the current state of preclinical and clinical results for single-stage cartilage repair procedures.

The authors reviewed a cohort of studies encompassing multiple single-stage techniques for cartilage repair including chondrocyte-matrix complex (CMC) and autologous matrix-induced chondrogenesis (AMIC) procedures. However, both of these single-stage cartilage repair procedures contain multiple subcategories. For example, CMC procedures encompass the heterogeneous group of both autologous chondrocyte implant (ACI) and juvenile allograft cartilage implantation (JACI) techniques. Similarly, AMIC includes enhanced microfracture-AMIC, membrane-covered microfracture with bone marrow concentrate, and membrane-covered bone marrow aspirate concentrate clot. This heterogeneity is a reflection of the current field of cartilage restoration. Currently, multiple technologies and techniques are being investigated simultaneously, and therefore there is no single "gold standard" procedure for cartilage restoration.

Furthermore, while the basic science supporting each of the aforementioned techniques is promising,[3-5] Zhang et al.[2] have done a commendable job pointing out the heterogeneity in biologic growth factors, stem cell concentrations, and immunogenicity in the various techniques. Not all bone marrow aspiration preparations or juvenile allograft cartilage compositions are equivalent,[6] and further preclinical work must be conducted to optimize the cellular composition of these and other biologics while limiting their immunogenicity.

As is the case for all systematic reviews, the quality of the results and the strength of the conclusions drawn from those results are directly correlated to the strength and quality of the input studies.[7] The topic at hand is relatively novel, and, as such, the volume of high-level, clinical studies is relatively low. Of the 13 clinical studies included, there is only one Level II study,[8] and no study with greater than 3-year follow-up. Despite the vast majority of clinical studies being Level IV evidence, Zhang et al.[2] appropriately applied strict inclusion and exclusion criteria and presented balanced clinical results. Overall, the results of the 13 clinical studies with minimum 2-year follow-up demonstrated single-stage cell-based techniques to be safe and largely comparable to 2-stage techniques in terms of defect fill and postoperative appearance.[2,9]

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Zhang et al.[2] concluded that "CMC and AMIC, as 1-step cartilage repair techniques, have the potential for homogenous distribution of chondrocytes and MSCs [mesenchymal stem cells], which could enhance chondrogenesis, have the ability to regenerate hyaline-like cartilage tissue and could be applied to cartilage repair by arthroscopy in clinical settings." It is our experience that the 2 most important words in the previous sentence are "potential" and "could," as they are suggestive of the promising future for single-stage cartilage repair techniques, but at the same time they serve as a reminder that much work must be done at both the preclinical and clinical level to reach the cartilage restoration "holy grail."

Alexander E. Weber, M.D.
Brian J. Cole, M.D., M.B.A.
Chicago, Illinois

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