Comment on Anterior Cruciate Ligament Reconstruction with Autografts Compared With Non-Irradiated Non-Chemically Treated Allografts

To the Editor:

We read with deep interest the recent article by Lamblin et al.,[1] "Anterior Cruciate Ligament Reconstruction with Autografts Compared with Non-Irradiated Non-Chemically Treated Allografts." This is an excellent job that we really appreciate. However, after reading the paper very carefully, we also found some worthwhile issues worth being explored.

First, this systematic review included 11 studies (Level of Evidence of I to III) in the final analysis. Unfortunately, according to their specific inclusion and exclusion criteria, one randomized controlled trial[2] was probably missing. The missing trial[2] was prospectively randomized into 3 groups, which were the autograft group (33 patients), the nonirradiated allograft group (34 patients), and the irradiated allograft group (32 patients). The average follow-up was 31 months (range 24 to 47 months), which met the minimum of 2-year follow-up. Also, it would not be excluded for providing insufficient outcome data or some other prestated exclusion criteria. Perhaps the authors need to clarify more clearly why this study[2] was excluded from the systematic review.

Second, 2 of the included studies were from the same particular trial.[3,4] One trial[3] indicated that their study was from May 1991 to August 1992, and the other one[4] was from May 1991 through November 1992. Both of them were conducted in the same sports medicine and orthopaedic center. The major difference between these studies was the different first author, which may have misled the authors. We have no idea whether these 2 duplicative studies will have an impact on the result.

Third, meta-analysis should only be considered when a group of studies is sufficiently homogeneous to provide a meaningful summary. In addition, sensitivity analysis is the study of how the uncertainty in the output of a mathematical model or system can be apportioned to different sources of uncertainty in its inputs. Furthermore, publication bias is a tendency on average to produce results that appear significant, because negative or near-neutral results are hard to publish. However, in this study, the heterogeneity and risk of publication bias were not reported, nor was the sensitivity analysis, which was not conducted. According to the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0, assessing publication bias and conducting sensitivity analysis are recommended, and approaches to addressing clinical heterogeneity also should be described.[5]

Finally, the authors did not retrieve gray literature. Gray literature is informally published written material that may be difficult to trace through conventional channels.[6] However, it is crucial for completing a systematic review and meta-analysis.

Above all, we respect the contribution of the authors and we are pretty sure the results of the data analysis are accurate.

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Note: The authors report that they have no conflicts of interest in the authorship and publication of this letter.

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Authors' Reply

First and foremost, the authors thank Dr. Yang et al. for their careful reading of our systematic review. After

closer examination, we agree that the investigation by Sun et al.[1] warranted inclusion and may have been inadvertently excluded because of the use of irradiated allografts. Additionally, the effect of duplicate publication bias must be acknowledged in comparative studies with updated follow-up.[2,3] Although negative results are underemphasized in the current literature, the selected studies in our review largely indicate a lack of statistically significant differences between autograft and nonirradiated, nonchemically treated allografts on specific clinical end points. Interestingly, Mariscalco et al.[4] recently performed a similar systematic review and also failed to demonstrate any significant differences in graft failure rate, laxity measures, patient-reported outcome scores, or combinations of these factors.

Heterogeneity was also assessed in the current study but not featured in the final publication. Similarly, the authors agree sensitivity analysis offers meaningful information in selected studies, and this methodology has been used in our previous publications evaluating outcomes after anterior cruciate ligament reconstruction.[5,6]

Again, the authors would like to thank you for your interest in our work.

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Mesenchymal Stem Cells Versus Fat Pad–Derived Cells

To the Editor:

We read the article "Mesenchymal Stem Cell Injections Improve Symptoms of Knee Osteoarthritis" in the April 2013 issue of your highly acclaimed journal with great interest.[1] We congratulate Koh et al. for their work, but we are very concerned about the erroneous use of the term "fat pad–derived mesenchymal stem cells (MSCs)" instead of "fat pad aspirate concentrate" or "fat pad–derived cells" (probably containing a small number of mesenchymal stem cells) in the article. It leads to serious confusion for the readers including ourselves.

To use the term "fat pad–derived MSCs," the cells should have been isolated from human adipose tissue by culture expansion and then characterized by the following: self-renewal, expression of specific cell surface markers, and multilineage differentiation. Thus the obtained cell population is relatively homogeneous,[2] which can be designated as "MSCs." The other term, "fat pad aspirate concentrate" or "fat pad–derived cells," means that the cell population is not isolated by culture expansion, so the cells are heterogeneous and may contain only a small number of MSCs.[2]

In the introduction to the article, Koh et al.[1] state that "Buda et al. advocated the use of a one-step technique in repairing osteochondral lesions of the knee with bone marrow–derived mesenchymal stem cell transplantation." However, the cells used in the study by Buda et al.[3] were not "MSCs" but were "bone marrow–derived cells" (in other words, "bone marrow aspirate concentrate"). It is clear that the title of the article only used the term "bone marrow–derived cells." We believe that it is a serious error to interchange the term "bone marrow–derived cells" with "bone marrow–derived MSCs" because it is well known that both entities are different from each other, and this error adds more confusion to the already confusing information in terms of the clinical results of various types of cell therapies.

Moreover, in the paragraph describing the surgical procedure and MSC harvesting technique, Koh et al.[1] described that "MSCs were derived and counted with a hemocytometer, as described previously."[4,5] However, in the referenced articles,[4,5] cells from the infrapatellar fat pad were cultured and expanded in MSC