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Does Treatment of Psoriasis Reduce Cardiovascular Comorbidities?

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Psoriasis has been associated with an increase in myocardial infarctions. Several registries have shown reductions in major adverse cardiovascular events in psoriasis patients and rheumatoid arthritis patients treated with tumor necrosis factor-α antagonists. Many assume that the reduction in cardiovascular events can be attributed to the anti-inflammatory effect of tumor necrosis factor blockers, but a 52-week study conducted by Bissonnette and coworkers failed to show a reduction in cardiovascular inflammation in psoriasis patients treated with adalimumab. Longer and larger studies are needed to explain why tumor necrosis factor-α blockade appears to reduce cardiovascular events in patients with severe psoriasis.

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An association between psoriasis and myocardial infarctions has been observed for decades. Over 30 years ago, the associations between psoriasis and cardiovascular risk factors such as diabetes and hyperlipidemia were noted, and some of those publications suggested that psoriasis was not an independent risk factor for heart disease (Török et al., 1982). It was a highly cited study by Gelfand et al. in 2006 that convincingly linked severe psoriasis as an independent risk factor to an increase in myocardial infarctions, particularly in young patients. Using prospective data collected from general practitioners in the United Kingdom using the General Practice Research Database from 1987–2002, adjustments for hypertension, diabetes, history of previous myocardial infarction, hyperlipidemia, cigarette smoking, age, sex, and body mass index were made. Over 500,000 control patients were compared with approximately 127,000 patients with mild psoriasis and 3,837 patients with severe psoriasis. The adjusted relative risk for myocardial infarction in a 30-year-old patient with mild psoriasis was 1.29 (95% confidence interval [CI] = 1.14–1.46), and for a 30-year-old with severe psoriasis, the adjusted relative risk was 3.10 (95% CI = 1.98–4.86) (Gelfand et al., 2006). The relative risk remained elevated, but less so, as older age groups were examined because the frequency of myocardial infarctions in the general population increases with age.

Increases in cardiovascular risk factors such as smoking, hypertension, diabetes, obesity, and metabolic syndrome have all been shown in psoriasis (Shapiro et al., 2007). Comorbidities like stroke and peripheral vascular disease are also increased in patients with psoriasis and can be directly related to severity of the disease (Kaye et al., 2008). Increases in inflammatory proteins and markers including C-reactive protein, osteopontin, leptin, and others have been shown in patients with psoriasis, suggesting that inflammation contributes to both diseases (Gisondi and Girolomoni, 2009).

Not every study shows an increase in heart disease in patients with psoriasis. Dowlatshahi et al. (2013) showed that psoriasis patients smoked more and had higher blood pressure and body mass index levels, but the adjusted carotid intima-media thickness was the same for psoriasis as for reference subjects. Ankle-brachial indexes, pulse wave velocities, and coronary artery calcium scores were also similar, as was the risk of incident cardiovascular disease, including coronary heart disease, stroke, and heart failure. That study, however, predominately looked at patients with mild psoriasis (Dowlatshahi et al., 2013). Similarly, in a study by Egeberg et al. (2017), all residents of Denmark older than 18 years were included. Adjusted hazard ratios for mild psoriasis did not show an increase in the risk of myocardial infarction (hazard ratio = 1.02, 95% CI = 0.96–1.09), and the risk in patients with severe psoriasis was only modestly increased (hazard ratio = 1.21, CI = 1.07–1.37) (Egeberg et al., 2017). A few other studies also question the increase in myocardial infarctions, but the vast majority of population-based studies, registries, and databases show an increase in myocardial infarctions, particularly in patients with severe disease.

With the growing body of information pointing to increases in myocardial infarction and risk factors for cardiovascular disease in patients with psoriasis, the question that has been asked by many is *Can we prevent heart attacks and other cardiovascular comorbidities of psoriasis by treating the psoriasis?* Observational studies involving numerous registries have reported reductions in myocardial infarctions in patients treated with tumor necrosis factor (TNF)-α antagonists. Many of those studies showing reduced cardiovascular events have come from registries of patients treated for rheumatoid arthritis. However, Wu and Poon (2014) recently showed that treatment of psoriasis with TNF-α inhibitors is associated with reduced frequency of myocardial infarctions. In a retrospective cohort study of over 1,500 patients with psoriasis or psoriatic arthritis, the hazard ratio for myocardial infarction for those psoriasis patients treated with TNF-α inhibitors compared with those not

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Clinical Implications

- Severe psoriasis has been associated with an increase in myocardial infarctions.
- In many registries, the use of TNF-α blockers is associated with a large reduction in the frequency of myocardial infarctions in patients with severe psoriasis.
- A 52-week study of adalimumab in patients with psoriasis failed to show a reduction in cardiovascular inflammation.

treated with TNF-α inhibitors was 0.26 (95% CI = 0.12−0.56) (Wu and Poon, 2014). The presumed explanation was a reduction in inflammation as manifested by clearing of psoriasis. Presumably, the accompanying reduction in inflammatory cytokines resulted in a reduction in atherosclerosis and cardiovascular disease.

In an earlier 30-patient pilot study published by Bissonnette et al. (2013) looking at vascular inflammation in the ascending aorta and carotid arteries, decreases in vascular inflammation were shown in psoriasis patients treated with adalimumab compared with placebo when data for the ascending aorta and carotid arteries were analyzed separately at 15 weeks (Bissonnette et al., 2013). It was therefore with great anticipation that we awaited the results of the longer-term studies of cardiovascular inflammation, expecting further proof that the TNF-α antagonist, adalimumab, would result in reduction of cardiovascular inflammation over 52 weeks. The 52-week study by Bissonnette et al. (2017) was a double-blind, placebo-controlled psoriasis trial of adalimumab that examined vascular inflammation using positron emission tomography-computed tomography to measure uptake of fluoro-2-deoxy-D-glucose in the ascending aorta and carotid arteries. This study, however, failed to show reduced vascular inflammation despite a reduction in high-sensitivity C-reactive protein in the adalimumab-treated patients (Bissonnette et al., 2017).

There are a number of reasons why this study may not have shown the anticipated reduction in cardiovascular inflammation. The registries showing reductions in cardiovascular disease have looked at thousands of patients treated for up to 10 years, and this study may be too small or of insufficient duration to show an effect. Moreover, even if we assume that the technology used to study vascular inflammation was sufficiently sensitive and specific to do so, it was the carotid arteries and ascending aorta that were studied, not the coronary arteries. Finally, we undoubtedly know less than we think about the factors linking cardiovascular inflammation, atherosclerosis, and coronary artery thrombosis, and undoubtedly TNF-α is not the only factor to be considered.

Despite the negative results in this study, we cannot ignore the studies of registries that have reported reductions in myocardial infarctions and deaths from cardiovascular disease in patients treated with TNF-α antagonists both for psoriasis and for rheumatoid and psoriatic arthritis. In patients with cardiovascular risk factors, TNF-α antagonists have been the medications we turn to for severe psoriasis, for good reasons. More data will be needed to show a definite effect, but existing observational data suggest that TNF-α blockers are likely to prove to be cardioprotective in this population.

CONFLICT OF INTEREST

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