

ORIGINAL ARTICLE

Surgery versus Physical Therapy for a Meniscal Tear and Osteoarthritis

Jeffrey N. Katz, M.D., Robert H. Brophy, M.D., Christine E. Chaisson, M.P.H., Leigh de Chaves, P.T., O.C.S., Brian J. Cole, M.D., M.B.A., Diane L. Dahm, M.D., Laurel A. Donnell-Fink, M.P.H., Ali Guermazi, M.D., Ph.D., Amanda K. Haas, M.A., Morgan H. Jones, M.D., M.P.H., Bruce A. Levy, M.D., Lisa A. Mandl, M.D., M.P.H., Scott D. Martin, M.D., Robert G. Marx, M.D., Anthony Miniaci, M.D., Matthew J. Matava, M.D., Joseph Palmisano, M.P.H., Emily K. Reinke, Ph.D., Brian E. Richardson, P.T., M.S., S.C.S., C.S.C.S., Benjamin N. Rome, B.A., Clare E. Safran-Norton, P.T., Ph.D., O.C.S., Debra J. Skonieczki, M.S.N., A.N.P., Daniel H. Solomon, M.D., M.P.H., Matthew V. Smith, M.D., Kurt P. Spindler, M.D., Michael J. Stuart, M.D., John Wright, M.D., Rick W. Wright, M.D., and Elena Losina, Ph.D.

ABSTRACT

BACKGROUND

Whether arthroscopic partial meniscectomy for symptomatic patients with a meniscal tear and knee osteoarthritis results in better functional outcomes than nonoperative therapy is uncertain.

METHODS

We conducted a multicenter, randomized, controlled trial involving symptomatic patients 45 years of age or older with a meniscal tear and evidence of mild-to-moderate osteoarthritis on imaging. We randomly assigned 351 patients to surgery and postoperative physical therapy or to a standardized physical-therapy regimen (with the option to cross over to surgery at the discretion of the patient and surgeon). The patients were evaluated at 6 and 12 months. The primary outcome was the difference between the groups with respect to the change in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) physical-function score (ranging from 0 to 100, with higher scores indicating more severe symptoms) 6 months after randomization.

RESULTS

In the intention-to-treat analysis, the mean improvement in the WOMAC score after 6 months was 20.9 points (95% confidence interval [CI], 17.9 to 23.9) in the surgical group and 18.5 (95% CI, 15.6 to 21.5) in the physical-therapy group (mean difference, 2.4 points; 95% CI, -1.8 to 6.5). At 6 months, 51 active participants in the study who were assigned to physical therapy alone (30%) had undergone surgery, and 9 patients assigned to surgery (6%) had not undergone surgery. The results at 12 months were similar to those at 6 months. The frequency of adverse events did not differ significantly between the groups.

CONCLUSIONS

In the intention-to-treat analysis, we did not find significant differences between the study groups in functional improvement 6 months after randomization; however, 30% of the patients who were assigned to physical therapy alone underwent surgery within 6 months. (Funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases; METEOR ClinicalTrials.gov number, NCT00597012.)

From Brigham and Women's Hospital (J.N.K., L.C., L.A.D.-F., S.D.M., B.N.R., C.E.S.-N., D.J.S., D.H.S., J.W., E.L.) and Boston University (C.E.C., A.G., J.P.) — both in Boston; Washington University, St. Louis (R.H.B., A.K.H., M.J.M., M.V.S., R.W.W.); Rush University, Chicago (B.J.C.); Mayo Clinic, Rochester, MN (D.L.D., B.A.L., M.J.S.); Cleveland Clinic, Cleveland (M.H.J., A.M.); Hospital for Special Surgery, New York (L.A.M., R.G.M.); and Vanderbilt University, Nashville (E.K.R., B.E.R., K.P.S.). Address reprint requests to Dr. Katz at the Orthopedic and Arthritis Center for Outcomes Research, Department of Orthopedic Surgery, Brigham and Women's Hospital, 75 Francis St., BC-4016, Boston, MA 02115, or at jnkatz@partners.org.

This article was published on March 19, 2013, at NEJM.org.

N Engl J Med 2013.

DOI: 10.1056/NEJMoa1301408

Copyright © 2013 Massachusetts Medical Society.

SYMPTOMATIC, RADIOGRAPHICALLY CONFIRMED osteoarthritis of the knee affects more than 9 million people in the United States.¹ Meniscal tears are also highly prevalent, with imaging evidence of a meniscal tear observed in 35% of persons older than 50 years of age; two thirds of these tears are asymptomatic.² Meniscal damage is especially prevalent among persons with osteoarthritis^{3,4} and is frequently treated surgically with arthroscopic partial meniscectomy. This procedure, in which the surgeon trims the torn meniscus back to a stable rim, is performed for a range of indications in more than 465,000 persons annually in the United States.⁵

The high prevalence of meniscal tears in patients with osteoarthritis of the knee and the observation that these lesions are often asymptomatic challenge the ability of clinicians to determine whether symptoms are caused by the tear, osteoarthritis, or both. Clinicians who suspect that the tear is symptomatic may refer the patient to a surgeon for arthroscopic partial meniscectomy. The role of arthroscopic surgery in patients with osteoarthritis has been studied in two randomized, controlled trials over the past decade. One trial⁶ compared arthroscopic débridement and lavage with a sham surgical procedure, and the other⁷ compared arthroscopic débridement with a nonoperative regimen. Neither trial showed a statistically significant or clinically important difference between the arthroscopic and nonoperative groups with respect to functional improvement or pain relief over a period of 24 months.^{6,7}

These landmark trials established that arthroscopic treatment was not superior to the other interventions in the treatment of knee osteoarthritis, but they did not focus on management of a symptomatic meniscal tear, which is a frequent indication for knee arthroscopy in patients with osteoarthritis of the knee. The efficacy of arthroscopic partial meniscectomy in symptomatic patients with a meniscal tear and osteoarthritis has been evaluated, to our knowledge, in only one randomized, controlled trial, which was a single-center study involving 90 patients.^{8,9} This study did not show a significant difference in pain relief or functional status between arthroscopic partial meniscectomy plus a physical-therapy regimen and physical therapy alone. Given the frequency and cost of arthroscopic partial meniscectomy and the paucity of data,

we designed the Meniscal Tear in Osteoarthritis Research (METEOR) trial to assess the efficacy of arthroscopic partial meniscectomy as compared with a standardized physical-therapy regimen for symptomatic patients with a meniscal tear and concomitant mild-to-moderate osteoarthritis.

METHODS

STUDY DESIGN AND OVERSIGHT

This randomized, controlled trial was conducted in seven U.S. tertiary referral centers. Details of the trial design and conduct have been published elsewhere.¹⁰ The study was approved by the Partners HealthCare Human Research Committee and overseen by a data and safety monitoring board assembled by the National Institute of Arthritis and Musculoskeletal and Skin Diseases. There was no commercial sponsorship of this trial. The first and last authors vouch for the accuracy of the reported data and analyses and the adherence of the study to the protocol; the protocol and the statistical analysis plan are available with the full text of this article at NEJM.org.

ENROLLMENT AND RANDOMIZATION

We enrolled symptomatic patients 45 years of age or older with a meniscal tear as well as osteoarthritis detected on magnetic resonance imaging (MRI) or radiography. Since osteoarthritis-defining features can be seen on MRI before changes consistent with osteoarthritis can be detected on radiography, patients with normal findings on radiography and cartilage defects on MRI were eligible. We required that patients have at least one symptom that was consistent with a meniscal tear¹¹ that had persisted for at least 1 month despite pharmacologic treatment, physical therapy, or limitation of activity. Detailed entry and exclusion criteria (including specific symptoms that were consistent with a meniscal tear) are provided in Table 1 in the Supplementary Appendix, available at NEJM.org.

Research coordinators at each center reviewed outpatient schedules to identify patients who were potentially eligible to participate in the study. The surgeon assessed eligibility criteria and referred eligible patients to the research coordinator, who introduced the study using a standardized script. Surgeons and coordinators told patients randomly assigned to physical therapy alone that they would have the opportunity to cross over to

arthroscopic partial meniscectomy over time if the patient and surgeon thought it was clinically indicated. Patients who wished to participate provided written informed consent and completed a baseline questionnaire.

Patients were then randomly assigned in a 1:1 ratio to a treatment group with the use of a secure program on the trial website. Randomization was conducted in blocks of varying size within each site, stratified according to sex and the extent of osteoarthritis on baseline radiography (either Kellgren–Lawrence grade 0 to 2 [no joint-space narrowing] or Kellgren–Lawrence grade 3 [<50% joint-space narrowing]).

After randomization, the patient was informed about the treatment assignment; the surgeon was informed as part of the surgical booking process. Treatment was generally scheduled within 2 to 4 weeks after randomization.

INTERVENTIONS

Teams of surgeon investigators met in person on two occasions and regularly by telephone conference call throughout enrollment, as did teams of physical therapists. These teams developed standardized surgical and physical-therapy interventions that were implemented in all study centers. Standardization was developed further in telephone conference calls and meetings with the use of case examples. All surgeons were fellowship-trained and performed at least 50 arthroscopic partial meniscectomies annually. Most of the therapists were board-certified.

Arthroscopic Partial Meniscectomy

The protocol called for surgeons to perform an arthroscopic partial meniscectomy by trimming the damaged meniscus back to a stable rim. Surgeons removed loose fragments of cartilage and bone, but this procedure did not involve penetration of the subchondral bone. Preoperative antibiotics were used routinely. Postoperatively, patients were allowed to bear weight as they were able. Bracing was not used. Patients were referred to a physical therapist for a postoperative standardized physical-therapy program with the use of the same protocol as that used in the physical-therapy group, described below.

Physical Therapy

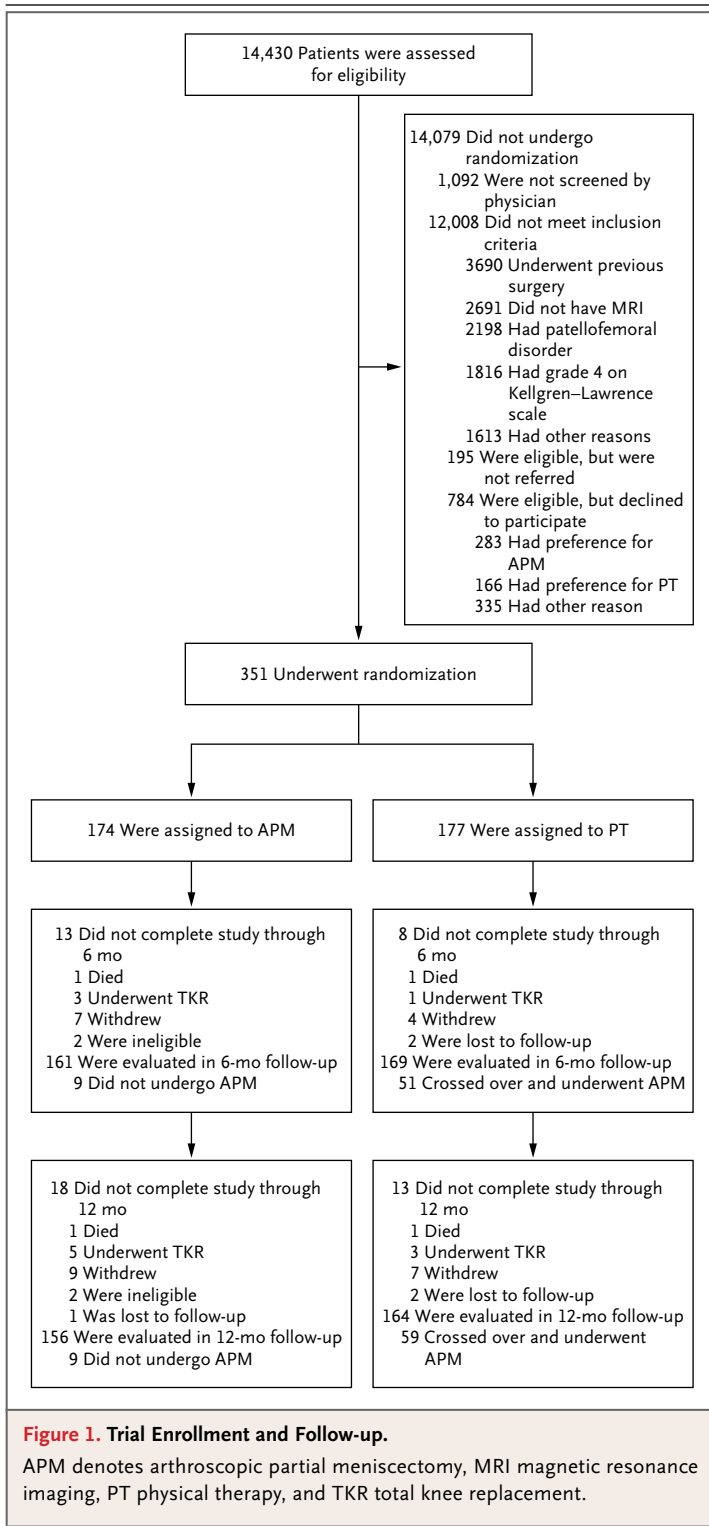
The physical-therapy protocol was developed by a team of experienced physical therapists. The pro-

ocol was based on literature supporting the effectiveness of land-based, individualized physical therapy with progressive home exercise for patients with knee osteoarthritis.^{10,12,13} The three-stage structured program was designed to address inflammation, range of motion, concentric and eccentric muscle strength, muscle-length restrictions, aerobic conditioning (e.g., with the use of a bicycle, elliptical machine, or treadmill), functional mobility, and proprioception and balance. Details of the physical-therapy program are described in Table 2 in the Supplementary Appendix. Criteria for advancing from stage I to II and from stage II to III included the level of self-reported pain, observed strength, range of knee motion, knee effusion, and functional mobility. At each stage, it was recommended that the patient attend physical-therapy sessions once or twice weekly and perform exercises at home. Patients progressed at their own pace; the duration of participation varied depending on the pace of improvement. Generally, the program lasted about 6 weeks.

In both the arthroscopic-partial-meniscectomy and physical-therapy groups, patients were permitted to receive acetaminophen and nonsteroidal antiinflammatory agents as needed. Intraarticular injections of glucocorticoids were permitted over the course of the trial.

OUTCOMES

The primary outcome was the difference between the study groups with respect to the change in the score on the physical-function scale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)¹⁴ from baseline to 6 months after randomization. WOMAC scores range from 0 to 100, with higher scores indicating worse physical function. The original statistical-analysis plan referred to the primary outcome as the WOMAC function score at 6 months, with adjustment for the baseline score. However, since the change in the WOMAC physical-function score is a standard outcome in assessing interventions for knee osteoarthritis and is more easily interpreted than the raw score at 6 months adjusted for the baseline score, we revised the primary outcome before analyzing the trial data. We specified 6 months as the time for assessment of the primary outcome because the clinical response to treatment is apparent by this time. We added a 12-month assessment to determine whether the response was stable.



ies involving patients with a meniscal tear,^{15,16} and the score on the physical-activity scale of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). Scores on both scales range from 0 to 100, with higher KOOS scores indicating more severe pain and higher SF-36 scores indicating greater physical activity.¹⁷ We also considered a binary outcome that was defined as improvement in the WOMAC physical-function score of at least 8 points (a clinically relevant difference specified a priori^{10,18,19}) without crossover to the other study group.

ASSESSMENTS

Questionnaires were administered at baseline and 3, 6, and 12 months after randomization. The primary outcome was assessed at 6 months, with the 3-month and 12-month assessments used to capture the trajectory and stability of the treatment response. Site coordinators contacted the participants by telephone every other week for the first 3 months after randomization and quarterly thereafter to ascertain adverse events and compliance with physical therapy. Surgeons, patients, and research staff were aware of the treatment assignments.

Radiographs of the weight-bearing knee were assessed at each study site by the participating surgeon on the basis of the Kellgren–Lawrence grade²⁰ and were then reassessed centrally (also on the basis of the Kellgren–Lawrence grade)²¹ by a musculoskeletal radiologist. The concordance between these readings was 71.8%. Readings performed at the clinical site were used for assessing eligibility and randomization strata, whereas central readings were used in the analysis. Analyses performed with readings at the clinical site did not materially differ from those performed with central readings.

STATISTICAL ANALYSIS

The primary analysis was implemented with an analysis of covariance with changes in the WOMAC physical-function score from baseline to 6 months as the dependent variable, treatment as the independent variable of interest, and study site as a covariate. Other covariates, such as age, sex, and baseline Kellgren–Lawrence grade, were balanced across groups and were therefore not included in the analysis. The primary analysis used a modified intention-to-treat approach in which patients who did not withdraw from the

Secondary outcomes were the pain score on the Knee Injury and Osteoarthritis Outcome Scale (KOOS), which has been used frequently in stud-

study were evaluated in the group to which they were randomly assigned. We performed three secondary analyses: an analogous intention-to-treat analysis of covariance with the use of either the KOOS pain score or the SF-36 physical-activity score as the dependent variables and a logistic regression, with adjustment for the study site, which used the binary outcome defined above. We prespecified one subgroup analysis based on the baseline radiographic grade (Kellgren–Lawrence grade 0 to 2 vs. Kellgren–Lawrence grade 3).^{10,22} Additional analyses with adjustment for uncertainty due to missing data are described in the Supplementary Appendix.²³

We powered the study to detect a 10-point difference in the WOMAC physical-function score between the arthroscopic-partial-meniscectomy and physical-therapy groups. This was the difference we noted in observational pilot data, and it is close to the minimal clinically important difference in the WOMAC physical-function score among patients with osteoarthritis.^{18,19} On the basis of a type I error rate of 5% and a power of 80%, and taking into account potential losses to follow-up and crossovers from the assigned group to the other group before the assessment of the primary outcome, we set the target sample size at 340 patients.

RESULTS

CHARACTERISTICS OF THE STUDY POPULATION

From June 2008 through August 2011, a total of 14,430 patients were screened in seven study centers, of whom 1330 (9.2%) were eligible. Of these patients, 351 (26.4%) were enrolled and randomly assigned to a treatment group (Fig. 1). The two groups were similar with respect to age, sex, race or ethnic group, baseline Kellgren–Lawrence grade of radiographic severity, and baseline WOMAC physical-function score (Table 1).

OUTCOMES

In the intention-to-treat analysis that was adjusted for the study site, the mean improvement in the WOMAC physical-function score from baseline to 6 months was 20.9 points in the group randomly assigned to arthroscopic partial meniscectomy, as compared with 18.5 points in the physical-therapy group (between-group difference, 2.4 points; 95% confidence interval [CI], -1.8 to 6.5) (Table 2 and Fig. 2A). Results of the

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Arthroscopic Partial Meniscectomy (N = 161)	Physical Therapy (N = 169)
Mean age — yr	59.0±7.9	57.8±6.8
Sex — no. (%)		
Male	71 (44.1)	72 (42.6)
Female	90 (55.9)	97 (57.4)
Race or ethnic group — no. (%)†		
White	138 (85.7)	142 (84.0)
Black	15 (9.3)	17 (10.1)
Hispanic	2 (1.2)	5 (3.0)
Other	6 (3.7)	5 (3.0)
Index knee — no. (%)		
Right	70 (43.5)	68 (40.2)
Left	91 (56.5)	101 (59.8)
Mean body-mass index	30.0±6.1	30.0±6.1
WOMAC physical-function score‡	37.1±17.9	37.5±18.3
KOOS pain score§	46.0±15.5	47.2±16.4
Mental Health Index 5 score¶	74.8±12.9	74.0±13.9
SF-36 physical-activity score	44.3±23.7	43.3±23.3
Kellgren–Lawrence grade — no. (%)**		
0	34 (21.1)	36 (21.3)
1	26 (16.1)	35 (20.7)
2	37 (23.0)	39 (23.1)
3	45 (28.0)	39 (23.1)

* Plus–minus values are means ±SD. There were no significant differences between the groups. Percentages may not sum to 100 because of rounding. The body-mass index is the weight in kilograms divided by the square of the height in meters.

† Race and ethnic group were self-reported.

‡ Scores on the physical-function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) range from 0 to 100, with higher scores indicating more limitation of physical function.

§ Scores on the pain scale of the Knee Injury and Osteoarthritis Outcome Scale (KOOS) range from 0 to 100, with higher scores indicating more pain.

¶ Scores on the Mental Health Index 5 range from 0 to 100, with higher scores indicating better mental health.

|| Scores on the physical-activity scale of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 to 100, with higher scores indicating greater physical activity.

** A Kellgren–Lawrence grade of 0 (no osteophytes or joint-space narrowing) indicates no osteoarthritis, a grade of 1 (questionable osteophyte) indicates possible osteoarthritis; a grade of 2 (definite osteophyte, no joint-space narrowing) indicates mild osteoarthritis, a grade of 3 (≥50% joint-space narrowing) indicates moderate osteoarthritis, and a grade of 4 (>50% joint-space narrowing) indicates severe osteoarthritis. In 11.8% of patients, Kellgren–Lawrence grades were not assessed centrally.

analysis (as originally specified) of the 6-month WOMAC physical-function score, adjusted for the baseline score, likewise did not show a clinically important or statistically significant difference

Table 2. Primary and Secondary Outcomes of the Trial.*

Outcome	Arthroscopic Partial Meniscectomy (N = 161)		Physical Therapy (N = 169)		Improvement from Baseline		Between-Group Difference in Improvement from Baseline
	Arthroscopic Partial Meniscectomy	Physical Therapy	Arthroscopic Partial Meniscectomy	Physical Therapy	Arthroscopic Partial Meniscectomy	Physical Therapy	
6 Months							
WOMAC physical-function score — mean (95% CI)	14.7 (12.0 to 17.5)	19.0 (16.3 to 21.7)	20.9 (17.9 to 23.9)	18.5 (15.6 to 21.5)	2.4 (–1.8 to 6.5) †		
KOOS pain score — mean (95% CI)	21.1 (18.3 to 23.9)	25.2 (22.4 to 28.0)	24.2 (21.3 to 27.1)	21.3 (18.4 to 24.2)	2.9 (–1.2 to 7.0)		
SF-36 physical-activity score — mean (95% CI)	69.2 (65.2 to 73.2)	66.1 (62.1 to 70.1)	24.2 (20.3 to 28.0)	23.1 (19.2 to 27.0)	1.1 (–4.4 to 6.6)		
Treatment success — no. (%) ‡	108 (67)	74 (44)					
Treatment failure — no. (%)	40 (25)	82 (49)					
WOMAC physical-function score improvement <8 points and no crossover — no./total no. (%)	32/40 (80)	31/82 (38)					
Crossover within 6 mo — no./total no. (%) §	8/40 (20)	51/82 (62)					
Data missing — no. (%)	13 (8)	13 (8)					
12 Months — mean (95% CI)							
WOMAC physical-function score	13.7 (11.2 to 16.2)	14.5 (12.0 to 16.9)	23.5 (20.5 to 26.5)	22.8 (19.8 to 25.8)	0.7 (–3.5 to 4.9)		
KOOS pain score	19.1 (16.4 to 21.9)	19.3 (16.6 to 22.0)	26.8 (23.7 to 30.0)	27.3 (24.1 to 30.4)	–0.4 (–4.8 to 4.0)		
SF-36 physical-activity score	69.0 (64.6 to 73.4)	71.4 (67.0 to 75.7)	25.0 (20.9 to 29.1)	28.1 (24.0 to 32.1)	–3.0 (–8.8 to 2.7)		

* Between-group differences may not equal the differences in change from baseline between the partial-meniscectomy and physical-therapy groups because of rounding. CI denotes confidence interval.

† This between-group difference was the primary outcome.

‡ Treatment success indicates an improvement in the WOMAC physical-function score of 8 points or more, with no crossover.

§ Eight patients in the partial-meniscectomy group crossed over to surgery within 6 months, and 1 crossed over after 6 months.

Figure 2. Scores on the WOMAC Physical-Function Scale and KOOS Pain Scale over the 12-Month Follow-up Period.

Panel A shows the scores on the physical-function scale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Panel B shows the scores on the pain scale of the Knee Injury and Osteoarthritis Outcome Scale (KOOS); scores on both scales range from 0 to 100, with higher scores indicating more severe symptoms. I bars indicate 95% confidence intervals. Panel C shows WOMAC physical-function scores in the APM group and in the PT group according to crossover status. The asterisk indicates that nine patients assigned to APM did not undergo surgery.

between groups (difference, 3.4 points; 95% CI, -0.04 to 6.8). In the intention-to-treat analysis of the KOOS pain score, the mean decreases (i.e., improvements) from baseline to 6 months were 24.2 points in patients assigned to arthroscopic partial meniscectomy versus 21.3 points in those assigned to physical therapy alone (between-group difference, 2.9 points; 95% CI, -1.2 to 7.0) (Table 2 and Fig. 2B). In intention-to-treat analyses of 12-month outcomes adjusted for study site, the two groups had similar changes from baseline in the WOMAC physical-function and KOOS pain scores (Table 2).

Among 330 active participants in the study, by 6 months of follow-up, 51 patients assigned to physical therapy alone (30.2%) had undergone arthroscopic partial meniscectomy, whereas 9 patients assigned to surgery (5.6%) had not undergone the procedure. An additional 8 active patients in the study (4.7%) who were assigned to the physical-therapy group crossed over to arthroscopic partial meniscectomy between 6 and 12 months. At 6 months, 67.1% of the patients assigned to arthroscopic partial meniscectomy had an improvement of at least 8 points in the WOMAC physical-function score and had not crossed over to the other study treatment, as compared with 43.8% of patients assigned to the physical-therapy group ($P=0.001$). Patients in the physical-therapy group who crossed over and underwent arthroscopic partial meniscectomy during the first 6 months had WOMAC physical-function scores at 12 months that were similar to those of patients assigned to the arthroscopic-partial-meniscectomy group (Fig. 2C). The proportion of patients who crossed over from physical therapy to arthroscopic partial meniscectomy ranged from 0.0 to 59.5% across study centers. In

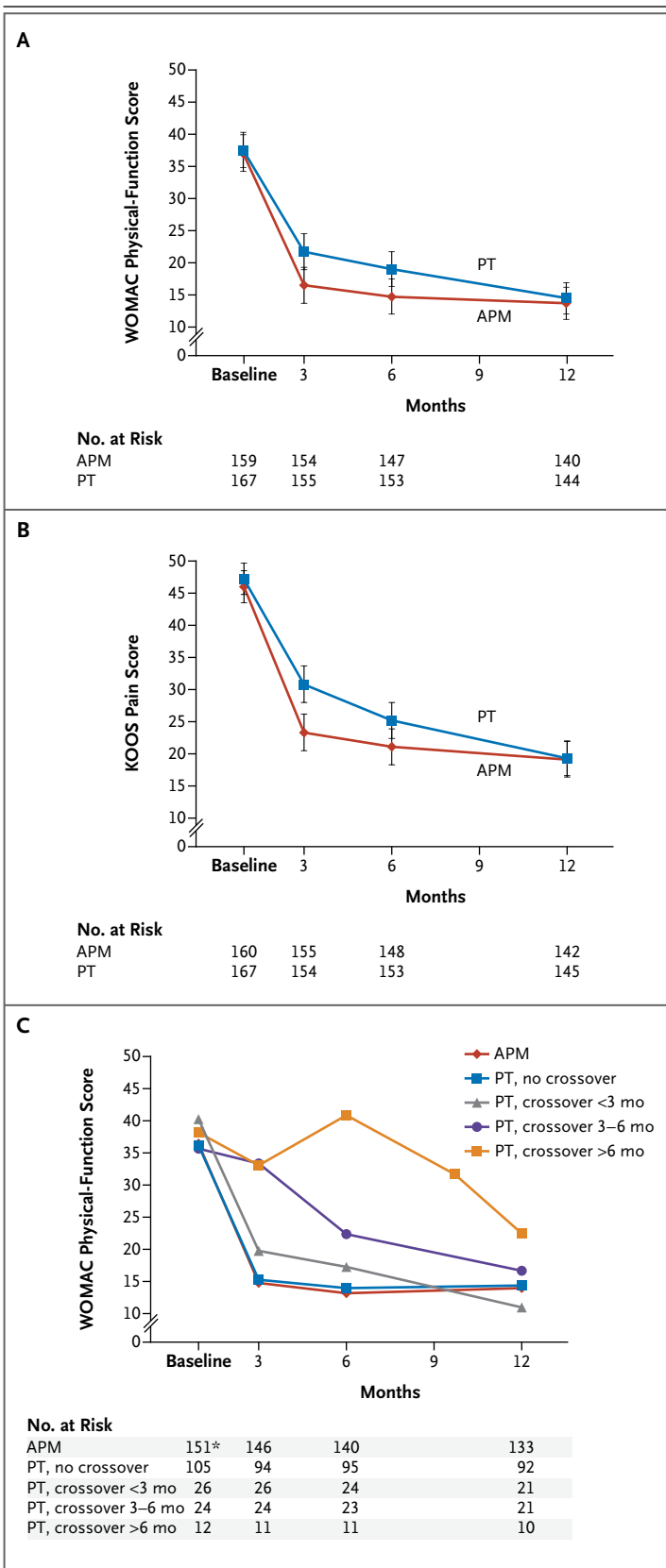


Table 3. Adverse Events at 12 Months in All Patients Assigned to Treatment.

Event	Arthroscopic Partial Meniscectomy (N=174)	Physical Therapy (N=177)
	<i>number of patients</i>	
Serious adverse events		
Cardiovascular		
Pulmonary embolism (fatal)	1	0
Acute myocardial infarction	1	0
Sudden death	0	1
Stroke	0	1
Hypoxemia	1	0
Total	3	2
Nonserious adverse events		
Musculoskeletal		
Pain from fall or other trauma	2	4
Tendonitis	3	0
Knee bursitis	0	1
Rupture of Baker's cyst	1	0
Knee pain	1	1
Pain in the back, hip, or foot	2	4
Cardiovascular		
Deep-vein thrombosis	2	0
Syncope	1	0
Atrial fibrillation	0	1
Skin	2	1
Other	1	1
Total	15	13

general, the patients assigned to receive physical therapy alone who crossed over to surgery did not have substantial improvement in functional status during the period from randomization until the time of crossover (Fig. 2C).

In the physical-therapy group, patients were scheduled for an average of 9.3 physical-therapy visits and attended an average of 8.4 visits (90.6%). In the arthroscopic-partial-meniscectomy group, patients were scheduled for an average of 7.4 visits and attended 6.9 visits (92.9%). In the physical-therapy group, 21 patients (12.4%) received intraarticular glucocorticoid injections, as did 9 patients (5.6%) in the arthroscopic-partial-meniscectomy group.

The between-group difference in functional improvement from baseline to 6 months did not differ significantly according to the Kellgren-

Lawrence grade of radiographic severity ($P=0.13$ for interaction) (Table 3 in the Supplementary Appendix).

ADVERSE EVENTS

There were no significant between-group differences in the frequencies of overall or specific adverse events. Over the 12-month period of follow-up, serious adverse events occurred in 3 participants assigned to arthroscopic partial meniscectomy and 2 participants assigned to physical therapy alone (including one death in each group); adverse events rated as mild or moderate in severity occurred in 15 participants in the arthroscopic-partial-meniscectomy group and 13 participants in the physical-therapy group (Table 3). Total knee replacement (coded not as an adverse event but rather as an indication for discontinuation from the study) was performed in 5 participants assigned to arthroscopic partial meniscectomy and 3 participants assigned to physical therapy alone (Fig. 1).

DISCUSSION

In this seven-center randomized, controlled trial involving symptomatic patients 45 years of age or older with a meniscal tear and imaging evidence of mild-to-moderate knee osteoarthritis, there were no significant differences in the magnitude of improvement in functional status and pain after 6 and 12 months between patients assigned to arthroscopic partial meniscectomy with postoperative physical therapy and patients assigned to a standardized physical-therapy regimen. These results were achieved with a 30% rate of crossover to arthroscopic partial meniscectomy at 6 months. At 12 months, among 169 participants (not all of whom provided data at the 1-year evaluation), the rate of crossover to surgery was 35%.

In a prior small, single-center, randomized, controlled trial comparing arthroscopic partial meniscectomy with standardized physical therapy for symptomatic patients with a meniscal tear and knee osteoarthritis, the two groups had similar functional outcomes at 6 months, and the similarity between the groups persisted through 5 years of follow-up.^{8,9} To our knowledge, this is the first large, multicenter, randomized, controlled trial to examine the efficacy of arthroscopic partial meniscectomy as compared with a standardized physical-therapy regimen.

Surgical randomized, controlled trials present methodologic challenges, including crossover from one group to the other.^{24,25} To account for crossovers, we defined an additional outcome a priori in which patients were deemed to have a successful treatment response if they had improvement of at least 8 points on the WOMAC physical-function scale (a clinically important difference) and they did not cross over from their assigned treatment. A total of 67% of patients assigned to arthroscopic partial meniscectomy met this threshold for success, as compared with 44% of patients treated with physical therapy alone. We acknowledge, however, that because the treatment assignments were not blinded, and because crossover could not occur in the arthroscopic-partial-meniscectomy group once the surgery had been performed, this secondary analysis was vulnerable to bias.

Several limitations of the study warrant discussion. First, because we enrolled only 26% of eligible patients, our findings must be generalized cautiously. The most frequent reason that patients declined enrollment was a strong preference for one treatment or the other. Since patients' preferences may be associated with treatment outcome, our trial may be vulnerable to selection bias. Participating surgeons may not have referred potentially eligible patients because they were uncomfortable randomly assigning these patients to treatment; this form of selective enrollment may also create bias.²⁶ Second, because the trial was conducted in academic referral centers, the findings should be generalized carefully to community settings. Third, we did not formally assess the fidelity of the physical therapists or surgeons to the standard intervention protocols. Finally, our study was not blinded, since our investigative group did not consider a sham comparison group feasible.

These limitations notwithstanding, the results of our trial may help guide management in the care of patients with knee symptoms, a meniscal tear, and imaging evidence of osteoarthritis. Our findings suggest that both arthroscopic partial meniscectomy and referral to physical therapy — with an opportunity to consider arthroscopic partial meniscectomy if substantial improvements are not achieved — are likely to result in considerable improvement in functional status and knee pain over a 6-to-12-month period. Given that improvements in functional status and pain

at 6 months did not differ significantly between patients assigned to arthroscopic partial meniscectomy and those assigned to physical therapy alone and that 70% of the patients in the physical-therapy group did not undergo surgery, these data provide considerable reassurance regarding an initial nonoperative strategy. It is uncertain whether patients who undergo arthroscopic partial meniscectomy are at greater risk for progression of underlying osteoarthritis than patients treated nonoperatively.²⁷⁻³⁰ Longitudinal assessment of imaging studies in our trial is planned to address this question.

In summary, symptomatic patients with a meniscal tear and imaging evidence of mild-to-moderate osteoarthritis who were randomly assigned to arthroscopic partial meniscectomy with postoperative physical therapy had improvements in functional status and pain at 6 months that did not differ significantly from the improvements in patients randomly assigned to a standardized physical-therapy regimen alone. However, 30% of patients assigned to the physical-therapy group crossed over to surgery in the first 6 months. These findings should help inform decision making by patients and their physicians.

Supported by grants (R01AR055557, K24AR057827, and P60AR047782) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health.

Dr. Brophy reports receiving fees for providing expert testimony on behalf of Genzyme on the use of Synvisc and grant support through his institution from the Orthopaedic Research and Education Foundation. Dr. Cole reports receiving consulting fees from Arthrex, Carticept, DJ Orthopedics, Genzyme, Johnson & Johnson, DePuy Orthopedics, Regentis, and Zimmer, lecture fees from Genzyme, fees for providing expert testimony for medical malpractice defense and third-party liability cases on personal injury and product liability, and royalties from Arthrex, DJ Orthopedics, Elsevier, and W.B. Saunders, holding equity in Carticept and Regentis, receiving grant support through his institution from Major League Baseball, Arthrex, Zimmer, ArthroSurface, Johnson & Johnson, and Medipost and fellowship support through his institution from DJ Orthopedics, Ossur, and Smith and Nephew. Dr. Guermazi reports receiving consulting fees from Merck Serono, Pfizer, and Genzyme, and holding stock in Boston Imaging Core Lab. Dr. Jones reports receiving consulting fees from Allergan and grant support through his institution from DJ Orthopedics, Stryker, Smith and Nephew, Breg, and Arthrex. Dr. Levy reports receiving consulting fees from Arthrex and royalties from VOT Solutions and Arthrex. Dr. Matava reports receiving consulting fees from ISTO Technologies, Schwartz Biomedical, and OsteSys, and grant support through his institution from Arthrex and Breg. Dr. Miniaci reports receiving consulting fees from ArthroSurface and Stryker and lecture fees, payment for the development of educational presentations, and travel support from ArthroSurface, holding stock in ArthroSurface, and receiving royalties from ArthroSurface for granted and pending patents regarding retrograde delivery of resurfacing devices, an articular surface implant and delivery system, and a system and method for a retrograde procedure and grant support through his institution from DJ

Orthopedics, Stryker, and Arthrex. Dr. Reinke reports receiving grant support through her institution from Smith and Nephew, DonJoy, and the National Football League. Dr. Smith reports receiving consulting fees from ISTO Technologies. Dr. Spindler reports receiving consulting fees from the National Football League and payment for patents from Connective Orthopedics on a biologic replacement for fibrin clots. Dr. Stuart reports receiving consulting fees and royalties from Arthrex and grant support through his institution from Stryker. Dr. J. Wright reports receiving consulting fees from DePuy Orthopedics. Dr. R. Wright reports receiving consulting fees from Flexion Therapeu-

tics and ISTO Technologies, and grant support through his institution from Smith and Nephew. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank the METEOR scientific advisory board (Thomas S. Thornhill, M.D., chair, John A. Baron, M.D., and Alan M. Jette, Ph.D.) for their advice; Nizar N. Mahomed, M.D., Sc.D., for support and scientific input; and the dozens of investigators and research staff and hundreds of patients across seven centers who participated in the trial.

REFERENCES

- Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. *Arthritis Rheum* 2008;58:26-35.
- Englund M, Guermazi A, Gale D, et al. Incidental meniscal findings on knee MRI in middle-aged and elderly persons. *N Engl J Med* 2008;359:1108-15.
- Bhattacharyya T, Gale D, Dewire P, et al. The clinical importance of meniscal tears demonstrated by magnetic resonance imaging in osteoarthritis of the knee. *J Bone Joint Surg Am* 2003;85:4-9.
- Sowers M, Karvonen-Gutierrez CA, Jacobson JA, Jiang Y, Yosef M. Associations of anatomical measures from MRI with radiographically defined knee osteoarthritis score, pain, and physical functioning. *J Bone Joint Surg Am* 2011;93:241-51.
- Kim S, Bosque J, Meehan JP, Jamali A, Marder R. Increase in outpatient knee arthroscopy in the United States: a comparison of National Surveys of Ambulatory Surgery, 1996 and 2006. *J Bone Joint Surg Am* 2011;93:994-1000.
- Moseley JB, O'Malley K, Petersen NJ, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002;347:81-8.
- Kirkley A, Birmingham TB, Litchfield RB, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2008;359:1097-107. [Erratum, *N Engl J Med* 2009;361:2004.]
- Herrlin S, Hällander M, Wange P, Weidenhielm L, Werner S. Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomized trial. *Knee Surg Sports Traumatol Arthrosc* 2007;15:393-401.
- Herrlin SV, Wange PO, Lapidus G, Hällander M, Werner S, Weidenhielm L. Is arthroscopic surgery beneficial in treating non-traumatic, degenerative medial meniscal tears? A five year follow-up. *Knee Surg Sports Traumatol Arthrosc* 2013;21:358-64.
- Katz JN, Chaisson CE, Cole B, et al. The MeTeOR trial (Meniscal Tear in Osteoarthritis Research): rationale and design features. *Contemp Clin Trials* 2012;33:1189-96.
- Niu NN, Losina E, Martin SD, Wright J, Solomon DH, Katz JN. Development and preliminary validation of a meniscal symptom index. *Arthritis Care Res (Hoboken)* 2011;63:208-15.
- Fransen M, McConnell S. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2008;4:CD004376.
- Fransen M, McConnell S. Land-based exercise for osteoarthritis of the knee: a metaanalysis of randomized controlled trials. *J Rheumatol* 2009;36:1109-17.
- Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to anti-rheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988;15:1833-40.
- Roos EM, Roos HP, Ekdahl C, Lohmander LS. Knee Injury and Osteoarthritis Outcome Score (KOOS) — validation of a Swedish version. *Scand J Med Sci Sports* 1998;8:439-48.
- Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS) — development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28:88-96.
- Ware JE Jr, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-83.
- Angst F, Aeschlimann A, Michel BA, Stucki G. Minimal clinically important rehabilitation effects in patients with osteoarthritis of the lower extremities. *J Rheumatol* 2002;29:131-8.
- Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. *Arthritis Rheum* 2001;45:384-91.
- Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthritis. *Ann Rheum Dis* 1957;16:494-502.
- Guermazi A, Hunter DJ, Li L, et al. Different thresholds for detecting osteophytes and joint space narrowing exist between the site investigators and the centralized reader in a multicenter knee osteoarthritis study — data from the Osteoarthritis Initiative. *Skeletal Radiol* 2012;41:179-86.
- Wang R, Lagakos SW, Ware JH, Hunter DJ, Drazen JM. Statistics in medicine — reporting of subgroup analyses in clinical trials. *N Engl J Med* 2007;357:2189-94.
- Little RJ, D'Agostino R, Cohen ML, et al. The prevention and treatment of missing data in clinical trials. *N Engl J Med* 2012;367:1355-60.
- Frobell RB, Roos EM, Roos HP, Rans-tam J, Lohmander LS. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med* 2010;363:331-42. [Erratum, *N Engl J Med* 2010;363:893.]
- Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical versus nonsurgical therapy for lumbar spinal stenosis. *N Engl J Med* 2008;358:794-810.
- Katz JN, Wright J, Levy BA, Baron JA, Losina E. Departures from community equipoise may lead to incorrect inference in randomized trials. *J Clin Epidemiol* 2011;64:280-5.
- Englund M, Lohmander LS. Risk factors for symptomatic knee osteoarthritis fifteen to twenty-two years after meniscectomy. *Arthritis Rheum* 2004;50:2811-9.
- Mills PM, Wang Y, Cicuttini FM, et al. Tibio-femoral cartilage defects 3-5 years following arthroscopic partial medial meniscectomy. *Osteoarthritis Cartilage* 2008;16:1526-31.
- Papalia R, Del Buono A, Osti L, Denaro V, Maffulli N. Meniscectomy as a risk factor for knee osteoarthritis: a systematic review. *Br Med Bull* 2011;99:89-106.
- Englund M, Guermazi A, Roemer FW, et al. Meniscal tear in knees without surgery and the development of radiographic osteoarthritis among middle-aged and elderly persons: the Multicenter Osteoarthritis Study. *Arthritis Rheum* 2009;60:831-9.

Copyright © 2013 Massachusetts Medical Society.