

Immediate Versus Delayed Meniscus Allograft Transplantation: Letter to the Editor

DOI: 10.1177/0363546515571065

Dear Editor:

We read with interest the article by Jiang and colleagues⁴ titled “Comparative Study on Immediate Versus Delayed Meniscus Allograft Transplantation: 4- to 6-Year Follow-up,” and we would like to express our comments to the authors. In this paper, the authors describe their clinical outcomes after immediate and delayed meniscus allograft transplantation (MAT). Patients in the immediate study group (IM) underwent MAT immediately after total meniscectomy, while those in the delayed study group (DE) underwent MAT after the report of knee symptoms mean time, 35 months after total meniscectomy (range, 9-92 months); both groups were compared to a control group of patients undergoing meniscectomy (ME). The authors reported significantly improved outcomes in the IM group compared to the DE group with respect to International Knee Documentation Committee (IKDC) scores (mean, 93; range, 85-99 vs mean, 74; range, 38-95; $P < .05$) and with respect to cartilage degeneration via radiographic/MRI analysis. Of note, there were no significant differences between any of the groups with regard to Lysholm score, Tegner score, joint narrowing, or meniscus extrusion.

While the findings of this study are of interest, the clinical ramifications of these results should be clearly delineated. Specifically, the main limitations are secondary to the small sample size and lack of clearly defined comparison group. Regarding the small sample size (8 patients in the IM group, 10 patients in the DE group), though significant findings were described, a power analysis should be included, as many of the other outcome variables were not adequately powered to find a difference. Further, it is difficult to explain the difference in IKDC between the IM and DE groups, but not between the IM versus ME groups, or between the DE versus ME groups. Thus, we are uncertain as to the clinical appropriateness of stating that immediate MAT is superior to delayed MAT as determined by IKDC when the authors report that both immediate and delayed MAT were no different compared to patients undergoing meniscectomy. Importantly, there were no differences between the IM and DE groups with respect to Tegner and Lysholm scores, which are clinically relevant in the MAT patient population.

Second, the comparison group is flawed as they are “randomly selected”⁴ and unmatched with regard to age, sex, transplanted compartment, and concomitant procedures, including ACL reconstruction, which adds further variability to the clinical interpretation of the statistical findings. The clinical details of the control group are not well described, as no information is given with regard to the length of symptoms before meniscectomy. Ideally, the comparison group for the IM group would be patients undergoing immediate meniscectomy, and the comparison group for the ME group would be patients who have developed symptoms after prior meniscectomy. Essentially, this would result in matched control groups for each treatment group that utilized the same inclusion criteria for each group. In addition, the difference in follow-up duration between the IM (mean, 51 months) and DE (mean, 72 months) groups is certainly worth mentioning, as a difference of 21 months is likely clinically relevant, even if not statistically different. Similarly, the difference in age between the IM (mean, 23 years) and DE (mean, 28 years) groups is likely also significant and underpowered, with P values of .058 (IM vs DE) and .055 (IM vs ME). We appreciate the difficulty in creating matched cohorts based on demographic variables and certainly understand that often with MAT, concomitant procedures are performed. However, the small sample size, inadequate matching, and lack of proper control groups in this study make the statistical outcomes difficult to interpret.

From a practical standpoint, multiple authors have reported on the short-, medium-, and long-term clinical outcomes following MAT.⁵⁻⁷ For the vast majority of patients, outcomes are satisfactory, regardless of the duration of time between the initial meniscus injury and/or index meniscectomy and MAT. Two recently published systematic reviews^{2,3} describe the outcomes of MAT in thousands of patients, noting overall good outcomes with improvements in pain and function for the majority of patients. In the review conducted by Verdonk’s group² consisting of 1136 grafts in 1068 patients, the duration of “delay” from injury to MAT was an average 10.7 years, with clinical improvement reported in the majority of patients. At this stage, it is clear that there is an “at risk” patient group that cannot compensate for the meniscectomized state; however, it is not clear as to what factors place patients into this category. Currently, when taking into account the cost of MAT, rehabilitation, and potential complications, it is difficult to recommend this surgery in asymptomatic patients. Interestingly, in 2003, Aagaard and colleagues¹ examined the effects of immediate versus delayed (3 months) MAT in a sheep model and found that at 6 months after surgery, immediate MAT reduced but did not prevent degeneration of the articular cartilage.

Pragmatically, meniscus allografts remain a scarce resource with many appropriately indicated patients waiting for a properly sized matched implant. In the United States there are between 500,000 and 700,000 meniscectomies performed each year. Radiographic progression may occur in up to 50% by 10 years, but clinical symptom onset lags behind this by at least another 5 to 10 years. Meniscus allografts

may predictably only last 5 to 7 years before they deteriorate anatomically. The addition of a meniscus implant to an asymptomatic patient can not only be associated with a serious complication that they would otherwise be able to avoid but present a scenario of obligatory activity modification if the patient wishes to avoid compromising their implant. Alternatively, given the lack of evidence between disease progression and activity profiles, the meniscectomized patient can return to activities rather predictably and most commonly for an indefinite period of time.

Certainly, the authors are to be commended for their comprehensive evaluation of what remains an extremely challenging patient population for even the most experienced of orthopaedic surgeons. In addition, the authors should be applauded for their ability to obtain postoperative MRI scans on all included patients. A controlled, adequately powered, prospective study with matched patient cohorts would be helpful to better understand the results presented here; however, such a study would be difficult, as the literature does not currently advocate for performing immediate MAT on asymptomatic patients. Clearly, more research is needed to better understand this patient population and the long-term effects of MAT.

Rachel M. Frank, MD
Adam Yanke, MD
Nikhil N. Verma, MD
Brian J. Cole, MD, MBA
Chicago, Illinois, USA

Address correspondence to Rachel M. Frank, MD (email: rmf Frank3@gmail.com).

The authors declared that they have no conflicts of interest in the authorship and publication of this contribution.

REFERENCES

1. Aagaard H, Jørgensen U, Bojsen-Møller F. Immediate versus delayed meniscal allograft transplantation in sheep. *Clin Orthop Relat Res*. 2003;406:218-227.
2. Elattar M, Dhollander A, Verdonk R, Almqvist KF, Verdonk P. Twenty-six years of meniscal allograft transplantation: is it still experimental? A meta-analysis of 44 trials. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(2):147-157.
3. Hergan D, Thut D, Sherman O, Day MS. Meniscal allograft transplantation. *Arthroscopy*. 2011;27(1):101-112.
4. Jiang D, Ao Y-F, Gong X, Wang Y-J, Zheng Z-Z, Yu J-K. Comparative study on immediate versus delayed meniscus allograft transplantation: 4- to 6-year follow-up. *Am J Sports Med*. 2014;42(10):2329-2337.
5. Saltzman B, Bajaj S, Salata M, et al. Prospective long-term evaluation of meniscal allograft transplantation procedure: a minimum of 7-year follow-up. *J Knee Surg*. 2012;25(2):165-176.
6. van der Wal RJP, Thomassen BJW, van Arkel ERA. Long-term clinical outcome of open meniscal allograft transplantation. *Am J Sports Med*. 2009;37(11):2134-2139.
7. Vundelinckx B, Vanlauwe J, Bellemans J. Long-term subjective, clinical, and radiographic outcome evaluation of meniscal allograft transplantation in the knee. *Am J Sports Med*. 2014;42(7):1592-1599.

Immediate Versus Delayed Meniscus Allograft Transplantation: Response

DOI: 10.1177/0363546515571066

Authors' Response:

Thank you for your interest in our study titled "Comparative Study on Immediate Versus Delayed Meniscus Allograft Transplantation: 4- to 6-Year Follow-up." We would like to respond as follows.

The difference in the International Knee Documentation Committee scores between the 3 groups in our study is in fact not difficult to explain. It is known that most of the meniscectomy patients would not complain of any discomfort in the relative short follow-up of 4 to 6 years. Therefore, in spite of the excellent performance of meniscus allograft transplantation (MAT), it was reasonable that both immediate and delayed MAT would be no different compared to patients undergoing meniscectomy. Moreover, in addition to the sensitivity of the scoring system itself, the advantages of chondroprotection might be a more important reason for the final recommendation, although both the Lysholm score and Tegner scores were clinically relevant for the MAT patients.

We apologize for the ambiguous description of the comparative groups. The phrase "randomly selected" meant that the postoperative results of those patients were not known in the selection for the objective comparison. In fact, the matching of the age, sex, and other factors was considered for a better comparison with the MAT group, although not ideal. We also agree with your suggestion of better designed control groups for future studies.

Indeed, as you pointed out, the difference in follow-up duration between the IM and DE groups (21 months) is likely clinically relevant. To reduce the impact caused by the different follow-up times, the preoperative to postoperative changes of all the parameters were also compared between the 3 groups in addition to the preoperative and postoperative values. As a matter of fact, the reason for the difference of the follow-up duration between the 2 groups was that the immediate MAT was not started at the same time as the delayed MAT. At first, the traditional indication for the MAT was followed in our department during the early period of MAT, namely, only symptomatic meniscectomy patients were enrolled for MAT then. About 2 years later, some meniscectomy patients were very anxious about the possible occurrence of the postoperative osteoarthritis and requested immediate MAT after meniscectomy. From then on, the immediate MAT came into our consideration for the small number of patients who persisted to ask for the MAT despite preventive MAT still not being recommended in our department. The immediate MAT was only done for patients with a strong request, and

total meniscectomy must have been done during operation. Compared to the medial meniscectomy, the total lateral meniscectomy was generally more commonly performed in the young patients.⁴ This might be the reason that more lateral MAT were included in the IM group.

Given that most of the studies of delayed MAT obtained overall good outcomes^{2,5} and the source of allograft meniscus is so limited with respect to so many meniscectomy patients, immediate MAT might be difficult to be comprehensively promoted. However, according to some studies,^{1,3} biochemical and biomechanical changes might also occur just after meniscectomy although there were no or only extremely mild chondral lesions at the time of delayed MAT. Those changes might not be corrected by MAT and lead to increasingly serious osteoarthritis. So the main superiority of the immediate MAT was the chondroprotective effect before those changes can occur, and the immediate MAT might be more necessary for those "at risk" patients. Since only a small number of the meniscectomy patients experienced the changes and complained of discomfort in a short time after meniscectomy, how to pick out the "at risk" patient group that cannot compensate for the meniscectomized state would be a great challenge and needs to be studied.

Lastly, it should also be noted that our study was meant only to evaluate and compare the short- to midterm results of the immediate and the delayed MAT, far from determining the precise necessity for all the meniscus injured patients.

Other animal studies or better designed prospective clinical studies with more patients are needed in the future.

Dong Jiang, MD
Jia-kuo Yu, MD, PhD
Beijing, China

Address correspondence to Jia-kuo Yu, MD (email: yujiakuo@126.com).

The authors declared that they have no conflicts of interest in the authorship and publication of this contribution.

REFERENCES

1. Aagaard H, Jørgensen U, Bojsen-Møller F. Immediate versus delayed meniscal allograft transplantation in sheep. *Clin Orthop*. 2003;406:218-227.
2. Lee BS, Kim JM, Sohn DW, Bin SI. Review of meniscal allograft transplantation focusing on long-term results and evaluation methods. *Knee Surg Relat Res*. 2013;25(1):1-6.
3. Mankin HJ, Dorfman H, Lippiello L, Zarins A. Biochemical and metabolic abnormalities in articular cartilage from osteoarthritic human hips. *J Bone Joint Surg Am*. 1971;53:523-537.
4. Montgomery SR, Zhang A, Ngo SS, Wang JC, Hame SL. Cross-sectional analysis of trends in meniscectomy and meniscus repair. *Orthopedics*. 2013;36(8):e1007-1013.
5. Vundelinckx B, Vanlauwe J, Bellemans J. Long-term subjective, clinical, and radiographic outcome evaluation of meniscal allograft transplantation in the knee. *Am J Sports Med*. 2014;42(7):1592-1599.