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**Controversial role of arthroscopic meniscectomy of the knee: A review**

Ha AY *et al.* Controversial role of arthroscopic partial meniscectomy

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**Abstract**

The role of arthroscopic partial meniscectomy (APM) in reducing pain and improving function in patients with meniscal tears remains controversial. Five recent high-quality randomized controlled trials (RCTs) compared non-operative management of meniscal tears to APM, with four showing no difference and one demonstrating superiority of APM. In this review, we examined the strengths and weaknesses of each of these RCTs, with particular attention to the occurrence of inadvertent biases. We also completed a quantitative analysis that compares treatment successes in each treatment arm, considering crossovers as treatment failures. Our analysis revealed that each study was an excellent attempt to compare APM with non-surgical treatment but suffered from selection, performance, detection, and/or transfer biases that reduce confidence in its conclusions. While the RCT remains the methodological gold standard for establishing treatment efficacy, the use of an RCT design does not in itself ensure internal or external validity. Furthermore, under our alternative analysis of treatment successes, two studies had significantly more treatment successes in the APM arm than the non-operative arm although original intention-to-treat analyses showed no difference between these two groups. Crossovers remain an important problem in surgical trials with no perfect analytical solution. With the studies available at present, no conclusion can be drawn concerning the optimum treatment modality for meniscal tears. Further work that minimizes significant biases and crossovers and incorporates sub-group and cost-benefit analyses may clarify therapeutic indications.

**Key words:** Arthroscopic partial meniscectomy; Meniscal tear; Knee osteoarthritis; Physical therapy; Randomized controlled trial; Crossover; Bias

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**Core tip:** Despite several recent high-quality randomized controlled trials, the efficacy of arthroscopic partial meniscectomy (APM) for meniscal tears remains controversial. In this review, we analyzed the five most important trials for potential inadvertent biases. Each study was found to have some combination of selection, performance, detection, and transfer biases that compromise its conclusion. We also completed an alternative analysis of their results that took into account the observed high crossover rates. This analysis suggested that two studies whose original conclusions showed no superiority of APM may in fact support APM.

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Observational studies, including longitudinal cohort studies, have suggested that arthroscopic partial meniscectomy (APM) is an effective treatment for meniscal tears[1-5]. More recent randomized controlled trials (RCTs) have suggested that non-operative regimens may provide equivalent symptom relief and functional improvement[6-10]. We have previously analyzed RCTs comparing APM with non-operative therapy specifically in the clinical setting of meniscal tears with concomitant osteoarthritis of the knee (MT-OAK) (Ha *et al*, submitted). That approach maximized internal validity but limited generalizability of the analysis. Therefore, there is value in analyzing reports of APM in a variety of clinical settings, understanding that the variable settings may increase variability but are more broadly generalizable. Occasionally, direct comparisons between outcome assessments cannot be made because of varying assessment instruments but outcomes can still be compared.

Our previous analysis of APM for MT-OAK identified two types of problems in the studies reviewed that compromised confidence in the study conclusions: (1) inadvertent biases within the structure of the RCTs; and (2) the large numbers of patients who crossed over from the non-operative to the operative groups. While the RCT is the methodological gold standard for establishing efficacy of treatments, bias may still occur within their structure that compromise their conclusions[11-15]. The second problem encountered is the evaluation of outcomes of patients who cross over from one treatment group to another, when they comprise a substantial portion of the study population[16]. Crossovers can be major confounders especially to an intention to treat (ITT) analysis and can obscure differences in the outcomes of two treatments[16,17]. Other methods of data analysis, each with their own limitations, may be useful as supplementary, but potentially more precise, analytical approaches[14].

In the present analysis, we review five RCTs reporting the efficacy of APM for meniscal tears in a variety of clinical settings. Particular attention is paid to the occurrence of biases within the RCT structure and the fidelity to the treatment assignment. Second, we employ an alternative quantitative analysis that examines the effects of crossovers upon the efficacy of APM.

Five RCTs comparing APM to non-operative treatment for meniscal tears with at least 6 mo follow-up were included in this analysis[6-10,18]. One study was excluded because it had not reported results beyond 3 mo[19]. Another study was excluded because it dealt with arthroscopic surgery for OAK rather than meniscal tears[20]. A third study was excluded whose results are not generally accepted because of methodological flaws making the data uninterpretable[21].

The five RCTs were first assessed for the presence of inadvertent bias within their structure. We used the framework proposed by Rudicel *et al*[15] to detect existing selection, performance, detection, or transfer biases. Furthermore, each RCT was individually assessed for the percentage of patients meeting the criterion for treatment success in both non-operative and APM groups. For this analysis, we used the definition of treatment success put forward by Katz *et al*[8]: Achieving improvement that is equal to or greater than the minimal clinically important difference (MCID) at the primary outcome time point compared to baseline without crossing over or requiring additional procedures. Data from either the original report or supplementary information provided directly by the authors was used to complete this analysis.

The Fisher exact test was used to test for statistical significance between the numbers of treatment successes in operative and nonoperative groups. SPSS, version 23.0 (IBM), was used for all statistical analyses. A biomedical statistician performed the statistical analyses.

The citations, meniscal pathology and associated conditions of the five RCTs reviewed are summarized in Table 1.

Herrlin et al[6,7] reported 96 patients with medial meniscal tears and Ahlback grade 0-1 osteoarthritis-comparable to Kellgren-Lawrence grade 0-2-between the ages of 45-64 followed for 5 years. The primary outcome was the change in knee injury and osteoarthritis outcome (KOOS) scores at 6-mo follow-up. Forty-seven were randomized to APM and exercise; 49 were randomized to exercise therapy alone. Thirteen/forty-nine (27%) of patients managed by exercise therapy were ultimately treated by APM. ITT analysis showed a 9-point difference on the KOOS Pain scale compared to baseline favoring APM, which was not statistically significant. Forty-two/forty-seven (89%) of operative group met the definition for treatment success compared to 34/49 (69%) of non-operative group (*P* = 0.023) (personal communication, May 18, 2015). The study had significant strengths including a homogeneous population and well standardized surgical and physical therapy protocols. However, the APM cohort had significantly poorer baseline characteristics, leading to possible selection bias. The study also experienced low enrollment of eligible patients (80/177, or 55%), high crossover rate, and was non-blinded.

Katz *et al*[8,16] followed for 12 mo 351 patients with meniscal tears and concomitant osteoarthritis of grades 0-3 by Kellgren-Lawrence criteria aged 45 years or older. The primary outcome was the change in the Western Ontario and McMaster Osteoarthritis Index (WOMAC) scores at 6-mo follow-up. One hundred and seventy-four were assigned to APM and physical therapy; 177 were assigned to physical therapy alone. 51/177 (29%) and 59/177 (33%) of patients initially managed by physical therapy underwent APM by 6 mo and 12 mo, respectively. ITT analysis showed a 2.4-point difference in on the WOMAC score compared to baseline favoring APM, which was not statistically significant. However, as noted in the original paper, a greater proportion of APM patients had successful treatment outcomes than that of physical therapy patients (108/161, or 67.1% *vs* 74/169, or 43.8%, *P* < 0.0001). This was a landmark study with a strong study design and large cohort size. However, this study suffers from low enrollment rate (351/1330, or 26%), inconsistent referral patterns from participating surgeons, and lack of blinding, leading to potential selection and detection biases. High crossover rate and large variability in the percentage of crossovers among participating centers (range 0%-60%) question protocol adherence and suggest potential performance and transfer biases.

Yim *et al*[10] reported 102 patients aged 43-62 years with degenerative horizontal tears of the posterior horn of the medial meniscus with OA of grades 0-1 by Kellgren-Lawrence criteria followed for 24 mo. The primary outcome was by Lysholm scores at 2 years follow-up. 50 patients were treated with APM and strengthening exercises; 52 were treated with strengthening exercises alone. Only 1/52 (2%) of patients assigned to nonoperative management crossed over to surgery. The results as analyzed in the original report showed no difference in the Lysholm scores between the two groups at 2 years follow-up. 45/50 (90%) of surgical patients met the definition for treatment success compared to 48/52 (92%) of non-surgical patients (*P* = 0.739) (personal communication, June 27, 2015). The strengths of this study include low loss to follow-up rate (2/108, or 2%), low crossover rate (1/52, or 2%), and relatively long follow-up period. Its weaknesses include: disproportionately large female study population (81/102, or 79.4%); sample size falling just short of the 54 patients per group required for 80% power; and low enrollment rate (108/162, or 66.7%). Finally, Lysholm scores are best suited for measuring outcomes after ligament surgery and may not have sufficient validity, sensitivity, and reliability for assessing degenerative tears of the meniscus[22].

Sihvonen *et al*[9] reported 146 patients aged 35-65 years with degenerative meniscal tears with OA of grades 0-1 by Kellgren-Lawrence criteria followed for 12 mo. The primary outcome measures were changes in the Lysholm and Western Ontario Meniscal Evaluation Tool (WOMET) scores at 12 mo post-op. Seventy patients were treated with APM; 76 underwent sham surgery. 5/76 (6.6%) of patients assigned to sham surgery were ultimately treated with APM (4 patients) or high tibial osteotomy (1 patient). 2/70 (2.9%) of patients assigned to APM were ultimately treated with additional arthroscopy (1 patient) or total knee replacement (1 patient). The results as analyzed in the report showed no differences in the changes in WOMET and Lysholm scores at 12 mo compared to baseline. A priori and post-hoc subgroup analyses did not show between-group differences. Forty-nine/seventy (70%) of the APM cohort met the definition for treatment success compared to 51/76 (67.1%) of the exercise cohort (*P* = 0.725) (personal communication, May 11, 2015). This study had many strengths, including its rigorous double-blinded, sham-controlled design, low loss to follow-up and crossover rates, and high enrollment rate (146/205, or 71.2%). This study’s weakness is its relatively narrow generalizability, having included only nontraumatic degenerative medial meniscal tears with no or very mild OA.

Gauffin *et al*[18] reported 150 patients aged 45-64 years with minimum 3 mo of meniscal symptoms and OA of grades 0-2 by Kellgren-Lawrence criteria, who had undergone 3 mo of prior physiotherapy, followed for 12 mo. The primary outcome measure was the change in KOOS Pain scores at 12 mo compared to baseline. Seventy-five patients were treated with arthroscopic surgery, and 75 patients were treated by 3 mo of physical exercises alone. Sixteen/seventy-five (21.3%) of patients assigned to physical therapy ultimately underwent surgery, whereas 9/75 (12%) originally assigned to surgery only completed physical exercises. This is the first RCT to report superiority of surgical management to physical therapy, by both ITT and as-treated analyses. In ITT analysis, the between-group difference in the changes in KOOS Pain scores from baseline was both statistically and clinically significant (10.6 points, *P* = 0.004). As-treated analysis accentuated this difference to 13.9 points (*P* < 0.001). However, the surgery group had more females and poorer baseline KOOS scores than the non-surgery group-a breakdown of randomization. Sixty-two/seventy-four (84%) of the surgical patients, whereas 36/56 (64%) of the non-surgical patients, met the definition for treatment success (*P* = 0.010). This study’s strengths include a high enrollment rate (150/179, or 83.8%), relatively long planned follow-up period of 3 years. The study’s weaknesses include heterogeneity in the surgeries performed, poor compliance to physiotherapy, and high loss to follow-up rate (20/150, or 13.3%) and crossover.

**DISCUSSION**

While RCTs are the best way to minimize bias in clinical trials, there are nonetheless opportunities for bias within the structure of an RCT and the use of this study design in itself does not ensure either internally or externally valid data[12]. Analysis of five RCTs reveals that they were excellent attempts to compare APM with non-surgical treatment but all suffered from potential inadvertent biases that reduce confidence in their conclusions.

Selection bias was the most frequently encountered bias in the five RCTs. This was often due to a low enrollment rate from the patients’ explicit preference for one treatment option to the other. Two studies suffered from unequal baseline characteristics between the surgical and non-surgical arms despite randomization. Performance bias was observed when intraoperative procedures and/or physiotherapy protocols were not standardized or determined a priori. Variability in supplemental therapy, such as unspecified use of non-steroidal anti-inflammatory drugs, and inconsistency among different participating medical centers can also lead to performance bias. Detection bias was also common, as only one RCT employed the double-blind methodology. We acknowledge that double blinding in surgical trials is challenging. However, a placebo effect may account for a significant part of response to surgery-up to 35% in some trials[23,24] - and therefore needs to be addressed[25]. Placebo also contributes to the effect of physical therapy and may need to be controlled[26,27]. Lastly, transfer bias occurs when there is a significant proportion of patients lost to follow-up or crossing over to the opposite study arm. One RCT had a high loss to follow-up rate, and three RCTs suffered from high crossover rates.

The American Academy of Orthopedic Surgeons has recommended using the minimum clinically important difference (MCID) to evaluate the clinical significance of treatment outcomes[28]. The MCID is the smallest change in an outcome score that corresponds to a change in a patient’s condition and thereby derives its clinical relevance. The MCIDs of two of the patient report outcome measures used in these studies, the WOMAC and the KOOS have been determined to be 9-12 points and 8-10 points respectively[22]. We analyzed each study according to the number of patients in each group reaching this clinically meaningful end point.

Using the definition of treatment success suggested by Katz *et al*[8], which occurs when the improvement in a patient’s outcome score is greater than or equal to the MCID without crossing over or requiring additional procedures, and the data reported in the original papers or communicated to us directly by the authors, we compared the percentage of patients meeting the definition of treatment success in each group for statistical significance. Two RCTs had significantly more patients treated successfully with APM, although their original ITT analyses showed no between-group differences. By this analysis method, three RCTs favor APM and two RCTs show no difference (Table 2).

ITT analysis remains the current gold standard for data analysis in RCTs. It has the advantages of preserving randomization and minimizing false positive (type I) errors; however, in the setting of high cross over rates, the ITT analysis does not reflect the treatment actually received and, therefore, may not accurately reflect the efficacy of treatment, leading to false negative (type II) errors[29,30]. The risk for a type II error is especially high when there is a significant number of patients who perform poorly with one treatment method and then show rapid improvement after crossing over. Noncompliance with assigned therapy may also exaggerate this feature and lead the ITT analysis to underestimate the potential benefit of a treatment. Additional analyses may therefore be useful[31,32]. An “as treated” analysis is an alternative, but it has been criticized for compromising initial randomization. Our analysis of treatment success can be considered a form of “as treated” analysis as it separates those patients who remained in their originally assigned groups from those who did not. However, we acknowledge that this analysis is not a generic solution to the crossover problem.

**CONCLUSION**

This review sought to approach the question of efficacy of APM and non-operative management for meniscal tears by examining five important RCTs. Special attention was paid to inadvertent biases they may harbor despite their RCT design. Many potential biases were identified. An alternative analysis to the conventional ITT analysis was completed, which showed that the data from three RCTs favor APM while two others show no difference between APM and non-operative management. Use of the RCT design in itself ensures neither internal nor external validity of study data. Crossovers remain a significant problem in surgical RCTs, but there are currently no suitable analytical methods that both preserve randomization and minimize type II errors. With the studies available at present, no conclusion can be drawn concerning the optimum treatment modality for meniscal tears. Further work on sub-group analysis and cost-benefit analysis may clarify therapeutic indications.

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**Table 1 Characteristics of included studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author/citation** | **Meniscal pathology** | **Associated osteoarthritis** | **Operative group treatment** | **Non-operative group treatment** |
| Herrlin *et al*[6,7] | Medial meniscal tear | Ahlback grades 0-1 | Exercise + APM | Exercise |
| Katz *et al*[8] | Meniscal tear | Kellgren-Lawrence grades 0-3 | Exercise + APM | Exercise |
| Yim *et al*[10] | Horizontal medial meniscal tear | Kellgren-Lawrence grades 0-1 | APM | Strength exercises |
| Sihvonen *et al*[9] | Meniscal tear | Kellgren-Lawrence grades 0-1 | APM | Sham surgery |
| Gauffin *et al*[18] | Meniscal tear | Kellgren-Lawrence grades 0-2 | Exercise + APM | Exercise |

APM: Arthroscopic partial meniscectom.

**Table 2 Outcomes of analysis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author/citation** | **Potential bias** | **Results as reported** | **Crossovers *n* (%)** | **Treatment success by group** |
| Herrlin *et al*[6,7] | SelectionDetectionTransfer | APM group showed 9-point greater improvement in KOOS Pain scores (NS) | 13/49 (27%) from PT to APM | APM - 42/47 (89%)PT - 34/49 (69%)(*P* = 0.023) |
| Katz *et al*[8] | SelectionPerformanceDetectionTransfer | APM group showed 2.4-point greater improvement in WOMAC scores (NS) | 51/177 (29%) from PT to APM at 6 months post-op. | APM - 108/161 (67%)PT - 74/169 (44%)(*P* < 0.0001) |
| Yim *et al*[10] | SelectionDetection | APM group showed 0.1-point greater improvement in Lysholm scores (NS) | 1/52 (2%) from PT to APM | APM - 45/50 (90%)PT - 48/52 (92%)(*P* = 0.739) |
| Sihvonen *et al*[9] | Narrow generalizability | Sham surgery group showed 2.5-point greater improvement in WOMET scores (NS) | 5/76 (6.6%) from sham to APM | APM - 49/70 (70%)Sham - 51/76 (67%)(*P* = 0.725) |
| Gauffin *et al*[18] | PerformanceDetectionTransfer | APM group showed 10.6-point greater improvement on KOOS Pain scores (*P* = 0.004) | 16/75 (21%) from PT to APM9/75 (12%) from APM to PT | APM - 62/74 (84%)PT - 36/56 (64%)(*P* = 0.010) |

APM: Arthroscopic partial meniscectom; NS: Not statistically significant.