Psoriasis and CVD: From the skin to the heart

The associations between cardiovascular events and psoriasis have been well documented in peer-reviewed literature. The key question, however, is why do these associations exist?

It is currently known that patients with psoriasis are more likely to experience myocardial infarctions and strokes, but not enough patients have been studied to provide the data necessary to yield definitive answers.

Joel M. Gelfand

Regarding therapeutics, an emerging body of data shows that statins can have a positive impact on CV events in the psoriasis setting, but statin adherence among individuals with psoriasis remains suboptimal. The psoriasis armamentarium has demonstrated a mixed bag of results, with some drugs showing improvement in CV outcomes and others leading to further comorbidity.

Joel M. Gelfand, MD, MSCE, FAAD, professor of dermatology and epidemiology, vice chair of clinical research and director of the Psoriasis and Phototherapy Treatment Center at the University of Pennsylvania Medical Center, sat down with Healio to discuss these associations and what the future may hold for patients with psoriasis and their cardiovascular risk.

Q: What CV comorbidities are most common in patients with psoriasis?

Gelfand: People with psoriasis are more prone to metabolic diseases and syndrome, including diabetes, dyslipidemia and hypertension. They are also more prone to CV events like myocardial infarctions and strokes. All of this can cause premature mortality. One thing we have learned about these events is that they are related to the severity of the skin disease. People who have more severe skin disease are more likely to develop these events.

Q: Is it understood why these associations exist?

Gelfand: We are still not sure precisely why. One idea is that the pathophysiology of inflammation in chronic skin disease that drives psoriasis can cause some of the effects that lead to an adverse CV profile, such as stickiness of platelets — leading to clots — and inflammation in blood vessels accelerating atherosclerosis, plaque rupture and major CV events.

Q: Does a specific form of psoriasis appear to be more associated with CV risks?

Gelfand: This one is also a challenge to answer precisely because that has not been studied thoroughly. That said, there does seem to be an association with body surface area (BSA). Specifically, every 10% increase in BSA impacted by psoriasis corresponds with a 20% higher risk for developing diabetes. But that's just one example. BSA likely effects the prognosis of other CV comorbidities, but we can't say this with any degree of certainty, and we have not drawn any specific conclusions about psoriasis in the genitals, scalp, nails or other anatomic areas and how those areas impact CV risk.

Q: Why are you unable to say this with certainty?

Gelfand: You really need very large studies with highly detailed information to study CV outcomes.

Q: Why have these studies not been conducted?

Gelfand: They require the prospective collection of data on tens of thousands of people. It is comparatively easy to accrue these numbers for diabetes or hypertension, which are more common and can be measured with a simple biomarker such as HbA1c or systolic blood pressure. It is considerably more difficult in diseases that are common but not that common, like psoriasis. The key issue with psoriasis in this regard is that it takes careful measurements of skin activity by a clinician because we lack an objective biomarker.

Q: Could you discuss some CV therapies that seem to improve psoriasis parameters?

Gelfand: In general, treating psoriasis successfully portends better outcomes in the skin, but also in terms of CV comorbidities. But this is also mainly a hypothesis at the moment that needs to be proven. In my group, we have done a series of placebo-controlled trials showing that therapies, ranging from ultraviolet light to TNF inhibitors, could improve cardiovascular outcomes by reducing inflammatory pathways like C-reactive protein (CRP) and IL-6. However, these are just biomarkers and may not predict events. From other fields, we know that using certain biologics like canakinumab (Ilaris, Novartis) or colchicine in people with heart disease can prevent myocardial infarctions. If a similar randomized placebo-controlled trial was done with a safety therapy like adalimumab (Humira, AbbVie) or guselkumab (Tremfya, Janssen), or one of our other biologics proving that they lower CV risk it would be a blockbuster. But they have not been studied yet.

Q: How about psoriasis treatments that are associated with increased risk for CV comorbidities?

Gelfand: There are a few that we are worried about. One is acitretin, which is

a pharmacologic version of vitamin A. It has been shown to elevate triglycerides and lipids. This could be managed with diet and exercise and lipid-lowering medications. The other one is cyclosporin, which elevates blood pressure, lipid levels and triglycerides. A third one to consider is tofacitinib (Xeljanz, Pfizer). Although this is a very effective anti-inflammatory drug that lowers CRP, for reasons not completely understood, it also can lead to thrombosis and pulmonary embolism.

Q: A recent study showed that statins may be beneficial for patients with severe psoriasis. Could you discuss these findings?

Gelfand: This is fascinating. Obviously, statins have been around for decades with incredibly reproducible results in lowering LDL cholesterol and an attractive safety profile. There was a recent meta-analysis suggesting that statins may improve psoriasis, particularly in severe disease, but this needs to be confirmed with larger trials. If there is one overarching issue with statins, it is that they are severely underused. Only 30% of Americans who could benefit from a statin are taking one; this is even true for people who have had CV events. It is just difficult for people to take a pill every day that doesn't change how they feel. Surprisingly, what we saw recently is that people with psoriatic disease are even less likely to be on a statin despite being at higher risk for CV disease. We are trying to understand why that is. One theory is that they mainly see specialists like dermatologists or rheumatologists who are less likely to check their cholesterol. Another thought is that people with chronic diseases such as psoriasis just don't want to be on another medication. However, we are still exploring these associations.

Q: Could you talk a little more about why patients do not want to take long-term medications?

Gelfand: It is just human nature. On a broad level, people do not like taking medications, especially ones that are purely for prevention and don't have any impact on how they feel or function. There is a whole field called behavioral economics where it's been shown that as people, we are predictably irrational. For example, studies have shown that just eliminating a $5 co-pay results in better statin adherence, even in wealthy individuals.

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Q: How can dermatologists help mitigate CV risks associated with psoriasis?

Gelfand: The American Academy of Dermatology/National Psoriasis Foundation has guidelines, as does the American College of Cardiology/American Heart Association. On a basic level, we need to educate our patients with psoriasis about these risks. More specifically, for individuals with psoriasis who are younger than 40, we encourage a heart-healthy lifestyle. We encourage them to exercise, not smoke and not drink alcohol in excess. They should get screened regularly for blood pressure, diabetes, lipids and other CV parameters. For those aged 40 years and older, we take the extra step of calculating their 10-year risk for a CV event. This can be done in primary care and includes all the factors you would expect, including age, smoking status, sex, blood pressure, cholesterol levels, etc. Because people with psoriasis are at increased risk for CV events compared with the general population, the score needs to be adjusted, multiplying it by 1.5 in those with moderate to severe psoriasis. Guidelines may also call for a coronary calcium score to see if calcium is present in the arteries of patients in whom it is unclear if they should go on a statin. Above all, we need to continually educate our patients about these risks.

Q: There is a trend toward team-based care for these patients. Could you discuss this approach?

Gelfand: This is critical. Psoriasis is a complex, multisystem disease. It is hard for one doctor to put it all together. In addition to the comorbidities that we have been discussing, worse mental health outcomes are also observed in populations with psoriasis as well as psoriatic arthritis. To streamline care, there should be a care coordinator who carefully goes through all the relevant information with patients to make sure they schedule their next appointment, whether it is with their dermatologist, primary care provider, rheumatologist, cardiologist, psychologist or other specialist. – *by Rob Volansky* Healio▸

For more information:

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Disclosure: Gelfand reports serving as a consultant for AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Janssen Biologics, Novartis Corp, UCB (DSMB); receiving research grants (to the Trustees of the University of Pennsylvania) from AbbVie, Boehringer Ingelheim, Celgene, Janssen, Novartis Corp, Ortho Dermatologics and Pfizer; and receiving payment for continuing medical education work related to psoriasis that was supported indirectly pharmaceutical sponsors.