

Smoking–Joint Erosion Link Questioned in RA

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Cigarette smoking does not appear to negatively influence the progression of radiographic damage in rheumatoid arthritis, a prospective study has shown. In fact, radiographic progression of disease was significantly less among heavy smokers than among moderate smokers and nonsmokers in the longitudinal observational investigation of rheumatoid arthritis patients.

Because smoking is an established risk factor for the development of rheumatoid arthritis (RA), investigators with the Swiss Clinical Quality Management (SCQM) project for RA—a population-based registry designed to monitor disease activity—hypothesized that smoking would exacerbate disease progression. Yet, a comparison of smokers and nonsmokers from the registry showed that radiographic joint damage progressed at an equivalent rate in both groups, reported Dr. Axel Finckh of the Geneva University Hospital and colleagues. “Furthermore, we observed a significant trend for reduced radiographic progression and generally more favorable functional scores among heavy smokers, suggesting that cigarette smoke does not accelerate RA disease progress,” the authors wrote (*Ann. Rheum. Dis.* 2007 [Epub doi: 10.1136/ard.2006.065060]).

The SCQM system requests at least yearly assessments of disease activity, radiographic damage, antirheumatic therapy, sociodemographic factors, and lifestyle characteristics, including cigarette-smoking history. The cohort for the current study included 2,004 registry patients for whom cigarette smoking history and at least two consecutive sets of radiographs were available.

Progression of radiographic joint damage, as measured by changes from baseline in radiographic damage scores, was the study’s primary outcome, and the progression of functional disability as measured by change from baseline in the Stanford Health Assessment Questionnaire (HAQ) disability index was the secondary outcome. The outcome analyses included data collected between March 1996 and November 2005.

Of the 2,004 patients eligible for study inclusion, 545 were current smokers consuming, on average 16 cigarettes per day, with a mean past smoking exposure of 20.6 pack-years. Of the 545 smokers, 55 were characterized as heavy smokers with a reported average intake of 33 cigarettes per day and 27.7 years of smoking and 489 met the criteria for moderate smokers, with an average of 13 cigarettes per day and 24.2 years of smoking.

The smokers were predominantly younger males with shorter disease durations and less joint erosions at baseline, the authors reported. There were no significant differences between smokers and nonsmokers with respect to other important risk factors for disease progression, such as rheumatoid factor seropositivity, antirheumatic therapy, glucocorticoid use, functional status, and educational level.

In both crude and adjusted models of radiographic progression, there was no evidence for more rapid progression among smokers than nonsmokers, according to the authors. “In the fully adjusted model, radiographic damage progressed by 2.79% at 2 years in nonsmokers compared to 2.51% in smokers.”

There was an inverse dose-response effect for heavy smokers, compared with moderate smokers and nonsmokers. “Specifically, radiographic erosions evolved significantly more slowly in heavy smokers [average 1.21% in 2 years] com-

pared to nonsmokers [2.86%], whereas erosive disease in moderate smokers [2.71%] progressed at a rate similar to that in nonsmokers,” the authors reported.

A sensitivity analysis examining current smoking exposure as a continuous variable and with an alternative categorization demonstrated a similar inverse dose-response effect as did analyses restricted to subgroups of patients with rheumatoid factor–positive disease, male patients, and patients treated with tumor necrosis factor inhibitors, according to the authors, who noted that “the strongest predictors of radiographic damage progression were disease duration, baseline radiographic damage, and rheumatoid factor.”

With respect to functional disability, “overall, mean HAQ scores tended to improve somewhat during the first years of the observation,” the authors reported, linking the improvements to the initiation of new antirheumatic therapies at the time of enrollment.

As for functional capacity relative to smoking status, “the evolution of HAQ scores did not differ significantly between smokers and nonsmokers,” the authors wrote, nor was there a significant inverse

dose-response effect in heavy smokers, compared with moderate smokers and nonsmokers. High baseline HAQ score, female gender, rheumatoid factor, and lower educational levels were strong predictors for functional disability.

The results of this study suggest, “that smoking may be more important in the initiation of RA than in the perpetuation of the erosive disease process,” the authors noted.

Previous studies have shown some protective effects of smoking in several inflammatory diseases, and nicotine specifically has been shown to have anti-inflammatory properties, which may support the current findings in RA patients, the authors wrote. Smoking or nicotine exposure should not be a therapeutic consideration. “Global health risks associated with smoking are much greater than those potential benefits,” they said.

The exclusion from the study of registry patients with no radiographic follow-up could potentially contribute to a selection bias, although there is no indication that the missing radiographic follow-up was associated with smoking and more severe radiographic progression, the authors wrote.

X-rays showed that RA progressed about 3% over 2 years in smokers and nonsmokers alike; the progression rate averaged 1% in heavy smokers.

Etoricoxib Caused Fewer GI Events Than Diclofenac in Arthritis Patients

The cyclooxygenase-2 inhibitor etoricoxib caused fewer clinically important upper GI events than the traditional NSAID diclofenac in a large study designed to reflect the real-world experience of treating osteoarthritis and rheumatoid arthritis.

The Multinational Etoricoxib and Diclofenac Arthritis Long-Term Program (MEDAL) pooled the results of three large randomized clinical trials involving nearly 35,000 patients treated at 1,380 sites in 46 countries. Unlike in most clinical trials, subjects in the MEDAL program were encouraged to use proton pump inhibitor therapy to protect against GI damage, and those at cardiovascular risk were encouraged to add low-dose aspirin to their regimens, investigators reported.

Etoricoxib and diclofenac had similar efficacy against arthritis. Upper GI events, primarily uncomplicated ulcers, were significantly less frequent with etoricoxib than with diclofenac. There was no difference between the two drugs in rates of more serious complicated events, reported Dr. Loren Laine and associates in the MEDAL program (*Lancet* 2007;369:465-73).

Significantly fewer patients taking etoricoxib discontinued treatment because of dyspepsia, compared with those taking diclofenac.

This study was sponsored by Merck Research Laboratories, which conducted the statistical analyses and was involved in data analysis, safety monitoring, and reporting.

—Mary Ann Moon

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