Psoriasis and Risk of Myocardial Infarction

To the Editor: The prospective cohort study by Dr Gelfand and colleagues found that patients with psoriasis had an increased adjusted relative risk for myocardial infarction (MI). In their conclusion, the authors state that psoriasis may confer an independent risk of MI, which is greater in young patients with severe psoriasis. Analyses were performed using conditional logistic regression, adjusted for age, sex, and other major cardiovascular risk factors (hypertension, diabetes, history of MI, hyperlipidemia, smoking, and body mass index).

Other studies have demonstrated the association of psoriasis with severe psychological morbidity, in particular with depression. Devrimci-Ozguven et al demonstrated that patients with psoriasis had significantly higher degrees of depression and more body cathexis problems than did patients with psoriasis had significantly higher degrees of disease. Moreover, disease-related psychological stress has been associated with an increased risk for coronary artery disease.

It therefore seems that several influencing and confounding factors, such as depression, psychological disorders, and disease-related stress, could have biased the findings of Gelfand et al. We believe that adjustment for these factors would result in a more accurate estimation of the actual additional risk of MI in patients with psoriasis.

Alevizos Alevizos, MD
alevisos@gmail.com
Department of General Practice and Family Medicine
Health Centre of Vyronas
Athens, Greece

Financial Disclosures: None reported.


To the Editor: Dr Gelfand and colleagues studied the risk of MI in patients with psoriasis. The authors found that psoriasis is an independent risk factor for MI, especially for young patients with severe disease, and hypothesized that exaggerated immune activity could lead to a higher risk for MI by linking Th1 diseases to atherosclerosis and coronary artery disease. However, the exact mechanism by which Th1-mediated diseases predispose patients to vascular disease remains unclear.

The study by Wakkee et al reviewed the mechanisms by which systemic inflammation results in an adverse effect on the cardiovascular risk profile in patients with psoriasis: oxidative stress, endothelial cell dysfunction, hyperhomocysteinemia, and platelet adhesion, together with well-known risk factors for MI such as hypertension and dyslipidemia. We have observed a higher prevalence of hyperhomocysteinemia in patients with psoriasis compared with healthy patients, and an inverse association between severity of psoriasis and plasma folate acid levels. Folate deficiency in patients with psoriasis could be due to an increased loss of folate acid (by rapid skin turnover) and reduced absorption from the intestine.

Hyperhomocysteinemia is an independent risk factor for coronary artery disease, stroke, and peripheral vascular disease. We have also found that hyperhomocysteinemia is directly associated with the Psoriasis Area and Severity Index, suggesting a potential explanation for the higher risk
for MI in patients with severe psoriasis that was found by Gelfand et al.

Mario Malerba, MD  
malerba@master.cci.unibs.it  
Department of Internal Medicine  
University of Brescia  
Brescia, Italy

Paolo Gisondi, MD  
Biomedical and Surgical Sciences  
University of Verona  
Verona, Italy

Alessandro Radaeli, MD  
Department of Internal Medicine  
University of Brescia

Gianpiero Girolomoni, MD  
Biomedical and Surgical Sciences  
University of Verona

Financial Disclosures: None reported.


To the Editor: Psoriasis is considered an immune-mediated inflammatory disease, such as rheumatoid arthritis or Crohn disease. Dr Gelfand and colleagues1 found psoriasis to be an independent risk factor for MI. This is consistent with similar findings in other immune-mediated inflammatory diseases, such as rheumatoid arthritis,2 and supports the systemic nature of the underlying inflammation. Atherosclerosis is regarded as an inflammatory process as well.3 The cascade of events that ultimately results in formation of atherosclerotic plaques begins with infiltration and retention of low-density lipoprotein and activation of endothelial cells. Platelets are the first blood cells to arrive at the scene, likely contributing to further endothelial activation and subsequent formation of an inflammatory cell infiltrate in the forming plaque.4

The notions of a crucial role of platelets in the formation of atherosclerotic plaques and psoriasis as a systemic inflammatory disease resulting in higher cardiovascular morbidity are supported by the finding that platelet activation, monitored by expression of adhesion molecule P-selectin, correlated with Psoriasis Area and Severity Index (a measure of disease severity); these activated platelets help to facilitate leukocyte extravasation.5 Contribution of P-selectin–expressing platelets to atherosclerosis has been shown in animal models in which interactions of activated platelets with monocytes and endothelium led to delivery of platelet-derived CCL5 and CXCL4, increased leukocyte binding to vascular cell adhesion molecule 1, and exacerbation of atherosclerosis.6 This may also occur in patients to a clinically relevant degree: analysis of coronary artery calcification as early evidence for cardiovascular disease showed that patients with psoriasis exhibited calcifications with significantly more frequency and severity compared with controls matched for all major known risk factors.6

Experimental evidence therefore supports the notion of psoriasis being a disease of systemic inflammation that in turn contributes to the comorbidity of MI. Further research may yield information on which to base recommendations for cardiac screening at an early stage. In addition, it will be interesting to investigate the effects of continuous anti-inflammatory therapies for psoriasis on the development of comorbidities.

Ralf J. Ludwig, MD  
r.ludwig@em.uni-frankfurt.de  
Wolf-Henning Boehncke, MD  
Department of Dermatology  
Clinic of the Johann Wolfgang Goethe University  
Frankfurt am Main, Germany

Financial Disclosures: None reported.

In Reply: Dr Alevizos and colleagues suggest that the association of psoriasis and MI that we observed may be due to psoriasis-associated depression. Although this possibility requires further research to fully address, confounding by depression is unlikely to explain our results.

First, the prevalence of severe depression in patients with psoriasis and the magnitude of this potential association have not been well established in large, broadly representative population-based studies. The authors refer to a small, specialty clinic–based study that demonstrated that patients hospitalized for psoriasis were more likely to be depressed, based on Beck Depression Inventory scores (mean score in mild-moderate depression range), compared with healthy controls.1 The correlation between depression scores and psoriasis severity was weak (r = 0.29) and it is unclear if these results would generalize to the broader population of patients with psoriasis we studied. Alevizos et al also refer to 1 large study of patients with psoriasis from Italy that found that patients with psoriasis had an average Center for Epidemiologic Studies-Depression scale score of 26.1, which is a borderline score between mild and major depression.2 This study was limited by a low response rate (48%), lack
of a control group, and lack of clarity as to the source population used to identify patients with psoriasis.

Second, studies of depression as an independent risk factor for MI have been inconsistent. Studies that have been positive have found only a modest association with depression (an approximately 1.5–2.0 adjusted relative risk for the subsequent development of coronary artery disease), making it unlikely that depression is a strong enough confounder to explain our results. Finally, there is no indication that the relative risk of MI due to depression varies by age, as was observed in our study.

Dr Malerba and colleagues suggest that the increased risk of MI we found may be due to elevated plasma homocysteine in patients with psoriasis. The increase in homocysteine levels in patients with psoriasis observed by Malerba et al was modest (5.6 μmol/L) and the correlation of homocysteine level with psoriasis severity was weak (r=0.30); therefore, homocysteine is unlikely to substantially explain our observations.

Drs Ludwig and Boehncke have shown that psoriasis may be an independent risk factor for coronary artery calcification, which provides important confirmatory data for our results. Furthermore, they provide data that psoriasis severity is strongly correlated with P-selectin (r=0.83, P<.001), which is expressed on activated platelets and has been implicated in the pathogenesis of atherosclerosis in animal models. Further studies will be necessary to determine the mechanism by which psoriasis confers an independent risk of coronary artery disease and MI, and how best to minimize this risk.

Joel M. Gelfand, MD, MSCE
Joel.gelfand@uphs.upenn.edu
Department of Dermatology
University of Pennsylvania
Philadelphia
Shanu Kohli Kurd, MHS
Jefferson Medical College
Philadelphia, Pa
Andrea L. Neumann, MD
Department of Dermatology
Albert Einstein School of Medicine
New York, NY
Daniel B. Shin, BA
David J. Margolis, MD, PhD
Department of Dermatology
University of Pennsylvania
Andrea B. Troxel, ScD
Center for Clinical Epidemiology and Biostatistics
University of Pennsylvania

Financial Disclosures: Dr Gelfand reported receiving grant support (grants to the Trustees of the University of Pennsylvania) from Biogen Idec, AMGEN, Centocor, and Astellas; and consulting agreements with Genentech, Novartis, Warner-Chilcott, AMGEN, Wyeth, Biogen Idec, and Centocor. Dr Margolis reported receiving grant support (grant to the Trustees of the University of Pennsylvania) from Biogen Idec and is also on the data and safety monitoring boards for Abbott, Biogen Idec (which is now Astellas), and Centocor, who have studies investigating drugs for psoriasis. None of the other authors reported financial disclosures.

©2007 American Medical Association. All rights reserved.


RESEARCH LETTER

Prevalence of Overweight Among High School Football Linemen

To the Editor: Obesity among professional football players has been documented, with recommendations that it be further investigated among amateur athletes. Adolescent overweight is related to unfavorable cardiovascular disease risk factors and predicts overweight in young adulthood. We therefore examined the prevalence of overweight and obesity in high school football linemen, the players who tend to be heaviest.

Methods. Data were obtained on 3683 linemen from publicly available varsity rosters, including 100% of the players from 251 (69%) of the 364 Iowa high school teams during fall 2005. At least 2 teams from each of Iowa’s 47 districts were included, making the sample likely to be representative of all players. Data for height, weight, and year in school were taken as reported on the roster. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Linemen were classified as at risk of overweight (BMI ≥85th and <95th percentile) or overweight (BMI ≥95th percentile) based on age-specific percentiles using the 2000 US Centers for Disease Control and Prevention growth charts. Prevalence was compared to 2003-2004 National Health and Nutrition Examination Survey (NHANES) data for boys aged 12 to 19 years (the group most closely matching the players’ ages).

Frequencies were also calculated for the percentage of players who would be classified as adult class II (BMI ≥35) and class III (BMI ≥40) obesity. Age (14.5 to 18.5 years) was assumed from the mid-age at each grade level (9 through 12); analyses using quarter-year ages did not change the results. Iowa high school football is categorized into classes based on school enrollment. These classes in decreasing enrollment size are 4A, 3A, 2A, 1A,