Do TNF Inhibitors Reduce the Risk of Myocardial Infarction in Psoriasis Patients?

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Association Between Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients With Psoriasis

Jashin J. Wu, MD; Kwun-Yee T. Poon, MS; Jennifer C. Channual, MD; Albert Yuh-Jer Shen, MS, MD

Objective: To assess whether patients with psoriasis treated with tumor necrosis factor (TNF) inhibitors have a decreased risk of myocardial infarction (MI) compared with those not treated with TNF inhibitors.

Design: Retrospective cohort study.

Setting: Kaiser Permanente Southern California health plan.

Patients: Patients with at least 3 International Classification of Diseases, Ninth Revision, Clinical Modification, codes for psoriasis (696.1) or psoriatic arthritis (696.0) (without antecedent MI) between January 1, 2004, and November 30, 2010.

Main Outcome Measure: Incident MI.

Results: Of 8845 patients included, 1673 received a TNF inhibitor for at least 2 months (TNF inhibitor cohort), 2097 were TNF inhibitor naive and received other systemic agents or phototherapy (oral/phototherapy cohort), and 5075 were not treated with TNF inhibitors, other systemic therapies, or phototherapy (topical cohort). The median duration of follow-up was 4.3 years (interquartile range, 2.9, 5.5 years), and the median duration of TNF inhibitor therapy was 685 days (interquartile range, 215, 1312 days). After adjusting for MI risk factors, the TNF inhibitor cohort had a significantly lower hazard of MI compared with the topical cohort (adjusted hazard ratio, 0.50; 95% CI, 0.32-0.79). The incidence of MI in the TNF inhibitor, oral/phototherapy, and topical cohorts were 3.05, 3.85, and 6.73 per 1000 patient-years, respectively.

Conclusions: Use of TNF inhibitors for psoriasis was associated with a significant reduction in MI risk and incident rate compared with treatment with topical agents. Use of TNF inhibitors for psoriasis was associated with a non–statistically significant lower MI incident rate compared with treatment with oral agents/phototherapy.


Commentary by April W. Armstrong, MD, MPH

Psoriasis is a common, immune-mediated disease that affects 3% of the US population and more than 125 million patients worldwide. Population studies have found that psoriasis patients have an increased prevalence of cardiovascular risk factors, including obesity, diabetes, hypertension, and dyslipidemia. Psoriasis patients also have a greater prevalence of coronary artery disease, myocardial infarction (MI), and cardiovascular death compared with the general population. This association of psoriasis with adverse cardiovascular outcomes may be most pronounced among young patients with severe psoriasis.

Whether systemic treatments for psoriasis modify the risk of major adverse cardiovascular events is a clinically significant question. Atherosclerosis is an inflammatory disease, and it is possible that reduction in tumor necrosis factor (TNF) and T(H)1-mediated inflammation could reduce rates of incident MI among patients with psoriasis. The currently approved biologic agents for treatment of psoriasis include TNF inhibitors as well as anti-IL12/23 monoclonal antibodies. The TNF inhibitors approved for treatment of psoriasis include adalimumab, etanercept, and infliximab.

In the August 2012 issue of the Archives of Dermatology, Wu and colleagues reported results from a retrospective cohort study that examined whether psoriasis patients treated with TNF inhibitors have a decreased risk of MI compared with psoriasis patients not receiving TNF inhibitors. The authors analyzed data from 8845 patients enrolled in the Kaiser Permanente Southern California (KPSC) health plan with either psoriasis or psoriatic arthritis and no antecedent MI history of MI. These patients were followed up for a median duration of 4.3 years. Among them, 1673 patients were treated with TNF inhibitors (adalimumab, etanercept, or infliximab) for a median duration of 685 days. After multivariate analysis, patients treated with TNF inhibitors had
approximately half the risk of developing MI (hazard ratio [HR], 0.50; 95% CI, 0.32–0.81) compared with psoriasis patients treated with topical agents. The authors also reported a differential strength of association based on age. Specifically, patients older than 60 years receiving TNF inhibitor therapy had a greater relative reduction in MI risk (HR, 0.32; 95% CI, 0.14–0.73), compared with those 60 years and younger (HR, 0.46; 95% CI, 0.25–0.88).

This novel work by Wu and colleagues examined a clinically important question regarding whether systemic treatments for psoriasis affect cardiovascular outcomes. The large, diverse, and stable membership of KPSC makes it an ideal data source to explore this research question with sufficient study power. The authors concluded that the use of TNF inhibitors was associated with a significant reduction in MI risk compared with treatment with topical agents.

Based on these study findings, should patients be treated with TNF inhibitors for psoriasis to reduce the risk of cardiovascular events? Before answering this question, consider other aspects of this study as well as the study context. First, the authors treated age as a dichotomous variable in multivariate analyses; it would be noteworthy to explore whether treating age as a continuous variable would affect the findings. Second, the question remains whether longer TNF treatment duration is associated with more favorable cardiovascular outcomes. Wu et al found that longer duration of TNF inhibitor therapy (>685 days) was not associated with significantly lower risk of MI (HR, 1.36; 95% CI, 0.64–2.90) compared with shorter treatment duration.

How do these study findings compare with other studies in the literature? Most epidemiologic studies have used medication records to define psoriasis severity because measures directly assessing psoriasis severity, such as Psoriasis Area and Severity Index (PASI) or Physician Global Assessment, are not routinely reported in clinical care. Wu et al divided the psoriasis patients into 3 groups based on their medication use: TNF inhibitor, oral medications or phototherapy, and a topical cohort. This classification is similar to the seminal work by Gelfand et al, in which psoriasis patients in the United Kingdom were defined as having severe disease if they used oral systemic treatment or phototherapy (biologic therapy was not widely used at that time) and mild disease if they had not used systemic treatment. With the reference group defined as patients without psoriasis, Gelfand et al found that those receiving oral or phototherapy had greater MI risk compared with patients receiving topical or no therapy. In both studies, without direct measures of psoriasis severity, it may be difficult to discern treatment effects from disease effects on MI risk. Despite similar study designs, the differences in the study findings were more than what would be expected from the differences in study design and populations.

Abuabara et al found no difference in MI risk in the systemic treatment group (including TNF inhibitors) compared with patients receiving UV-B phototherapy. The authors identified an interaction with age, in which patients 50 years or older receiving systemic therapy (including TNF inhibitors) had no difference in risk for MI compared with those receiving UV-B. Importantly, when the models were analyzed with each individual treatment category (including TNF inhibitors) compared with UV-B, the results did not change significantly. Thus, no overall reduction in MI risk was observed in patients receiving TNF inhibitors compared with phototherapy.

Ahlehoff et al found that among a Danish psoriasis cohort with severe psoriasis, biologic treatments (with >80% representing TNF inhibitors) were associated with significantly lower risk of composite outcome of death, MI, and stroke compared with those treated with nonbiologic, nonmethotrexate, anti-inflammatory medications. However, when a different composite outcome comprising cardiovascular death, MI, and stroke was assessed, no significant differences in risk were observed between these 2 groups.

Why have these studies reached different conclusions? Differences in all the aforementioned study findings could be attributed to different patient populations, definition of the reference group, and methods for categorizing treatments. Although the absolute differences should not be compared among these studies, the relative directionality of these relationships may be informative.

At the current time, data from population studies are not sufficient to determine with certainty whether TNF inhibitors are beneficial in reducing incident MI in patients with psoriasis. Future population studies need to incorporate direct assessment of psoriasis severity, explore the relationship between treatment duration and MI rates, and thoroughly evaluate interaction terms in analysis models. The gold standard remains a randomized controlled trial to evaluate the cardiovascular effects of TNF inhibitors in patients with psoriasis.

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Armstrong has served as investigator, advisor, and/or speaker to AbbVie, Amgen, Janssen, Eli Lilly, Merck, and Pfizer.

REFERENCES