Depression Is Associated with an Increased Risk of Psoriatic Arthritis among Patients with Psoriasis: A Population-Based Study

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Ryan T. Lewinson[1,2], Isabelle A. Vallerand[1,3], Mark W. Lowerison[3], Laurie M. Parsons[4], Alexandra D. Frolkis[1,3], Gilaad G. Kaplan[3,5], Andrew G.M. Bulloch[3,6,7], Mark G. Swain[5], Scott B. Patten[3,6] and Cheryl Barnabe[3,8]

The factors that contribute to the development of psoriatic arthritis (PsA) among patients with psoriasis are not well known; however, systemic inflammation is believed to be important. On the basis of recent laboratory work demonstrating that major depressive disorder (MDD) is associated with increased systemic inflammation, we hypothesized that patients with psoriasis who develop MDD are at increased risk of subsequently developing PsA. We utilized The Health Improvement Network, a primary care medical records database, to identify 73,447 individuals with psoriasis. Patients were followed up to 25 years until the development of the primary outcome of PsA or the censor date. The exposure of interest was the development of MDD. Cox proportional-hazards models showed that patients with psoriasis who developed MDD were at significantly increased risk of subsequently developing PsA compared with patients who did not develop MDD, even after accounting for numerous covariates (hazard ratio 1.37, 95% confidence interval 1.05−1.80, $P = 0.021$). This result was maintained through numerous sensitivity analyses. These data support the hypothesis that MDD increases the risk of developing PsA among patients with psoriasis, suggesting a need for heightened prevention and management of MDD in patients with psoriasis.

INTRODUCTION

Psoriasis is an inflammatory skin disease characterized by pruritic, erythematous, scaling papules, and plaques (Nestle et al., 2009). Approximately 8.5% of patients with psoriasis have psoriatic arthritis (PsA) (Ogdie et al., 2013), which is characterized by psoriasis plus inflammation of joints and other extra-articular manifestations. Although many studies have highlighted potential risk factors for PsA development, such as psoriasis severity (Reich et al., 2009), obesity (Love et al., 2012), alcohol use (Wu et al., 2015), and smoking (Li et al., 2012), the pathophysiologic mechanisms that contribute to the development of PsA among patients with psoriasis are not well known.

Given the similar genetic and inflammatory associations between psoriasis and PsA (Huffmeier et al., 2010; Veale et al., 2005), immune activation to external stressors is a proposed mechanism (Barnas and Ritchlin, 2015). It is believed that elevated systemic inflammation contributes to more severe psoriatic disease (Dowlatshahi et al., 2013), suggesting the possibility of a particular "threshold" that is crossed leading to manifestations beyond skin disease.

Recently, it has been demonstrated that individuals with major depressive disorder (MDD) have elevated serum inflammatory markers such as tumor necrosis factor-α (Dowlati et al., 2010), and that increased levels of tumor necrosis factor-α are associated with reduced activity of serotonin transporters (Krishnadas et al., 2016) relevant to MDD pathophysiology. Also, both psoriasis and PsA are associated with MDD (Dalgard et al., 2015; Dommasch et al., 2015; Kurd et al., 2010), commonly attributed to the physical and/or cosmetic disability incurred by psoriatic disease. The concept of high levels of systemic inflammation driving psoriatic disease severity (Dowlatshahi et al., 2013) warrants an investigation on whether the presence of MDD may in fact predispose to PsA in patients with psoriasis. In addition, MDD is known to be associated with poor health behaviors such as unhealthy diet and physical inactivity (Trudel-Fitzgerald et al., 2016), which could also contribute toward the development of PsA. Population-based studies are ideal to address the role of MDD in PsA development, given their large and nationally representative samples, lengthy follow-up times, and ability to determine risk of incident PsA given an MDD exposure in patients with psoriasis.

[1]Leaders in Medicine Program, Cumming School of Medicine, Calgary, Alberta, Canada; [2]Biomedical Engineering Program, Schulich School of Engineering, Calgary, Alberta, Canada; [3]Department of Community Health Sciences, Cumming School of Medicine, Calgary, Alberta, Canada; [4]Division of Dermatology, Cumming School of Medicine, Calgary, Alberta, Canada; [5]Division of Gastroenterology, Cumming School of Medicine, Calgary, Alberta, Canada; [6]Department of Psychiatry, Cumming School of Medicine, Calgary, Alberta, Canada; [7]Department of Physiology and Pharmacology, Cumming School of Medicine, Calgary, Alberta, Canada; and [8]Division of Rheumatology, Cumming School of Medicine, Calgary, Alberta, Canada

Correspondence: Cheryl Barnabe, University of Calgary, 3330 Hospital Drive NW, Calgary, Alberta T2N 4N1, Canada. E-mail: ccbarnab@ucalgary.ca

Abbreviations: CI, confidence interval; HR, hazard ratio; IQR, interquartile range; MDD, major depressive disorder; PsA, psoriatic arthritis; THIN, The Health Improvement Network

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Our objective was to evaluate clinical data to elucidate the possible role of MDD in the progression of inflammatory disease from one organ system (the skin) to involving multiple organ systems, and thereby highlight a possible risk factor for PsA development among patients with psoriasis. We hypothesized that patients with psoriasis and comorbid incident MDD would be at a greater risk of developing PsA compared with those who have psoriasis without comorbid incident MDD.
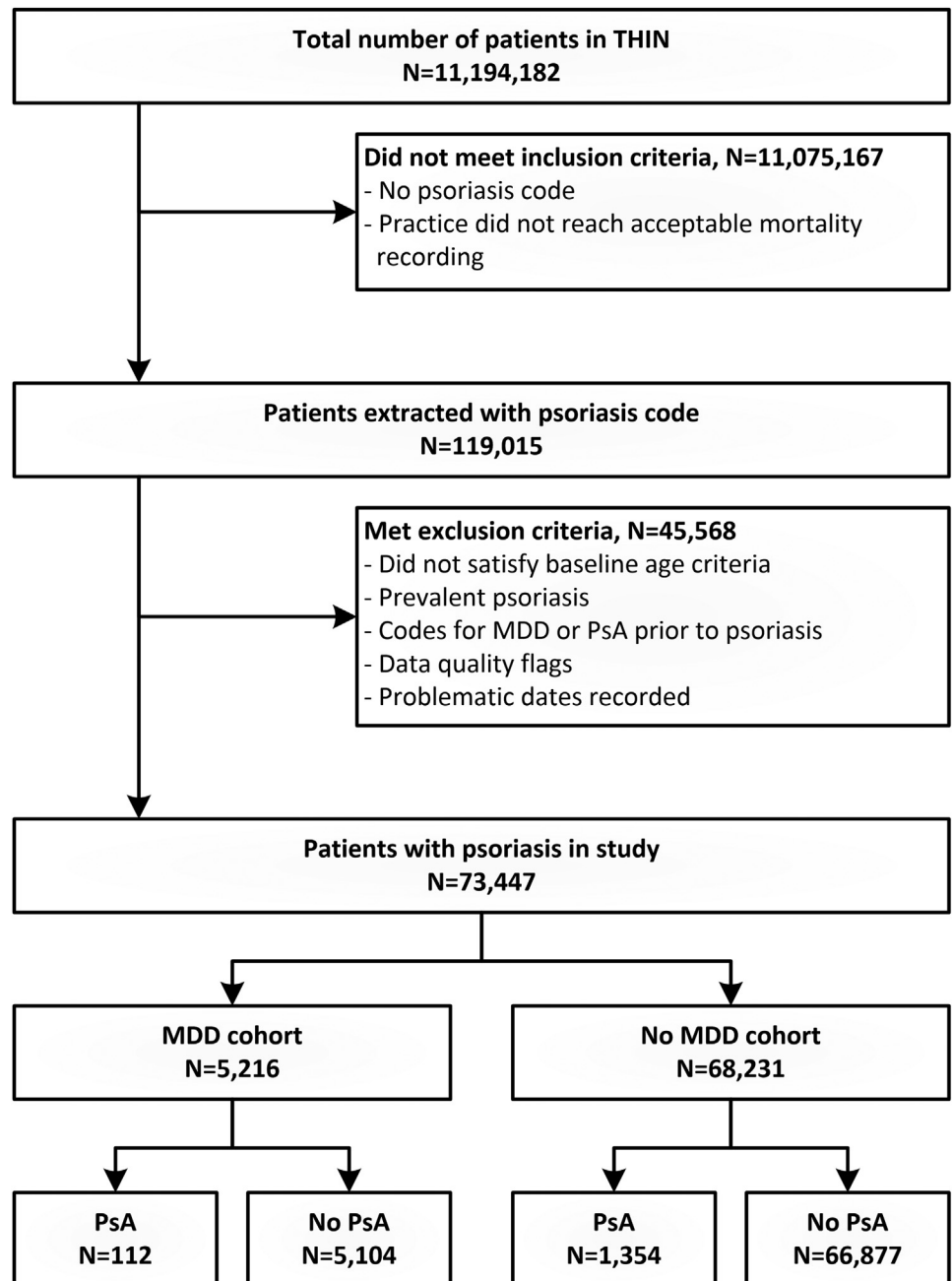
RESULTS

Participants and descriptive data

We utilized The Health Improvement Network (THIN), a general practice medical records database in the United Kingdom (UK), to identify 73,447 individuals with an incident psoriasis diagnosis who were followed until the development of PsA or the censor date (Figure 1). The median (interquartile range, IQR) age at psoriasis diagnosis was 49.5 years (IQR 19.0 years). The median follow-up time in the study was 5.1 years (IQR 6.9 years).

Between the study start time at psoriasis diagnosis and the study end point at PsA diagnosis or censor date, we identified 5,216 (7.1%) patients with psoriasis who developed MDD. Among those who developed MDD, the median time from psoriasis diagnosis to MDD diagnosis was 3.1 years (IQR 4.7 years). Those who developed MDD were more likely to be younger, female, current smokers, with at least one comorbidity, socially deprived, and with moderate-severe psoriasis,

Figure 1. Study flow diagram. The figure shows the approach for identifying eligible patients with psoriasis within THIN and then identifying those who subsequently developed major depressive disorder (MDD) and/or psoriatic arthritis (PsA). THIN, The Health Improvement Network.