Editorial Commentary

Microfracture for cartilage repair in the knee: current concepts and limitations of systematic reviews

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This is an editorial on the article "*Microfracture for cartilage repair in the knee: a systematic review of the contemporary literature*" by Orth *et al.*, published in *Knee Surgery, Sports Traumatology, Arthroscopy*, January 2019 (1).

Articular cartilage injuries are a common and challenging problem in the knee joint. Approximately 12% of the population was estimated to have a cartilage lesion in the knee (2). The prevalence of cartilage lesions was up to 66% in knee arthroscopic procedures (3,4). It is expected that the recent growth in sports participation will further increase the prevalence of cartilage lesions (5). Cartilage lesions have the potential to progress into larger and higher grade disease, ultimately resulting in osteoarthritis, because cartilage has almost no intrinsic healing capacity due to its avascular nature and minimal chondrocyte migration and propagation (2,6).

Microfracture (MFx) is a marrow stimulation technique achieved by subchondral bone perforation to recruit autologous mesenchymal stem cells to a cartilage defect (7). The recruited stem cells differentiate into fibrochondrocytes, which fill and remodel the injured area to form a fibrocartilage clot. The clot is composed primarily of type I collagen and is different from the native hyaline cartilage, which contains a large amount of type II collagen (8). The procedure has gained popularity over the last decades, and some surgeons have considered it as first-line treatment for cartilage injury (7). This popularity might be due to the minimally invasive and technically simple procedure. Further, MFx has been shown as the most cost-effective procedure among the surgical options for cartilage lesion, including osteochondral autograft transfer (OATS) and autologous chondrocyte implantation (ACI) (2,9). According to a large insurance database, about 78,000 MFx are performed annually in the United States (7).

Many previous studies have reported the advantages of MFx via short- to mid-term clinical and radiographic results (10,11). However, there have been concerns regarding suboptimal repair with fibrocartilage infill, subchondral osseous overgrowth, questionable durability of fibrous cartilage, and deterioration of clinical improvement over long-term follow-up (8,9,11,12). Several issues, including usefulness of biologic augmentation and rehabilitation protocol, require further study (2,13).

The present study is a systematic review evaluating novel clinical data following MFx for knee articular cartilage injury and was conducted with contemporary studies published between 2013 and 2018. The study demonstrated the encouraging long-term clinical efficacy following 'classic' MFx without adjuvant treatment. However, the included study designs were of moderate quality and lacked appropriate standardization.

Although many studies on MFx have been accumulated, limited systematic reviews on the procedure have been conducted. Previous review articles provided generalized objective evidence on the clinical advantages and concerns of MFx (10,11). However, they included relatively old, non-contemporary studies that offered limited insight into current trends of studies about MFx (14). The present

review of contemporary studies will be valuable in this regard and will help surgeons acquire up-to-date knowledge about MFx.

One of the most important issues of MFx is the sustainability of improved clinical outcomes following the procedure. The concern originates from different mechanical properties of fibrocartilage from native cartilage, which makes it less durable and more prone to wear over time (15). A systematic review by Mithoefer *et al.* (10) reported that MFx provided excellent short-term efficacy at 2 years following the procedure; however, after 2 years, 47% to 80% of patients showed a decline in function from the initial improvement. Recent reviews demonstrated that such suboptimal favorable status, lower than initial improvement but higher than preoperative level, was maintained over a mid-term follow-up period. Krych *et al.* (5) reported that the overall mean preoperative Tegner score was 2.7 and improved to 3.9 (1 year), 5.4 (2 years), and 5.0 (5 years) following MFx. A review by Kraeuter *et al.* (16), including studies with at least 5-year follow-up and an overall mean follow-up duration of 7 years, also showed that clinical advantages of MFx were maintained up to mid-term follow-up and were not significantly different from those of ACI in most included studies.

The present review, including six current studies with long-term follow-up (over 10 years), evaluated the long-term clinical advantage of MFx more clearly, compared with previous reviews. In aggregate, there seemed to be clinical efficacy during the 10–15 years after MFx; the procedure provided good function and pain relief within the 5 years after surgery, while less extensive but largely satisfying improved clinical outcomes were found up to postoperative 15 years. MFx seems to be a cost-effective procedure able to provide a long-term favorable result if accompanied by necessary concomitant surgery in appropriate indications.

It is encouraging that this long-term favorable result was obtained from classic MFx without any adjuvant procedure. Recently, classic MFx has been modified to increase efficacy by improving repair tissue quality and durability. Many biologic augmentation materials have been improved in the forms of intra-articular adjuvant (adipose-derived mesenchymal stem cell, bone marrow concentrate, platelet-rich plasma, polyglycolic acid, and hyaluronic acid) or scaffolding matrix (collagen I/III matrix, chitosan polymer matrix, collagen II and glycosaminoglycans from porcine decellularized biomembrane, and polyglycolic acid-hyaluronic acid cell-free matrix) (13,15). Arshi *et al.* (13) described that, even though early studies were heterogenous and extremely limited in quality, individual trials regarding MFx with biologic augmentation reported both equivalent and superior clinical outcomes compared with an MFx-only procedure.

The reliability of a systematic review depends on the qualities of included studies. For this reason, several reviews on MFx have only used level I or II studies as their materials (2,9,14,17,18). In the present study, overall study quality was moderate; an average modified Coleman Methodology score (mCMS; generally used methodological quality assessment tool) was 64 points (categorized as fair). This score was similar to those of previous reviews by Mithoefer (average 58.2; fair) (10) and Krych *et al.* (average 62.3; fair) (5) but lower than that by Devit *et al.*, who only included high-quality studies with a mCMS greater than 65 (average 79; good) (14). Although inclusion of only high-level studies would have risk of bias excluding valuable studies that did not report outcomes with a high level of evidence (10), systematic review with high-quality contemporary studies will be required to help generate more reliable current knowledge about MFx.

In addition, there was lack of standardized clinical evaluation, rehabilitation protocols, and radiographic assessment in the present study. There was more critical heterogeneity within the involved MFx studies compared with reviews on different procedures. Many reviews on MFx, including the present study, have shown severe heterogeneity in patient demographics (age, body mass index, duration of preoperative symptoms, or preoperative activity level), lesion characteristics (acute or chronic, size, or location), surgical technique or concomitant procedures (meniscectomy or ligament reconstruction), definition of failure (pain or additional procedure), rehabilitation protocol (frequency of CPM, duration until return to sports, or intensity of physical activities), and follow-up period (10,11,14,16,17). In particular, the lack of standardization in clinical evaluation was most serious (10,11,14,17). Mithoefer *et al.* (10) reported that as many as 15 different knee scales were used for clinical evaluation in their included studies; in the present study, 10 scales were used for evaluating clinical outcomes. Such heterogeneities have prohibited meta-analysis of aggregate data in many systematic reviews, including the present study (1,10,11,14,16,17). It will be necessary to standardize the included materials to perform a meta-analysis and achieve generalized objective evidence on MFx.

In conclusion, the present study will help orthopedic surgeons acquire up-to-date knowledge about commonly used MFx. The procedure seems to provide satisfying clinical results

for a long-term follow-up period of 10–15 years if accompanied by necessary concomitant surgery in appropriate indications. These clinical efficacies of MFx are expected to be more consistent and prolonged according to development of biologic augmentation techniques (13). Systematic reviews using more standardized and high-quality studies are required to achieve valid and reliable evidence regarding MFx in the context of cartilage repair strategies.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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