



## Nursing Considerations When Treating Patients with Moderate to Severe Psoriasis and Associated Comorbidities

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### Expert Commentary

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Psoriasis is a chronic, immune-mediated disease characterized by recurring and remitting inflammatory disease, ranging from mild-to-severe and affecting the skin, the scalp, and sometimes the joints. Psoriasis affects approximately 2% of the general population,<sup>1</sup> with a peak onset in young adulthood. Psoriasis has a detrimental impact on quality of life and may lead to emotional suffering and frustration. Moreover, approximately 20% to 25% of patients with psoriasis have extensive disease requiring systemic therapy.<sup>2</sup>

Psoriasis is linked to a number of comorbid conditions that can seriously impact a patient's overall health. Psoriasis patients are at increased risk for obesity, diabetes, hyperlipidemia, hypertension, heart failure, myocardial infarction and lymphoma.<sup>3-7</sup> In addition, patients with psoriasis may suffer from depression, and frequently smoke and consume alcohol in excess.<sup>8-10</sup> Indeed, a recent study indicates that there is an increased risk of death in patients with severe psoriasis with the relative risk of mortality greatest in younger patients compared to older patients.<sup>11</sup> Although the associated comorbid conditions are more commonly observed in patients with moderate-to-severe psoriasis, these conditions can also be observed in patients with mild psoriasis.<sup>12</sup>

Traditional treatment approaches for psoriasis are aimed at controlling symptoms of the disease. Patients with mild-to-moderate psoriasis can generally be managed with topical therapies. For patients with moderate-to-severe psoriasis, systemic therapies have dramatically improved patient outcomes. These treatments include phototherapy, traditional systemic medications (eg, acitretin, methotrexate, and cyclosporine), and the newer biologic agents. The biologic agents work to control the inflammatory response that underlies psoriasis. For example, the tumor necrosis factor (TNF) inhibitors (eg, adalimumab, etanercept, and infliximab) control inflammation by binding to TNF- $\alpha$ , a proinflammatory cytokine, which is over expressed in psoriatic skin and joints. In contrast, the T-cell inhibitors block T-cell migration and activation (efalizumab), or inhibit T-cell activation and selectively reduce memory T cells (alefacept) in psoriatic skin.

In order to provide optimal care for their patients, dermatology nurses should recognize the relationship between psoriasis and associated comorbid conditions, and be knowledgeable of recent advances in treatment options for patients with psoriasis. This Dermatology Express Report™ reviews data and strategies for treating patients with psoriasis and associated comorbidities with TNF inhibitors presented at a CE-certified satellite symposium held during the Dermatology Nurses' Association 26th Annual Convention, March 25-27, 2008, in Las Vegas, Nevada.

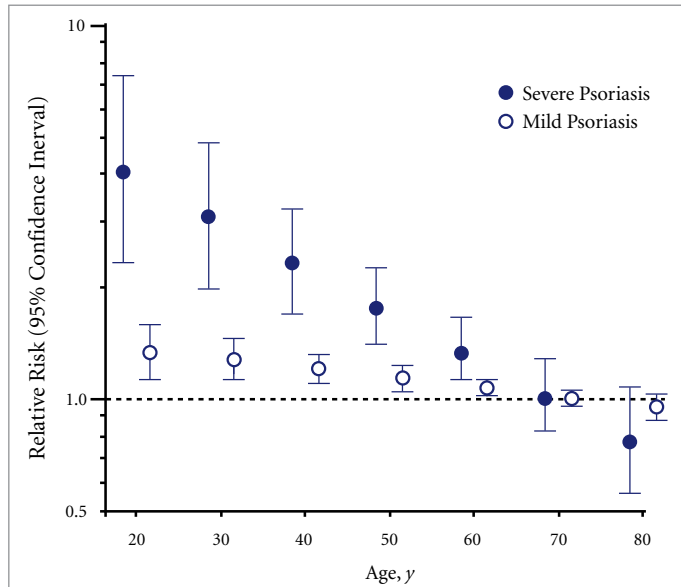
### Psoriasis Patients are at Increased Risk for Comorbid Conditions

Obesity is associated with more severe psoriasis<sup>3</sup> and is reported about twice as frequently among psoriasis patients as in the general population.<sup>4</sup> "Patients with psoriasis, especially when it is moderate-to-severe, likely have health concerns that extend beyond the condition of their skin," said Jennifer Clay Cather, MD, Division of Dermatology, Department of Internal Medicine, Baylor University Medical Center, Dallas, Texas.<sup>13</sup> There is a pathophysiological link between obesity and psoriasis, and common inflammatory mechanisms. Intra-abdominal fat is an endocrine organ that releases pro-inflammatory cytokines such as TNF- $\alpha$  and IL-6.<sup>14</sup> These cytokines which are overexpressed in psoriasis plaques are known to contribute to features of the metabolic syndrome, such as hypertension, dyslipidemia and insulin resistance.<sup>15</sup> Another marker of inflammation associated with both the metabolic syndrome and psoriasis is high-sensitivity C-reactive protein (hsCRP). It has been established that hsCRP levels  $\geq 1$  mg/L signal an intermediate risk for cardiovascular disease, while levels  $> 3$  mg/L indicate high risk. Obese patients with moderate-to-severe psoriasis have been observed to have elevated hsCRP levels.<sup>16</sup> "We have been surprised at the hsCRP levels we have seen—levels as high as 30 mg/L—in patients," Dr. Cather commented.

Dr. Cather emphasized that the presence of moderate-to-severe psoriasis, in itself, puts patients at increased risk for cardiovascular disease. A prospective, population-based cohort study was completed in the United Kingdom, of adults aged 20 to 90 years, to determine the risk of myocardial infarction in patients with psoriasis.<sup>5</sup> Data were collected by general practitioners as part of a patient's medical record and stored in the General Practice Research Database between 1987 and 2002, with a mean follow-up of 5.4 years. A total of 556,995 control patients and patients with mild ( $n = 127,139$ ) and severe psoriasis ( $n = 3837$ ) were included in the study. Adjustments were made for hypertension, diabetes, history of

myocardial infarction, hyperlipidemia, age, sex, smoking, and body mass index. Investigators determined that there were 11,194 myocardial infarctions (2.0%) within the control population and 2,319 (1.8%) and 112 (2.9%) myocardial infarctions within the mild and severe psoriasis groups, respectively. The incidences per 1000 person-years for control patients and patients with mild and severe psoriasis were 3.58 (95% confidence interval [CI], 3.52-3.65), 4.04 (95% CI, 3.88-4.21), and 5.13 (95% CI, 4.22-6.17), respectively (Figure 1). The investigators concluded that psoriasis may confer an independent risk of myocardial infarction and that the relative risk was greatest in young patients with severe psoriasis.

Figure 1. Risk of Myocardial Infarction in Patients With Psoriasis.<sup>[adapted from 5]</sup>



Adjusted relative risk is shown on a log scale.

Patients with psoriasis are at increased risk for other comorbidities including the metabolic syndrome. Investigators compared 581 adult patients hospitalized with moderate-to-severe plaque psoriasis and 1044 hospital-based controls who were assessed for chronic vascular and metabolic disorders.<sup>6</sup> A distinct pattern of chronic disorders was observed in patients with psoriasis (Table 1). Significantly, there was a 5-fold risk for metabolic syndrome. The metabolic syndrome, a chronic inflammatory state, is defined by the presence of at least three of the following: hypertension, hypertriglyceridemia, reduced HDL, insulin resistance, and abdominal obesity or increased waist circumference (> 35 inches in women and > 40 in men).<sup>17</sup> The individual components of the metabolic syndrome also occur disproportionately in the setting of psoriasis. Thus, patients with moderate-to-severe psoriasis are at increased risk for myocardial infarction, metabolic syndrome, type 2 diabetes, hypertension, hyperlipidemia, coronary heart disease.

### TNF Inhibitors Improve Cardiovascular Risk Profiles

A number of studies have indicated that TNF inhibitors may lower the risk for developing cardiovascular disease. Investigators completed a study to determine whether TNF inhibitors modify cardiovascular risk profiles in patients with rheumatoid arthritis (RA).<sup>18</sup> The levels of lipoprotein, hsCRP, and IL-6 were determined in 33 patients with RA treated with adalimumab and 13 control patients, before and after 2 weeks of treatment. In patients treated with adalimumab, the mean concentrations of HDL-cholesterol were significantly higher

Table 1. Cardiovascular Risk Factors in Patients With Moderate-to-Severe Psoriasis.<sup>[adapted from 6]</sup>

CVD Risk Factor	Odds Ratio
Type 2 diabetes	2.48
Hypertension	3.27
Hyperlipidemia	2.09
Coronary heart disease	1.96
Metabolic syndrome	5.29
Smoking	2.96
Regular alcohol consumption	3.33
Heavy alcohol consumption	3.61

after 2 weeks of treatment [0.86 (SD = 0.30) mmol/L versus 0.98 (SD = 0.33) mmol/L,  $P < 0.01$ ], whereas LDL and triglyceride levels were not significantly changed. Additionally, a significant decrease in hsCRP [86.1 (SD = 54.4) mg/L versus 35.4 (SD = 35.0) mg/L,  $P < 0.0001$ ], and IL-6 [88.3 (SD = 60.5) pg/mL versus 42.3 (SD = 40.7) pg/mL,  $P < 0.001$ ] concentrations was seen in this group. No change in lipid profile, hsCRP, or IL-6 levels were seen in the control group. Similarly, infliximab has been shown to increase the HDL-cholesterol levels in RA patients,<sup>19</sup> and etanercept has been shown to lower hsCRP levels in patients with psoriasis and psoriatic arthritis.<sup>16</sup>

TNF inhibitors also have been shown to protect against cardiovascular deaths.<sup>20</sup> Investigators examined the risk of cardiovascular disease in patients with RA treated with TNF inhibitors, compared to a standard RA population. Of 983 total patients in the combined cohort, 531 received etanercept or infliximab during the study period. Cardiovascular disease was defined as the first inpatient care or death from cardiovascular disease without inpatient care for cardiovascular disease prior to study entry. First cardiovascular disease events in those treated versus not treated with TNF blockers were estimated, using age and sex adjusted incidence density computations with treatment and disease severity markers as time-dependent covariates. In patients treated with TNF inhibitors, the age-sex adjusted incidence rate of first CVD event was 14.0/1000 person-years at risk (95% CI 5.7–22.4), compared with 35.4/1000 person-years (95% CI 16.5–54.4) in those not treated. Controlling for disability, the age-sex adjusted rate ratio was 0.46 (95% CI 0.25-0.85,  $P = 0.013$ ) in patients treated with TNF inhibitors versus patients not treated. These results suggest that the risk of developing CVD is lower in patients with RA treated with TNF blockers.

Collectively, these findings suggest that TNF inhibitors may be better agents for controlling comorbidities when compared to other treatment options for psoriasis. “We want to improve lipid profiles, reduce hsCRP and reduce IL-6. These drugs are doing that,” Dr. Cather noted. While the studies were in RA patients, the data can be extrapolated to the psoriasis population, Dr. Cather maintained. Noting the need to address cardiovascular risk factors, she emphasized, “We can impact patients’ lives as ‘interventional dermatologists.’ We can control systemic inflammation and reduce cardiovascular events.”

### Obesity and Dosing of Biologic Agents

Studies have demonstrated that weight affects the efficacy of biological agents in patients with psoriasis. For instance, infliximab is a

weight-dosed medication for the treatment of moderate-to-severe psoriasis. Investigators completed a subgroup analysis of pooled data from three clinical trials that evaluated the use of infliximab in patients with moderate-to-severe psoriasis.<sup>21</sup> Patients received 3 mg/kg or 5 mg/kg of infliximab at 0, 2, and 6 weeks. The common primary endpoint was the percentage of patients who achieved a  $\geq 75\%$  improvement in Psoriasis Area and Severity Index (PASI) score by week 10. The analysis demonstrated that patients who were either obese (BMI  $> 30 \text{ kg m}^{-2}$ ) or overweight (BMI 25 to  $< 30 \text{ kg m}^{-2}$ ) had a similar PASI 75 response to patients with ideal body weight (BMI  $< 25 \text{ kg m}^{-2}$ ) (Figure 2). These studies demonstrated that infliximab is an efficacious weight-based medication for the treatment of moderate-to-severe psoriasis.

In contrast to infliximab, etanercept is a fixed-dose medication. Investigators completed a subgroup analysis of pooled data from three clinical trials that evaluated the use of etanercept in patients with moderate-to-severe psoriasis.<sup>22</sup> Patients received etanercept at 50 or 100 mg/week. The primary efficacy endpoint in the studies was a  $\geq 75\%$  improvement in the PASI score at week 12. The analysis demonstrated that in both treatment groups, patients weighing more than 200 lbs had lower PASI 75 scores when compared to patients that weighed less than 200 lbs (Figure 3). Significantly, a greater percentage of patients weighing less than 200 lbs achieved a PASI 75 at each dose, when compared to patients weighing more than 200 lbs.

The link between psoriasis and obesity has implications not only for overall health but for the efficacy of treatment with biologic agents. Adequate dosing of biologic agents in obese patients requires consideration of a patient's weight, as the weight-based agents (eg, infliximab, efalizumab) appear to be more effective in treating obese patients with moderate-to-severe psoriasis than fixed-dose agents (eg, adalimumab, alefacept, etanercept).<sup>23</sup>

### Role of the Nurse: Impacting Healthcare of the Obese Patient with Psoriasis

In several countries, nursing has been repeatedly found to be one of the most trusted professions.<sup>24</sup> Nurse initiated follow-up in children and adults can be more effective than interventions involving physicians and the office visit. Nurses are also traditionally more patient-centered and use appropriate culturally tailored approaches when interacting with patients. Therefore, nurses play a unique and important role in identifying at-risk populations for obesity. "You will notice that most of our most severe psoriatics tend to be obese," said Ms. Melodie Young, MSN, RN, A/GNP-c Modern Dermatology, A Baylor-Health Texas Affiliate Dallas.<sup>25</sup> "Obesity is a significant health problem and is not something we can ignore because we are dermatologists." She suggested that dermatology staff should not only try to clear the skin but also treat the comorbidities. By doing this nurses can improve the quality of life as well as the overall health of their psoriasis patients.

Ms. Young indicated that dermatology nurses can be pro-active when treating their patients with psoriasis. Ms. Young recommended giving patients a comprehensive exam and to assess body fat using BMI or waist circumference. Nurses should also evaluate a patient's risk factors including blood pressure, cholesterol levels, and blood glucose levels, and determine whether there is a family history of obesity-related disease. Nurses can also educate patients about the importance of life-style changes such as losing weight, increasing exercise, quitting smoking and controlling blood pressure and cholesterol.

Figure 2. Infliximab PASI 75 Response at 10 Weeks by BMI.<sup>[adapted from 21]</sup>

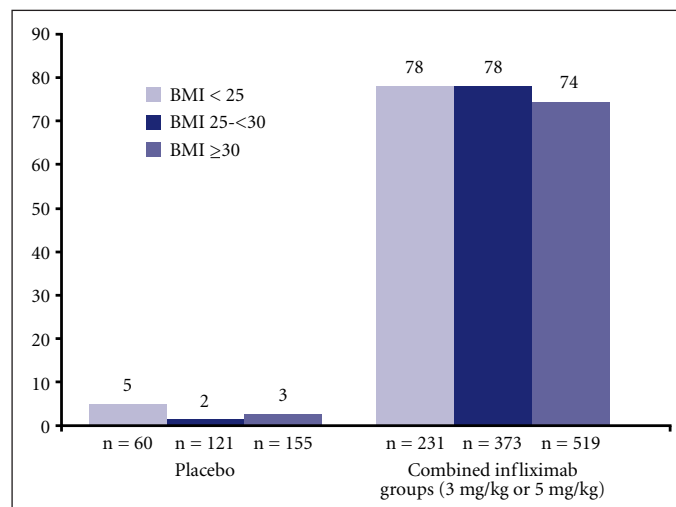
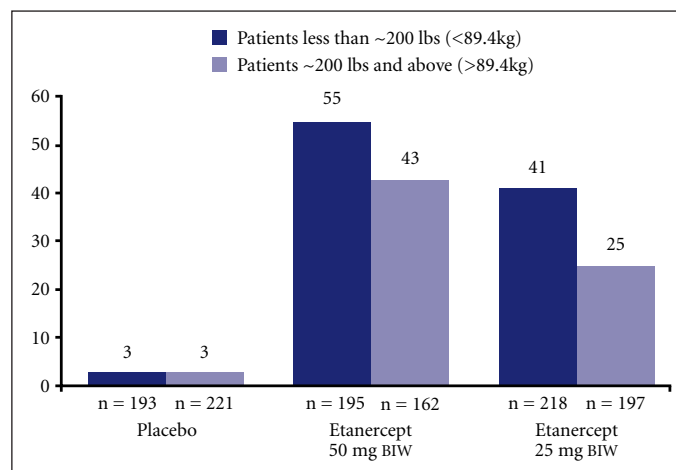


Figure 3. Etanercept PASI 75 Response at Week 12 by Dose and Weight.<sup>[adapted from 22]</sup>



Dermatology nurses should know the differences and be familiar with the treatment options for psoriasis, especially the biologic agents. They should know the dosing schedules and routes of administration, and be familiar with the efficacy, safety, and tolerability profiles of each of the agents. In addition, they should know which medications are more effective in the obese patients.

In conclusion, psoriasis patients with comorbidities present special challenges to the dermatology nurse. Psoriasis is associated with a higher incidence of comorbidities, including obesity, metabolic syndrome and cardiovascular disease. Patients with moderate-to-severe psoriasis should be screened for associated comorbidities especially if obese. TNF inhibitors are more likely to control comorbidities in patients with severe psoriasis when compared to other medications. Adequate dosing of biologic agents in overweight and obese patients may require consideration of a patient's weight, as weight-based medications may be more effective in treating obese patients with psoriasis than fixed-dose medications. As trusted health care professionals, nurses are in the best position to work with patients to improve their psoriasis and decrease their associated comorbidities and related health conditions.

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### DISCLOSURES:

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