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The Newsletter on Musculoskeletal Medicine

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Mobilization With Movement Improves Pain and Function on Knee Osteoarthritis

CME Article by Ellen Hoffmeister

Ms. Hoffmeister is a freelance medical writer in Camp Hill, Pennsylvania.

The author, faculty, and staff in a position to control the content of this CME activity have disclosed that they and their spouses/life partners (if any) have no financial relationships with, or financial interests in, any commercial companies relevant to this educational activity.

Learning objective: *After completing this activity, physicians should be better able to evaluate the evidence for mobilization with movement as an appropriate treatment for patients with knee osteoarthritis.*

Key Words: Knee, Osteoarthritis, Mobilization, Pain

The findings of a recent study suggest that mobilization with movement (MWM) provides a local and widespread hypoalgesic effect, increases knee flexion range of motion (ROM), increases knee flexor and extensor strength, and improves physical function in patients with osteoarthritis (OA). (See Alkhawajah and Alshami, 2019.)

Researchers Hani A. Alkhawajah, MSc, and Ali M. Alshami, MD, of Imam Abdulrahman Bin Faisal University in Dammam, Saudi Arabia, explain that MWM is a manual therapy that has been shown to increase joint ROM, enhance muscle function,

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Factors That Predict Radiographic Progression of Ankylosing Spondylitis

CME Article by Ellen Hoffmeister

Ms. Hoffmeister is a freelance medical writer in Camp Hill, Pennsylvania.

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Learning objective: *After completing this activity, physicians should be better able to describe factors that may impact the progression of ankylosing spondylitis.*

Key Words: Ankylosing spondylitis, Progression

Male sex, presence of baseline damage, active disease state, and higher inflammatory markers confer a high risk for the progression of ankylosing spondylitis (AS), according to a recent study. (See Sari et al., 2019.)

Ismail Sari, MD, MSc, of the Division of Rheumatology in the Department of Medicine at Toronto Western Hospital in Toronto, Canada, and colleagues add that treatment with tumor necrosis factor inhibitors (TNFi) showed a disease-modifying effect by slowing the rate of radiographic progression.

Sari et al. note that structural spinal damage is a known feature of AS, which is characterized by new bone formation (i.e. syndesmophytes) in the spine. They write that currently conventional radiography is the gold standard for assessment of the extent and severity of spinal disease caused by AS.

They also cite studies demonstrating that up to 50% of AS patients show some degree of spinal progression in two years of follow-up, and that pain and stiffness due to disease activity and structural damage are the main contributors toward physical function impairment. Further, a number of predictors of spinal disease progression, including baseline structural damage, higher

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Movement Improves Pain and Function

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and treat specific pathologies. "To our knowledge, three studies have attempted to investigate the effects of MWM in patients with knee OA. These studies were either case series or randomized controlled trials (RCTs) that used other treatment procedures in addition to MWM," they write.

Alkhawajah and Alshami note that studies that particularly investigate the widespread hypoalgesic effects of MWM in patients with knee OA are lacking. Therefore, the aim of their randomized double-blind controlled trial was to investigate the immediate and short-term effects of MWM on function and local and distant pain in patients with knee OA compared with sham MWM.

What Methods Did Researchers Use?

The researchers recruited patients who were treated in the Department of Physiotherapy at King Fahd Hospital. They included those 40 years or older with unilateral or bilateral knee OA with a Kellgren-Lawrence (KL) grade equal to or higher than 2 who fulfilled the classification criteria of the American College of Rheumatology for knee OA, reported peak knee pain of greater than 3 on a visual analog scale (VAS) over the previous 24 hours, and were able to walk at least 6 m.

The researchers excluded patients who had knee or lower limb surgery; had received an intra-articular corticosteroid or hyaluronic acid injection within the past six months; reported current or past (within four weeks) oral corticosteroid use; had inflammatory or neurologic disorders; had altered sensation (to cold, heat, or pressure) around their knee; exhibited cognitive difficulties; had low back-related leg pain; or had any contraindication to manual therapy.

Blinded to the allocation, participants were recruited consecutively and randomly allocated to either a treatment group (MWM) or a sham group (sham MWM).

An experienced physiotherapist trained in the use of MWM, blind to the measurements until data analysis, administered treatment to all patients. Mobilization with movement techniques were performed using a sustained medial, lateral, anterior, posterior, or rotation glide of the tibia during active knee flexion and extension. The glides were tested in all possible directions while the patient was in the supine position, in the following order: frontal plane (medial/lateral), sagittal plane (anterior/posterior), and rotation.

The researchers selected the direction that relieved pain to the lowest level and improved knee range most as the glide for treatment. If the movement was not painful, overpressure was added at the end range. The therapist examined the glide direction in weight bearing if there was no

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pain in the supine position. If several glide directions showed similar effects in the supine position, the therapist performed these tests in a weight-bearing position to determine the most effective glide direction.

In the treatment group, the therapist applied the glide force on the tibia with the knee in midrange. This force was maintained while the patient was flexing and extending the knee to full range. Overpressure was performed at the end range. The MWM treatment technique was repeated 10 times for three sets.

Patients in the sham group were handled similarly to those in the treatment group, but did not take the glide of direction. Alternatively, the therapist's hands lightly touched the knee skin without pressure, with one hand on the tibia and one on the femur. Active knee flexion and extension movements, however, were performed 10 times for three sets.

Outcome measures included a VAS for pain, the pressure pain threshold (PPT) test, the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index, the Timed Up and Go (TUG) test, and knee strength and knee ROM. Measurements were taken at baseline, immediately after intervention, and two days later. Of note, the researchers examined PPT on the affected knee and on the middle deltoid, 10 cm away from the acromion of the ipsilateral shoulder, to investigate any widespread changes in sensitivity at a distant site.

The researchers explain that the primary analysis was performed on an intention-to-treat basis, including all randomized participants. For continuous outcomes, the least square means and their 95% confidence intervals were estimated using a linear mixed model (LMM) for repeated measures with participants as a random effect, baseline score as a covariate, and outcomes at two follow-up visits as a dependent variable. For the WOMAC, which was measured with a single follow-up time (i.e. two days), the researchers used analysis of covariance (ANCOVA) with baseline value as a covariate.

What Results Do Researchers Report?

Alkhawajah and Alshami found that, while 44 patients satisfied the criteria, four were excluded because of tibial osteotomy, altered sensation around their knees, and/or because they were unable to walk 6-m distance with or without an aid.

At baseline, patients in the treatment and sham groups had an average age of 56.5 and 56.6 years, respectively. The treatment group comprised 13 male and seven females; the sham group comprised 12 males and eight females. Their average body mass index was 32.6 in the treatment group and 33.3 in the sham group. Patients' duration of symptoms was 51 months in the treatment group and 48 months in the sham group. More patients in both groups had OA in the right knee and a KL grade of 2.

The researchers report that the group-by-time interaction for the LMM was statistically significant for VAS, PPT at the knee and at the shoulder, TUG, knee flexor strength, knee extensor strength, and knee flexion ROM.

Alkhawajah and Alshami write that the results show significantly greater mean changes from baseline for knee flexion ROM in the treatment group compared with the sham group at follow-up visits one and two; the mean between-group difference was 12.8 and 8.3, respectively. Compared with those receiving sham MWM, the patients who received MWM demonstrated an immediate and greater decrease in pain, a greater increase in PPT at both the knee and shoulder, a greater decrease in TUG time, a greater increase in knee flexor and extensor strength, and a greater increase in knee flexion ROM, but not in extension ROM.

Two days after intervention, patients who received MWM demonstrated a greater decrease in pain, a greater increase in PPT at the shoulder, a greater decrease in TUG time, a greater increase in knee flexor and extensor strength, and a greater increase in knee flexion ROM compared with those who received sham MWM. However, no significant differences were found between the treatment and sham groups in PPT at the knee or knee extension ROM. The ANCOVA revealed no significant differences between the two groups in the total score or any subscale of the WOMAC.

What Do Researchers Add About Findings?

In the discussion of the findings, Alkhawajah and Alshami note that a strength of their study is that a sham treatment was used, which is considered more appropriate than no or usual treatment as a control. They also state that a limitation of the study is its short-term design, which may suggest that the immediate changes of any outcome cannot be extrapolated to long-term changes. "However, significant improvements in pain, function, ROM, and muscle strength were noted in this study, as in previous studies," they state.

In conclusion, they write that, although this study demonstrated immediate and short-term effects that persisted for two days after the intervention, more research is needed to determine the long-term efficacy of this approach. ■

Disclosures: None declared.

Reference

Alkhawajah HA and Alshami AM, The effect of mobilization with movement on pain and function in patients with knee osteoarthritis: A randomized double-blind controlled trial, *BMC Musculoskeletal Disorders*, 2019; 20:452.

Predict Radiographic Progression

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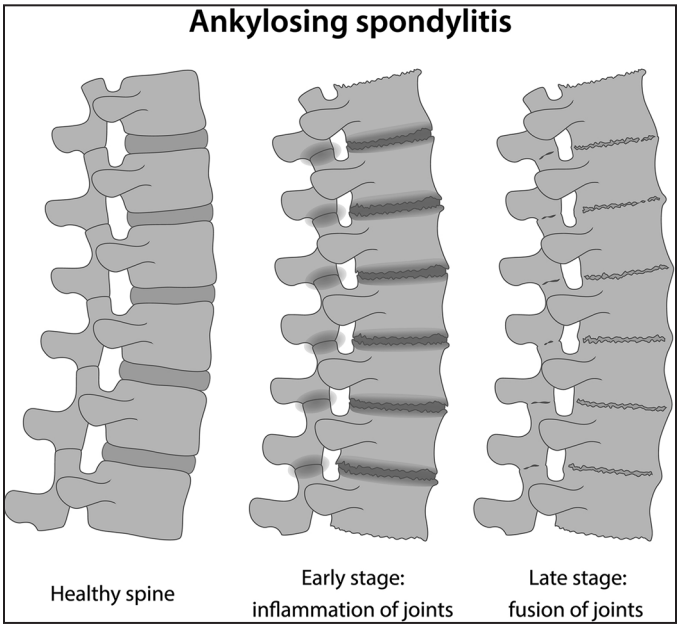
inflammatory burden, male sex, positivity for HLA-B27, and smoking, have been described previously.

They write that nonsteroid anti-inflammatory drugs (NSAIDs) and TNFi treatments are the cornerstone therapies in the management of AS. "Aside from being clinically effective, some reports suggest a beneficial effect on structural damage in AS, particularly with the use of TNFi," they add. Using a longitudinal observational cohort of AS patients, Sari et al. sought to identify progression rates and factors predictive of spinal progression. As a secondary aim, they analyzed the effect of TNFi on radiographic progression in these patients.

Sari et al. note that, at the individual level, structural disease progression was not linear and was highly variable.



What Methods Did Researchers Use?

The researchers recruited patients from the Toronto Western Hospital Spondylitis Clinic. In that cohort and using a standardized protocol, adult axSpA patients (18 years or older) are followed up on an annual basis and their data, including clinical (disease activity, Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] and Ankylosing Spondylitis Disease Activity Score [ASDAS]) and functional parameters (Bath Ankylosing Spondylitis Functional Index [BASFI]), medication history (TNFi and disease-modifying antirheumatic drugs [DMARDs] treatment), and laboratory studies are systematically collected. Patients also undergo conventional radiographs at two-year intervals.

Patients were included in the current study if they were classified as having AS, based on the modified New York criteria, and had available lateral views of cervical and lumbar x-rays on at least two time points, with a minimum interval of 18 months.

A study coordinator identified 354 patients who fulfilled the inclusion criteria. Their radiographs were anonymized and two experienced readers scored the spinal radiographs independently but in chronological order using the modified Stokes Ankylosing Spondylitis Spine Score (mSASSS). Radiographs with more than three missing vertebral corners (either cervical or lumbar) were excluded from the analysis. Starting from baseline, up to five follow-up sets, corresponding to 10 years of follow-up, were available for analysis. Total, cervical, and lumbar mSASSSs were assembled for each period. Researchers defined a change of two mSASSS units in two years as disease progression.

Researchers also collected information on other patient characteristics, including demographic, clinical (e.g. presence of extraspinal manifestations), laboratory (erythrocyte sedimentation rate and C-reactive protein [CRP]), and medication history. They used the following ASDAS cut-off scores for disease activity: inactive disease (<1.3), low disease activity (1.3–2.1), high disease activity (2.1–3.5), and very high disease activity (>3.5).

In patients receiving TNFi, Sari et al. calculated total exposure and exposure between each radiograph interval. In assessing the TNFi effect, they calculated the change and progression rates in the following two-year radiographic interval (e.g. in a patient receiving TNFi in the radiographic interval zero to two, change in mSASSS was calculated for the years two to four).

What Did Researchers Find?

After the exclusion of patients, primarily due to the presence of complete ankylosis at baseline, 350 patients were included in the study. Most of the patients (76%) were male, with an average age of 38.4 years. Patients' mean symptom duration at baseline was 14.9 years, 75.1% were positive for HLA-B27, and 46.6% had evidence of syndesmophytes.

Sari et al. note that, at the individual level, structural disease progression was not linear and was highly variable. At the group level, however, the mean mSASSS increased from 9.3 units at baseline to 17.7 units by the sixth year. They observed the same trend for cervical and lumbar segments separately, with more progression in the cervical spine.

Mean changes in total mSASSS between the radiographic intervals zero to two, two to four, and four to six years were 1.23, 1.47, and 1.52, units, respectively. The corresponding progression rates for the given periods were 24.3%, 26.9%, and 19.7%, respectively. When considering all periods, the average change in total

mSASSS over two years was 1.34 units. Overall, 24.3% of the group showed progression according to the defined criteria of at least 2 units in two years' time.

Sari et al. report that there were 230 patients (65.7%), with a mean age of 38 years and 78.7% of whom were male, who were treated with TNFi at some point during their follow-up. The mean duration of antitumor necrosis factor (anti-TNF) use was 5.2 years.

The researchers identified patients who were on an anti-TNF for a period of at least 12 months, then calculated the change in mSASSS and rate of progression over the following two-year interval. There were 67 patients who had been treated with TNFi before their baseline radiographic studies (i.e. change in mSASSS calculated in the year zero to two) and 80 patients on TNFi in the interval zero to two (i.e. change in mSASSS calculated in year two to four). The same approach was used for TNFi-naïve patients. Compared with conventional treatment, TNFi-treated patients had lower mSASSS change in the spinal segments in the subsequent two-year radiographic interval, but the differences were not statistically significant.

In a time-adjusted univariable linear analysis, male sex, presence of baseline syndesmophytes, baseline CRP, high and very high disease activity state according to ASDAS-CRP, and TNFi use were significantly predictive of mSASSS change over time. On the other hand, symptom duration, presence of HLA-B27, smoking status, BASFI, and clinical variables including presence of radiographic hip disease, uveitis, psoriasis, inflammatory bowel disease, and DMARD and NSAID use showed no associations with mSASSS progression.

In Cox multiple regression analysis, aside from disease duration and BASDAI, male sex, presence of baseline damage, and log CRP were predictive of radiographic progression. In a second model, after correcting for the aforementioned variables, total TNF use in years was an independent predictor of progression. In a third model, prior TNFi use was included and found not to be associated with progression.

What Do Researchers Add About Findings?

Sari et al. reiterate that their study demonstrated a progressive increase in the mean mSASSS on average 1.34 units over two years; 24.3% of the group progressed according to the criteria of mSASSS of equal to or greater than two units; male sex, baseline spinal damage, high disease activity, increased inflammatory markers, and treatment with TNFi were predictors of progression; and at least one-year use of TNFi therapy was associated with decreased progression rate in the next radiography interval and 20% reduction in the rate of spinal progression.

In this study, radiographic progression and related measures were evaluated based on total mSASSS. However, the researchers note that they did not analyze the development of syndesmophytes and bridging syndesmophytes separately, which can be considered to a limitation of the study. They also did not calculate an NSAID index, which prevented more sensitive analysis related to the use of these medications on radiographic progression.

They also acknowledge the limitations related to mSASSS scoring itself. In this scoring system only anterior vertebral corners of the cervical and lumbar spine are counted. As the thoracic segment, posterior vertebral corners and facet joints are not included, the true rate of radiographic progression is expected to be higher, they write. ■

As the thoracic segment, posterior vertebral corners and facet joints are not included, the true rate of radiographic progression is expected to be higher.

Disclosures: None declared.

Reference

Sari et al., Factors predictive of radiographic progression in ankylosing spondylitis [published online ahead of print November 1, 2019], *Arthritis Care & Research*; doi:10.1002/acr.24104.

Perspective

Physically Active RA Patients Are Less Likely to Report Cognitive Difficulties

Thirteen percent of the cohort met HHS guidelines for exercise, and 8.1% entered the cohort with a history of cardiovascular disease.

Researchers report that physical activity protects against the development of frequent symptoms of word finding, memory, and concentration difficulties in patients with rheumatoid arthritis (RA). (See Shadick et al., 2019.)

Nancy A. Shadick, MD, MPH, of Harvard Medical School and Brigham & Women's Hospital in Boston, Massachusetts, and colleagues also found that antitumor necrosis factor (anti-TNF) therapy was protective for the development of worsening memory. They also note that female sex predicted an increase in concentration difficulties, indicating the complex role that clinical, demographic, and psychosocial factors can play in how RA patients assess their cognitive function.

Shadick et al. cite studies that indicate individuals with inflammatory diseases, such as RA, have an increased prevalence of cognitive impairment. They state that measurable cognitive impairment is estimated to occur in 30% to 71% of patients with RA in several studies, whereas other studies have demonstrated an association between cognition and disease activity.

The researchers write that lifestyle factors, such as inactivity and obesity, contribute to cognitive decline in the general population. However, little is known about how these factors may affect individuals with conditions such as RA.

Patients and Methods

In their analysis, Shadick et al. used data from the Brigham and Women's Arthritis Rheumatoid Arthritis Sequential Study (BRASS), a large prospective, observational cohort. Enrollment for the registry began in March 2003 and is ongoing. Patients (18 years or older) with either new onset or established RA are recruited from the practices of rheumatologists. All diagnoses of RA are then verified according to either the American College of Rheumatology criteria or were the clinical opinion of a rheumatologist.

BRASS participants consent to annual visits, where updated information on demographics, disease activity, medication use, comorbidities, psychosocial variables, and functional status is obtained. Additionally, serum is collected yearly.

Shadick et al. followed up BRASS participants who completed at least two consecutive annual assessments for up to 10 years. The researchers collected clinical and functional questionnaire data from these participants, including yearly self-reported memory, concentration, and word-finding difficulties, graded from "never" to "often."

The researchers used generalized estimating equation models to examine the role of exercise (defined as those meeting the Department of Health and Human Services [HHS] physical activity guidelines of 75 minutes of vigorous or 150 minutes of moderate aerobic activity per week); body mass index; sleep; depression (using the Mental Health Index-Depression); Disease Activity Score (DAS)28 C-reactive protein (CRP) 3 score; and disease-modifying antirheumatic drug and corticosteroid use from the previous year as predictors of cognitive symptoms that progressed to "often" compared with the previous year.

Results

Shadick et al. report that of the 1219 participants entering the study, 127 (10.4%) described either poor memory, poor concentration, and/or word-finding difficulties as occurring often and were excluded from further analysis.

The remaining 1092 participants had a mean age of 56.5 years, were mostly female, and more than half had a college degree. The study cohort's mean follow-up duration was 5.4 years (range: 1–10.9 years). The majority of subjects were white.

The mean disease duration among all participants was 12.8 years. DAS28-CRP3 scores averaged 3.6, indicating moderate disease activity. Approximately 28% currently used corticosteroids and 38% were using anti-TNF therapy at study entry.

Thirteen percent of the cohort met HHS guidelines for exercise, and 8.1% entered the cohort with a history of cardiovascular disease. By the end of the 10-year study period, 11.4% reported at least one symptom as occurring often, compared with 10.4% at baseline.

Shadick et al. explain that, although trend lines demonstrated an increase in the frequency of all of the cognitive symptoms, only memory symptoms increased significantly over time, from 6.3% to 8.8% by study end. Rheumatoid arthritis patients who took TNF inhibitors and those who were active were less likely to report a worsening of memory.

Those who were active were also less likely to report word-finding difficulties occurring often. No other factor predicted an increase in reports of word-finding difficulties. Worsened concentration was more likely to be reported as "often" one year later among those RA patients who were female, had a higher DAS28-CRP3 score, or those who were not active.

The researchers also examined whether individuals who dropped out of the study (at a rate of approximately 5% per year) were more likely to have an increase in cognitive symptoms before dropout. They evaluated the frequency of each of the cognitive symptoms at a patient's last visit before dropping out and compared it with those who remained in the study. After analysis, they did not find that the subjects who dropped out had more cognitive symptoms of poor memory, word-finding difficulties, or trouble with concentration at multiple time points.

Strengths and Limitations

Shadick et al. write that their study is of value in that it provides longitudinal data on the frequency of cognitive symptoms in RA. Further, the researchers documented over 10 years that a variety of symptom symptoms occur in RA patients and that the frequency of memory difficulties increases over time. Additionally, although subjects in the study were highly educated and cognitively well enough to complete questionnaires, subjects who dropped out did not do so because they more likely had cognitive symptoms.

The researchers also note several study limitations. These include a lack of neurocognitive testing as a comparison of impairment; thus, the relationship of perceived cognitive function to actual cognitive function is unclear.

Although it did not appear that subjects who dropped out had an increased frequency of cognitive symptoms, suggesting that this may be a cause for attrition, a stable cohort study could have provided more accurate data on the prevalence of cognitive symptoms over time. "Having access to a parallel analysis of a normal control group would also clarify the comparative prevalence of these complaints," they write.

The researchers also note that while they queried subjects in the cognitive domains previously reported as impaired in RA patients, their questions do not come from a validated questionnaire. Therefore, they acknowledge that they do not have any data on validity, reliability, or sensitivity to change.

Although the researchers chose the outcome transitioning to symptoms described as "often" from either "never" or "sometimes," these transitions are not equivalent. In addition, while an increase in memory symptoms reported "often" appears to be small, many more subjects reported cognitive symptoms that "sometimes" affected them. These symptoms may also be clinically meaningful.

Shadick et al. suggest more testing in a randomized controlled setting. "Future studies should investigate the functional sequelae of these cognitive complaints, whether longitudinal follow-up of these individuals predicts an increase in cognitive impairment or dementia, and whether an increase in exercise may ward off these debilitating outcomes," they write. ■

Having access to a parallel analysis of a normal control group would also clarify the comparative prevalence of these complaints.

Disclosures: Shadick received consulting fees from Bristol-Myers Squibb. Researcher Michael E. Weinblatt, MD, received consulting fees from Abbvie, Amgen, Bristol-Myers Squibb, Corrona, Crescendo Bioscience, GlaxoSmithKline, Horizon, Lilly, Pfizer, Roche, Samsung, and Scipher; and owns stock options in Lycera, Canfite, Scipher, Vorso, and Inmedix.

Reference

Shadick N et al., The impact of exercise, lifestyle, and clinical factors on perceived cognitive function in patients with rheumatoid arthritis: Results from a prospective cohort study, *ACR Open Rheumatology*, 2019; 1(10):620–6. doi:10.1002/acr2.11088.

Trends and Innovations

Ultrasound Imaging Endpoints Fail to Provide Benefit in Patients With Early Rheumatoid Arthritis

According to researchers, incorporating ultrasound information in treatment decisions does not lead to reduced MRI inflammation or less structural damage in patients with early rheumatoid arthritis (RA). (See Sundin et al., 2019.)

Ulf Sundin, MD, of the Department of Rheumatology at Diakonhjemmet Hospital in

There was no significant difference in angle from baseline between the study arms at any time.

Oslo, Norway, and colleagues add that the systematic use of ultrasound does not provide benefit in treat-to-target follow-up of these patients. Sundin presented the researchers' findings at the American College of Rheumatology's 2019 Annual Meeting.

In an abstract of the presentation, Sundin et al. write that there is debate about whether treatment outcomes in early RA would be improved by targeting imaging remission, assessed by ultrasound or MRI, in addition to clinical remission.

They note that primary analyses within an earlier trial (i.e. the ARCTIC trial) did not show a beneficial effect of adding structured ultrasound assessment to a treat-to-target strategy. (See Haavardsholm et al., 2016.) However, ARCTIC reported a trend toward less radiographic progression in the ultrasound arm. In their new analysis of the ARCTIC trial data, Sundin et al. investigated whether an ultrasound-guided strategy would lead to reduced MRI inflammation or structural damage compared with a conventional treat-to-target strategy.

Analysis Strategy

The ARCTIC trial included 230 early RA patients who were naïve to disease-modifying antirheumatic drugs (DMARDs). Study patients, age 18 to 75 years, were randomized 1:1 to an ultrasound strategy targeting a Disease Activity Score (DAS) less than 1.6, no swollen joints, and no power-Doppler signal in any joint, or a conventional strategy targeting DAS less than 1.6 and no swollen joints.

The researchers explain that all patients were treated by the same DMARD escalation algorithm starting with methotrexate, then combination therapy methotrexate, sulfasalazine, and hydroxychloroquine, and then biologic DMARD. In the ultrasound arm, treatment was stepped up if indicated by the ultrasound score, overruling the DAS and swollen joint count.

MRI of the dominant hand was performed on six occasions and scored in chronological order by a blinded reader, according to the OMERACT RA MRI Scoring System. At baseline and at least during one follow-up visit, 218 patients (ultrasound n = 116, conventional n = 102) had MRI; all of these results were analyzed.

The researchers computed a combined inflammation by normalized summation of the synovitis, tenosynovitis, and bone marrow edema scores, and a combined damage score by normalized summation of the erosion and joint space narrowing scores. Mean change from baseline to each follow-up was estimated by a linear mixed model adjusted for baseline score, age, sex, and anti-CCP (anticyclic citrullinated peptide) status. Sundin et al. calculated the proportion of patients in each treatment arm with MRI erosive progression after two years, using the smallest detectable change (0.61) as cut-off.

Results Confirm Earlier Findings

Sundin et al. note that the groups were well balanced in terms of baseline characteristics, except that 72% of the ultrasound arms were women vs. 52% of those assigned to conventional target-to-treat. Patients mean age was approximately 51 years and mean time between symptom onset and enrollment was about seven months.

The researchers also report that there were no statistically significant baseline differences between the arms in either of the combined MRI scores. The mean combined MRI inflammation score decreased during the first year (one-year change in ultrasound arm −64.2, conventional arm −59.4), and maintained at the same level throughout the second year.

There was no significant difference in angle from baseline between the study arms at any time. The mean combined MRI damage score showed a small increase over time, without any significant difference between study arms. In the ultrasound arm, 39% of patients had MRI erosive progression vs. 33% in the conventional arm.

In a press conference at the meeting and reported in *MedPage Today*, study researcher Espen Haavardsholm, MD, PhD, of the University of Oslo, said that the ultrasound imaging merely added to treatment costs

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Snapshot

History of Abuse Tied to Worse Fibromyalgia

In a presentation at the American College of Rheumatology's 2019 Annual Meeting, researchers reported that stressors such as abuse have a wide range of detrimental effects on patients with fibromyalgia syndrome (FMS). (See Gota et al., 2019.)

Carmen Gota, MD, of the Cleveland Clinic in Cleveland, Ohio, and colleagues based their presentation on a study of 593 consecutive patients with FMS treated at the clinic.

In an abstract of their presentation, Gota et al. state that it has been proposed that the FMS phenotype is determined by genetic factors, lack of physical exercise, mood disorders, maladaptive pain responses, and both current and past stressors, including a history of abuse. "In this study, we examined the predictive role of a history of abuse on FMS severity measures, and the association between self-reported abuse and socioeconomic status, symptoms, psychiatric comorbidities, and disability," they write.

Enrollees

Gota et al. enrolled all consecutive patients clinically diagnosed with FMS who answered the question "Do you have a history of abuse?" and numerous other questions related to sociodemographics, comorbidities, and fibromyalgia signs and symptoms. Patients' characteristics were compared between those who reported a history of abuse and those who did not. The researchers then performed linear regression analysis to determine the predictive effect of a history of abuse.

The mean patient age was 43.8 years and 87% were female. A history of abuse—sexual, physical, or both—was reported by 223 (38%) patients. Fibromyalgia patients with a history of abuse had worse socioeconomical status as measured by higher percentages of single and divorced patients, lower education level, lack of private insurance and greater reliance on Medicare and Medicaid, lower employment rates, and higher disability compared with those without abuse.

A higher prevalence of personal and family history of psychiatric comorbidity was found in patients with a history of abuse. Substantially more patients with abuse histories were currently seeing psychiatrists (41.3% vs. 26.8%) or had done so previously (73.5% vs. 56.8%); past or present alcohol abuse (17.0% vs. 9.7%) was also markedly more common.

Results

Fibromyalgia severity scores, pain disability index, fibromyalgia impact questionnaire, and health assessment disability index were all higher in patients with FMS and a history abuse, compare to those without abuse.

These ranged from presence of tender points (56.5% vs. 44.3%) and generalized weakness (84.0% vs. 76.8%) to numbers of doctor visits in the past six months (11.6 vs. 8.0). Pain disability index scores averaged 6.0 for those with abuse histories vs. 5.1 for patients without.

The researchers also found that a linear regression model was strongly predictive of FMS severity from abuse, exercise, nonrefreshing sleep, current stressors, depression, and anxiety.

In their conclusion, Gota et al. recommend that clinicians inquire about abuse in all patients evaluated for FMS, as this may give more clarity to the nature and severity of the FMS presentation and prompt the need for psychological interventions. ■

The researchers also found that a linear regression model was strongly predictive of FMS severity from abuse, exercise, nonrefreshing sleep, current stressors, depression, and anxiety.

Disclosures: None declared.

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Patients With Early Rheumatoid Arthritis

Continued from page 32

without providing clinical value, at least when used to guide treatment. (See Gever, 2019.) But Haavardsholm emphasized that the findings do not mean ultrasound has no role in RA management. It may still be useful when clinical findings are inconclusive, for example. ■

Disclosures: None declared.

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Best of the Rest

Emergency Departments: Super-Expensive Back Care

Emergency departments (EDs) in the United States remain important venues for the evaluation and treatment of acute and chronic low back pain—and other pain conditions. However, they boost costs dramatically compared with urgent care centers and the offices of primary care physicians.

Refuges for the Poor, the Disadvantaged, the Disabled, and the Uninsured

Emergency departments in the United States are often the clinics of first and last resort for the poor, the disadvantaged, and the disabled. They all too often provide primary care for the uninsured and underinsured. And they serve as beacons for patients seeking opioids and other pain-killing drugs.

There are few reliable nationwide data on the exact number of back pain visits in emergency rooms. According to the Healthcare Cost and Utilization Project (HCUP), there were 137.8 million ED visits in the United States in 2014. And there has been a substantial increase in ED visits over the years, with the total number of visits increasing 14.8% between 2006 and 2014. (See HCUP, 2017.)

According to HCUP, the three leading medical reasons for ED visits in 2014 were abdominal pain, nonspecific chest pain, and back problems. The number of visits specifically attributed to back problems in 2014 was 4,158,800. However, this probably significantly underestimates the total number of visits among patients with back pain. There were over 10 million ED visits attributed to sprains and strains and superficial injuries, and several million attributed to mental health and substance-abuse disorders.

Emergency Room Care 12 Times More Expensive Than Primary Care

A recent report from UnitedHealth Group.com—the largest private health insurance provider in the United States—pointed out that visiting an ED is an exorbitantly expensive method of receiving care for common conditions. (See UnitedHealth Group, 2019.)

Among its clients, the 10 most common conditions treated in EDs are bronchitis, cough, dizziness, flu, headache, low back pain, nausea, sore throat, strep throat, and upper respiratory infections. UnitedHealth estimated that in 2018, there were a total of 46 million ED visits by individuals with private insurance. Of these, the health insurance company estimated that 18 million were completely avoidable. They could have been treated more efficiently and less expensively in primary care settings.

The cost discrepancies between ED and typical primary care settings are stunning. The average cost of treating the 10 abovementioned conditions in an ED was $2032. Similar care in an urgent care facility cost $193, and care provided in a primary care physician office tallied $167.

So average ED care for these 10 conditions is 10 times higher than that delivered in an urgent care center and 12 times higher than services provided in a primary care setting. According to UnitedHealth, the extra costs stem largely from hospital facility fees (which tallied an average $1069) and higher costs for diagnostic testing. Average costs for radiology, pathology, and laboratory tests averaged $335 at an ED, compared with $31 at a physician office.

So among the 18 million avoidable ED visits by privately insured individuals, there is the potential for $32 billion in savings—based on an average savings of $1800 per person. ■

Disclosures: None declared.

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Coming Soon

- No Evidence That Platelet-Rich Plasma Injections Improve Outcomes After Achilles Tendon Rupture
- Bisphosphonates Beneficial in Lessening Fracture risk in Women Treated for Breast Cancer
- Remote Ischemic Preconditioning Reduces Risk of Myocardial Injury in Hip Fracture

Lippincott's Bone and Joint Newsletter CME Quiz

To earn CME credit, you must read the CME articles and complete the quiz and evaluation assessment survey on the enclosed form, answering at least 70% of the quiz questions correctly. **Select the best answer and use a blue or black pen to completely fill in the corresponding space on the enclosed answer form.** Please indicate any name and address changes directly on the answer form. If your name and address do not appear on the answer form, please print that information in the blank space at the top left of the page. Make a photocopy of the completed answer form for your own files and send the original answer form to Wolters Kluwer, Continuing Education Department, PO Box 1543, Hagerstown, MD 21741-9914 by **February 28, 2022.** Only two entries will be considered for credit.

Online quiz instructions: To take the quiz online, **log on to your account at www.lbjnewsletter.com,** and click on the "CME" tab at the top of the page. Then click on "Access the CME activity for this newsletter," which will take you to the log-in page for **http://cme.lww.com**. Enter your ***username*** and ***password.*** Follow the instructions on the site. You may print your official certificate ***immediately***. Please note: Lippincott CME Institute ***will not*** mail certificates to online participants.

Online quizzes expire on the due date.

1. How many patients were included in the study conducted by Hani A. Alkhawajah, MSc, and Ali M. Alshami, MD?

A. 33
B. 36
C. 40
D. 46

2. More patients in both the treatment and sham groups had OA in the _____ knee and a KL grade of _____.

A. right, 2
B. right, 3
C. left, 2
D. left, 3

3. Alkhawajah and Alshami write that the results show significantly greater mean changes from baseline for knee flexion ROM in the treatment group compared with the sham group at follow-up visits one and two, with the mean between-group difference of _____ and _____, respectively.

A. 14.8, 7.4
B. 12.8, 8.3
C. 14.8, 7.4
D. 12.8, 7.4

4. Two days after intervention, no significant differences were found between the treatment and sham groups in PPT at the knee or knee extension ROM.

A. True
B. False

5. The researchers examined PPT on the affected knee and on the _____ to investigate any widespread changes in sensitivity at a distant site.

A. infraspinatus
B. latissima
C. middle deltoid
D. teres major

6. In the study conducted by Ismail Sari, MD, MSc, and colleagues, what percentage of patient had evidence of syndesmophytes at baseline?

A. 37.5%
B. 46.6%
C. 61.2%
D. 75.1%

7. Sari et al. note that, at the group level, the mean modified mSASSS increased from 9.3 units at baseline to _____ units by the sixth year.

A. 10.1
B. 12.2
C. 15.8
D. 17.7

8. Overall, _____ of the study patients showed progression according to the defined mSASSS criteria of at least 2 units in two years' time.

A. 19.7%
B. 24.3%
C. 26.9
D. 31.7%

9. How many study patients had been treated with TNFi before their baseline radiographic studies?

A. 67
B. 75
C. 80
D. 94

10. In a time-adjusted univariable linear analysis, male sex, presence of baseline syndesmophytes, high and very high disease activity, and TNFi use were among the factors significantly predictive of mSASSS change over time.

A. True
B. False

Bone and Joint in Brief

Insurers Failing to Cover Non-Drug Therapies

By many accounts, insurance companies have not embraced the recommendations of the 2017 American College of Physicians [ACP] guideline that nonpharmacologic therapies should be the first line of treatment for chronic back pain.

That guideline recommended greater use of multidisciplinary rehabilitation, acupuncture, mindfulness-based stress reduction (MBSR), tai chi, yoga, progressive relaxation, biofeedback, cognitive behavioral therapy (CBT), and spinal manipulation for chronic back pain.

Robert Bonakdar, MD, and colleagues used data from the 2017 Essential Health Benefits benchmark plans to study minimum insurance coverage levels of these treatments in 46 states.

"Analysis of the 2017 EHB benchmark plans that represent the minimum benefits required in all states demonstrated that, other than [spinal] manipulation, there was significant lack of coverage for nonpharmacological treatments recommended by the ACP guidelines for chronic LBP. Although state EHB coverage policies should reflect current evidence, our analysis reveals a disconnect between evidence-based recommendations and official guidelines."

There was a particularly notable lack of coverage for widely recommended behavioral health treatments such as cognitive behavioral therapy and biofeedback, which in many plans were only available for mental health diagnoses. (See *Global Advances in Health and Medicine*, 2019; 8: 2164956119855629.)

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MDs Still Coprescribing Opioids and Benzodiazepines

The United States has seen a significant dip in the rate of opioid prescription for chronic pain in the wake of the Centers for Disease Control and Prevention (CDC) guideline on prescribing opioids for chronic pain (www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm). But what about the impact of this guideline on the coprescription of opioids and benzodiazepines—a potentially lethal combination that has drawn warnings across medical settings?

Molly W. Jeffery, PhD, and colleagues performed a retrospective cohort study using claims data obtained from a US national database of medical and pharmacy claims for 3,598,322 adult commercially insured patients and 1,299,142 Medicare Advantage (MA) beneficiaries with no recent history of cancer, sickle cell disease, or hospice care who ever used prescribed opioids from January 1, 2014, through March 31, 2018.

They found only small (but statistically significant) decreases in the coprescription of opioids and benzodiazepines in the two years after the guideline.

"Co-prescription of opioids and benzodiazepines was common among this sample of commercially insured and MA beneficiaries, both before and after the release of the CDC guidelines," according to Jeffery et al. "After guideline release, the extent of co-prescribing decreased by a modest amount in people using opioids long term, but not those using opioids short term. There was no change associated with the guidelines in the intensity of coprescribing for any population. Future studies focused on identifying patterns of physician response to these guidelines may provide insight into who was affected by the guideline release on coprescription of opioids and benzodiazepines."

So why is this important? As the authors point out, "the risk of overdose in people taking both opioids and benzodiazepines increases with opioid dose." (See *JAMA Network Open*, 2019; 2(8): e198325. doi:10.1001/jamanetworkopen.2019.8325.)

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Reducing the Use of Unvalidated Diagnoses and Disease Labels

The spinal medicine field stands out for the excessive use of unvalidated disease labels and unvalidated diagnostic methods. Some common diagnoses—from sacroiliac joint pain to degenerative disc disease; from piriformis syndrome to myofascial pain disorders—have never been validated scientifically. And diagnostic guesswork does not portend well for patients or healthcare systems.

The entire medical field is making a major effort to reduce the level of medical errors. The use of unvalidated disease labels and diagnostic methods obviously raises the risk of medical errors, potentially compromising patient outcomes and heightening risk of malpractice litigation for physicians.

The best way of reining in the use of unvalidated diagnostic labels would be through more definitive research. Since there is no "gold standard" for many of the most controversial diagnoses, the best way of validating them would be through the performance of large, high-quality, independently financed, randomized controlled trials—to see whether these diagnoses and labels improve patient outcomes.

Another way of limiting the use of unvalidated diagnoses might be to have groups of physicians (or other healthcare providers) offer diagnostic possibilities rather than single providers.

Harvard researcher Michael Barnett, MD, et al. recently analyzed data from the Human Diagnosis Project (Human Dx), a large online database through which physicians and medical trainees solve user-submitted cases.

They tested the accuracy of diagnoses from individual physicians, groups of two physicians, and groups of multiple physicians in a variety of medical conditions.

The study found that multiple physicians outperformed individual MDs even in groups as small as two (62.5% vs. 75.1% accuracy), with accuracy increasing up to groups of nine (85.6% accuracy) across a broad range of medical cases and common symptoms such as chest pain or fever. "The magnitude of the increased accuracy with even small teams was surprising," said Barnett in an accompanying statement from Harvard." And nonspecialist groups routinely outperformed specialists.

This approach would pose a distinctive challenge in the back pain area—where the most accurate diagnosis in most cases would be no diagnosis.(See *JAMA Network Open*, 2019; 2(3): e190096.)

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