

EDITORIALS

Atopic eczema and cardiovascular disease

Eczema joins the list of inflammatory conditions linked to CV risk

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There is growing evidence that people with severe chronic inflammatory diseases may be at higher risk of cardiovascular (CV) disease, independent of more traditional CV risk factors. Population based studies using primary care databases have demonstrated higher CV risk associated with rheumatoid arthritis,^{1,2} psoriatic arthritis not prescribed a disease-modifying anti-rheumatic drug,² and severe psoriasis.² However, the subject remains controversial with conflicting evidence.³ Some of the ongoing uncertainty may be due to a dose-response effect—increased CV risk is confined to those with severe inflammation.

Previous evidence regarding the risk of CV disease in patients with atopic eczema has been inconsistent.^{4,5} In a linked article, Silverwood and colleagues (doi:10.1136/bmj.k1786) report a study using the UK Clinical Practice Research Datalink (CPRD) to investigate CV risk in 387 439 UK adults with atopic eczema, matched by age, sex, and location to 1 528 477 controls.⁶ Moderate disease severity was defined by receipt of at least two potent topical corticosteroid prescriptions in one year or treatment with a topical calcineurin inhibitor. Severe disease was indicated by phototherapy or systemic immunomodulator therapies.

Data on all standard CV risk factors, such as smoking, hyperlipidaemia, diabetes, and hypertension were available in patients' CPRD records and multivariable analyses controlled for these confounders. During an average of five years of follow-up after initial diagnosis, the risk of CV death was 30% higher in patients with severe eczema, the risk of heart failure was 70% higher, and the risks of myocardial infarction, unstable angina, and atrial fibrillation were about 40% higher than in controls. Severe eczema was associated with a 20% increased risk of stroke, with a 99% confidence interval for the adjusted hazard ratio of 1.01 to 1.48. A dose-response effect was observed, with CV risks increasing from mild to moderate to severe eczema. Adjusted risks were attenuated when all atopic eczema was grouped together, but remained significant for most CV outcomes.

Silverwood and colleagues also considered the effect of disease activity, identifying patients who had at least two eczema entries a year in their records for more than half of their follow-up period. A similar dose-response effect was observed, albeit with

smaller magnitude of effects. Strengths of the study include its large sample size and data acquisition from primary care, allowing a full spectrum of disease severity to be included. Availability of relatively comprehensive records of standard CV risk factors in CPRD allowed most potential confounders to be accounted for in the multivariable analysis. The dose-response effect observed with both eczema severity and eczema activity supports the observed association.

The authors used a validated algorithm to identify patients with atopic eczema, consisting of entry of an atopic eczema diagnostic Read code in CPRD combined with two separate atopic eczema treatment codes. The algorithm has a positive predictive value of 82% (95% confidence interval 73% to 89%) in identifying patients with atopic eczema. Turning this figure on its head means that one fifth of the patients in the exposed cohort did not have atopic eczema, however this would tend to attenuate the magnitude of the hazard ratios observed. One additional point is that, while the authors adjusted for acquired CV risk factors, it is possible that shared genetics between atopic eczema and CV disease represents an unadjusted confounder, because a family history of CV disease was not included in the multivariable analysis.

A sensitivity analysis investigating the use of high dose oral corticosteroids was consistent with the main analysis. However, the authors make the point that their results cannot differentiate the disease from treatment. For example, there may be a systemic effect of prolonged topical corticosteroid application on the CV system.

What are the implications for patients and doctors? For patients with severe or more active eczema, the evidence from the Silverwood and colleagues study makes the case for targeted screening of standard CV disease risk factors. We may need to rethink thresholds for primary prevention interventions in this patient group, by factoring in severe eczema as an independent CV disease risk factor.

The results may also have ramifications for allocation of healthcare resources in eczema. Prevention of CV disease by better control of severe eczema will contribute to the justification for expensive next generation biologic drugs that are becoming available for atopic eczema. Exploring whether these eczema drugs reduce CV events in patients with severe eczema is the

next important step. One further extrapolation is to consider CV disease prevention as a potential outcome in long term eczema trials.

The results from Silverwood and colleagues have helped to clarify the conflicting evidence regarding atopic eczema and CV risk. Severe eczema has joined a growing list of chronic inflammatory conditions that may, in those with severe disease activity, contribute an independent increase in CV disease risk.

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