ACI Versus Microfracture: The Debate Continues

Commentary on an article by Gunnar Knutsen, MD, PhD, et al.: “A Randomized Multicenter Trial Comparing Autologous Chondrocyte Implantation with Microfracture: Long-Term Follow-up at 14 to 15 Years”

Freddie H. Fu, MD, and Ashish Soni, MD, FRCS

Because of the limited regenerative potential of articular cartilage, management of symptomatic chondral defects places us in a very challenging situation. The quest for the ideal treatment modality, in which mechanically functional hyaline cartilage can be regenerated around and in the defect site, is ongoing. In the last few years, multiple products and techniques that claim to provide improved outcomes, but have never been tested in controlled trials, have entered the market.

Microfracture, autologous chondrocyte implantation (ACI), and the osteochondral autograft transfer system (OATS) have been around for the last 2 decades. They have been studied extensively, but Level-I studies are few in number. In a systematic review of Level-I and II studies, Magnussen et al. concluded that no 1 technique produces superior clinical results for these defects. Results were found to be inconsistent and contradictory, which could be due to multiple factors such as heterogeneity of the study sample, location of lesions, associated procedures, and age of the lesion, to name a few.

In this study, the authors presented the 15-year results of their randomized controlled trial (RCT) comparing ACI and microfracture. The study is an extension of previously published 2-year and 5-year follow-up investigations. Consistent with their previously published results, the authors showed no difference between treatment groups in any of the outcome measures. However, they reported a failure rate of 42.5% and 32.5% in the ACI and microfracture groups, respectively. Greater than half of the patients had radiographic evidence of osteoarthritis as determined by the Kellgren and Lawrence scale. Limitations of this study are the lack of a control group, an ambiguous definition of failure, and the small number of patients.

If we follow the results of the study, microfracture is the clear winner, being a single-stage, low-cost arthroscopic procedure compared with ACI, which is technically demanding, expensive (can cost from $20,000 to $40,000), and associated with increased morbidity, given that a 2-stage operation is required, with the initial stage usually performed by miniarthrotomy. In this ever-evolving field of cartilage regeneration, it is possible that the techniques used in the study more than 15 years ago are no longer relevant today.

When this study was designed, ACI was only a few years old. It is a technically demanding procedure, and the technique has evolved over the years. With a failure rate of approximately 60% from 1 of the 4 centers in the study, the learning curve could have contributed toward poor results. Also, 1st generation ACI, which is known to have a higher risk of hypertrophy and delamination in comparison with the 2nd and 3rd generations of ACI, was used in the study. Basad et al. noticed superior results with 3rd-generation ACI in comparison with microfracture for the treatment of lesions of >4 cm2 at 2 years.

The condition of the subchondral plate is an important factor to consider. If it is compromised, then OATS or osteochondral allograft might be the procedure of choice as it can restore the entire osteochondral unit. In this study, 28% of the patients had osteochondral defects and the authors did not mention whether the ACI technique was modified, i.e., a sandwich technique was used. If the standard ACI technique was used in the presence of a compromised subchondral plate, the lesion would have healed with poor-quality cartilage and possibly led to early failure.

The size of the lesion is another important variable. Knutsen et al., at the 2-year follow-up of the same RCT, showed that lesions of >4 cm2 did worse with microfracture, but ACI demonstrated no correlation between the size of the lesion and the clinical outcome. Basad et al. noticed similar results. Goyal et al., in their systematic review of Level-I and II studies, found that small-sized lesions and younger patients had good results with microfracture in the short-term, but treatment failures increased and osteoarthritis was observed after 5 years.

As the evidence stands currently, microfracture has favorable results for small (≤4 cm2), contained chondral defects. ACI has more favorable outcomes than microfracture for larger, contained defects. Management of these defects should be individualized, depending on the size and site of the lesion, patient age, type of sport, level of sports activities, chronicity, condition of subchondral bone, and, most importantly, the stability and alignment of the knee.
Nevertheless, this landmark study represents, to our knowledge, the longest follow-up investigation comparing microfracture and ACI to date. Perhaps even more impressive is the dropout rate of only 2.5% after 15 years. The completeness of this well-designed randomized study is not only commendable but also important in providing an understanding of the long-term effects of the treatments investigated.

Freddie H. Fu, MD
Ashish Soni, MD, FRCS*
University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

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References