Risk of Myocardial Infarction Increased With Systemic Sclerosis

Written by Wayne Kuznar

Evidence of macrovascular involvement and premature atherosclerosis in patients with systemic sclerosis (SSc) has been emerging. The risk of myocardial infarction (MI) was found to be increased in patients with incident SSc in a large population-based study discussed by J. Antonio Avina-Zubieta, MD, PhD, University of British Columbia, Vancouver, Canada.

In SSc, cardiovascular disease is the leading non-SSc cause of death [Tyndall AJ et al *BMJ* 2010]. Previous studies in which a link between SSc and premature atherosclerosis was discovered did not adjust for medication use and other relevant confounders or they relied on selected populations, obscuring the true risk of MI in this population [Nordin A et al. *Arthritis Res Ther* 2013; Ngian GS et al. *Ann Rheum Dis* 2012].

Using administrative health data from all 4.7 million residents of British Columbia, Canada, Prof. Avina-Zubieta and colleagues sought to estimate the risk of MI in patients with incident SSc at the general population level and to assess time trends in the risk of MI in relation to the onset of SSc. Some 1245 patients with SSc were identified from the database. Each patient was matched to 10 controls from the general population based on birth year, sex, and calendar year of exposure, for a total of 12,678 controls. The risk of incident MI in the SSc cohort relative to the general population was adjusted for age, sex, and comorbidities. The mean Charlson comorbidity index was 1.1 in the SSc cohort and 0.3 in the matched controls. At the time of SSc diagnosis, mean patient age was ~53 years. Consistent with the disposition of SSc, >80% of the study population were women.

Over an average follow-up of 3.5 years, incident MI occurred in 89 of the SSc group and in 289 controls, for an incidence rate of 20.2 per 1000 person-years among the SSc cohort and 5.3 per 1000 person-years among the controls. Using a multivariable adjusted model, the relative risk (RR) of incident MI was 4.1 (95% CI, 3.1 to 5.4) in the SSc cohort compared with the general population. The increased adjusted RR of MI in the SSc cohort remained significant on sensitivity analyses adjusting for potential unmeasured confounders (Table1).

When analyzed according to the follow-up period, the age- and sex-adjusted RR of MI among patients with SSc was highest within the first year of follow-up, at 8.2 (95% CI, 5.3 to 12.4; Table 2).

The increased RR of MI among patients with SSc was attenuated with longer duration of follow-up, to an age- and sex-adjusted RR of 3.1 during follow-up Years 1 through 5, and 1.4 with >5 years of follow-up.

Table 1. Sensitivity Analysis, Adjusting for Potential Unmeasured Confounders

Hypothetical Prevalence	Hypothetical Odds Ratio	MI Risk of SSc Adjusted RR (95% CI)
10%	1.3	4.1 (3.1–5.3)
10%	3.0	3.6 (2.7–4.7)
20%	1.3	4.0 (3.1–5.3)
20%	3.0	3.1 (2.3–4.1)

Table 2. Risk of MI According to Follow-up Period

Age-Sex Adjusted RR	< 1 Year of Follow-Up	1–5 Years of Follow-Up	> 5 Years of Follow-Up
RR (95% CI)	8.2 (5.3–12.4)	3.1 (2.1–4.4)	1.4 (0.9–3.4)

When analyzed according to age, the adjusted RR of MI in SSc patients was highest in the group aged 45 to 59 years old (RR, 7.4; 95% CI, 3.5 to 15.7 compared with the group aged <45 years).

The findings support increased vigilance in cardiovascular disease prevention, surveillance, and risk modification in patients with SSc, said Prof. Avina-Zubieta.

Patellofemoral Brace Reduces Pain, Bone Marrow Lesion Volume in Knee Osteoarthritis

Written by Wayne Kuznar

Bone marrow lesions may represent a viable target in the treatment of osteoarthritis (OA). David T. Felson, MD, University of Manchester, Manchester, United Kingdom, described a randomized clinical trial in which a patellofemoral (PF) knee brace reduced both the volume of bone marrow lesions in the PF joint and PF-related knee pain.

Bone marrow lesions represent lesions in subchondral bone caused in part by focal stress in the OA knee joint. Focal contact stress across the joint during weight bearing can cause bone trauma that leads to bone marrow lesions. Bone marrow lesions predict later cartilage loss at the same anatomic location and correlate with pain and pain severity. For these reasons, and because bone marrow lesion volumes fluctuate substantially in as little as 6 weeks [Felson DT et al. *Osteoarthritis Cartilage* 2012], bone marrow lesion volume appears to be a good short-term structural outcome measure in OA trials, said Prof. Felson. PF bracing can increase contact area in the PF joint [Powers CM et al. *Clin J Sports Med* 2004], with the potential to reduce contact stress and shrink bone marrow lesions, he said, in explaining the rationale for a study of bracing in the disease.

Patients aged 40 to 70 old (n=126) with daily knee pain ≥40 mm on a 1- to 100-mm visual analog scale (VAS) during a PF activity (eg, climbing or descending stairs, kneeling, prolonged sitting or squatting) for 3 months, a radiographic Kellgren-Lawrence Grade 2 or worse in the PF joint or PF OA worse than tibiofemoral disease, and confirmed PF joint tenderness on clinical examination were randomized to 6 weeks of treatment with a PF brace or no treatment.

The primary symptom outcome was the change in pain as measured on the VAS during nominated aggravating activity. The primary structural outcome was bone marrow lesion volume in the PF joint as assessed on contrast-enhanced magnetic resonance imaging. Tibiofemoral bone marrow lesion volume served as an untreated control region. In the treatment group, braces were worn for a mean of 7.35 hours per day. Five patients in the bracing group and one in the no-treatment group withdrew from the trial before completion.

In the bracing group, pain on the VAS during the nominating activity decreased by 18.16 mm, compared with a 1.29-mm reduction in the no-treatment group (p<0.001). Improvements in the Knee Injury and Osteoarthritis Outcome Score pain subscale and activities of daily living subscale were also significantly superior in the bracing group (p=0.02 for each vs no treatment; Table 1).

Table 1. Randomized Trial Results

Variable	No Brace Group	Brace Group	Between Groups Difference	
Change @ 6 weeks	Mean change (95% CI)	Mean change (95% CI)	Mean difference in change (95% CI)	p
Primary Symptom Outcome: Nominated VAS (0–100)	–1.29 (–6.39, 3.80)	–18.16 (–23.88, –12.44)	16.87 (9.30, 24.43)	<0.001
Primary Structural Outcome: BML Volume in PF joint (in mm^3)	102.66 (–292.80, 498.12)	–554.92 (–964.02, –145.82)	–657.58 (–1226.57, –88.59)	0.02
Secondary Structural Outcome: BML Volume in TF Joint (in mm^3)	1.79 (–492.67, 496.26)	198.08 (–313.44, 709.60)	196.29 (–515.15, 907.73)	0.59

BML=bone marrow lesion; PF=patellofemoral; VAS=visual analog scale.

PF bone marrow lesion volume decreased by a mean of 554.92 mm^3 in the bracing group, compared with a mean increase of 102.66 mm^3 in the no-treatment group (p=0.02). There was no significant difference between groups in the mean change in tibiofemoral bone marrow lesion volume or in synovitis volume.

The reduction in the size of bone marrow lesion volumes in the PF but not the tibiofemoral joint is consistent with a compartment-specific effect of the brace, concluded Prof. Felson.

Higher Incremental Cost-Effectiveness Ratios Seen With Biologics in the TEAR Trial

Written by Muriel Cunningham

As additional treatments have been approved for rheumatoid arthritis (RA), researchers have used clinical trial data to analyze the cost effectiveness of these new drugs. Since 1998, more than 30 cost-effectiveness analyses (CEAs) have been conducted, with highly variable results. Kaleb Michaud, PhD, National Data Bank for Rheumatic Diseases and the University of Nebraska Medical Center, Omaha, Nebraska, USA, presented the CEA results of patient-level data from the Treatment of Early Aggressive Rheumatoid Arthritis trial [TEAR; NCT00259610], a large, randomized, double-blind clinical study.

The objective of the TEAR trial was to determine the best strategy for treating patients with early RA [Moreland LW et al. *Arthritis Rheum* 2012]. Eligible patients were adults who had RA for <3 years, limited exposure to disease-modifying antirheumatic drugs, seropositivity or erosions, and at least 4 swollen and 4 tender joints on the 28-joint count. At baseline, patients were randomized to 1 of 4 treatments:

1. immediate treatment with methotrexate (MTX) plus etanercept (IE)
2. immediate triple therapy (IT) consisting of MTX plus sulfasalazine plus hydroxychloroquine
3. MTX monotherapy with a step-up to MTX plus etanercept (SE)
4. MTX monotherapy with a step-up to triple therapy (ST)

Step-up occurred at Week 24 in patients with active disease, defined as Disease Activity Score in 28 joints using the erythrocyte sedimentation rate (DAS28-ESR) ≥3.2. Patients were followed for up to 2 years. The primary outcome measure was the mean DAS28-ESR score from Weeks 48 to 102.

A total of 755 patients were randomized in the trial. At baseline, participants had a mean duration of RA of 3.6 months (range, 0 to 41.4), a mean (standard deviation [SD]) DAS28 of 5.8 (1.1), and an average of 14.3 (6.8) painful joints with 12.8 (6.0) swollen joints. At the Week 24 time point, both immediate treatment groups had significant decreases in DAS28 compared with the SE and ST groups (p<0.0001). However, in the primary analysis of results from Weeks 48 to 102 the four treatment arms had comparable improvement (p=0.55) [Moreland LW et al. *Arthritis Rheum* 2012].

A Markov simulation model with a societal perspective was utilized to estimate the costs and quality-adjusted life years (QALYs). The following inputs