

# Psoriasis, psoriatic arthritis and cardiovascular risk: are we closer to a clinical recommendation?

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The issue of vascular risk in chronic arthropathies and especially the magnitude of such risk and its clinical implications in daily practice are of considerable current importance. Similarly, the relative risk across distinct arthropathies and other chronic inflammatory conditions is debated. Ogdie *et al*<sup>1</sup> report associations between psoriasis, psoriatic arthritis (PsA), rheumatoid arthritis (RA) and an increased risk of major adverse cardiovascular events (MACE—myocardial infarction, stroke and cardiovascular death) in data derived from the UK primary care registry. Results are stratified by use of disease-modifying antirheumatic drugs (DMARDs). The risk for MACE appeared overall highest among patients with RA, and higher for DMARD users than non-users in RA and psoriasis. By contrast, combined risk of all outcomes was increased less in patients with PsA, and here, DMARD users had lower risks than non-DMARD users.

The statistical and epidemiological methods applied here are apparently sound, and important new information on increased cardiovascular risk in PsA, together with reaffirmation of earlier findings in psoriasis and RA, is presented. Limitations include their categorical adjustments for lipids and hypertension rather than adjustment for continuously measured risk factors. In addition, their somewhat arbitrary use of treatment (DMARDs) as a proxy marker of disease severity is challenging but pragmatic. On the one hand, those not receiving DMARDs should have lower disease activity, but, on the other, DMARDs attenuate inflammation and potentially lower vascular risk. There is also the possibility that some patients with PsA were missed and categorised as having psoriasis or RA. Nevertheless, if the results are accepted as valid, cardiovascular risk appears similarly elevated (by ~40–50%)

for patients with RA and severe psoriasis, whereas combined cardiovascular risk seems less elevated in PsA (~20%). That noted, the important outcome of risk of death from cardiovascular disease (as used in the SCORE risk calculator: <http://www.escardio.org/communities/EACPR/Documents/score-charts.pdf>) appeared not to be higher in the latter group, whereas it was clearly so in RA and severe psoriasis.

What are the implications of these findings? The authors conclude that cardiovascular risk should be addressed with vigilance in all three conditions. The medical community in general now understands systemic inflammation to be a risk pathway for the development of cardiovascular disease, with RA being the exemplar condition underpinning this understanding.<sup>2–5</sup> Thus, a call to address cardiovascular risk in such conditions is perhaps not a surprise. Systemic inflammation levels are generally much lower in psoriasis than in RA, as assessed at least by serum C-reactive protein, suggesting that C-reactive protein is not serving as an appropriate surrogate in this condition for inflammation, or that other, as yet imperfectly appreciated, pathways may contribute to accelerated vascular risk in psoriasis. In this respect, it is noteworthy that patients with psoriasis usually present with higher body mass index than patients with RA and have higher diabetes risk, comprising dual cardiovascular risk factors that are worthy of attention in their own right.<sup>6</sup> Further research to dissect out mechanisms for accelerated vascular risk in psoriasis and PsA seems warranted, with perhaps particular focus on those with early-onset and severe psoriasis.

Perhaps the more interesting question is whether the evidence is sufficiently robust to start using a cardiovascular risk multiplier in psoriasis or PsA? Currently, European League against Rheumatism (EULAR) consensus suggests a 1.5-fold increase in cardiovascular risk in RA in the presence of two out of three criteria (from the following: duration >10 years, rheumatoid factor or anti-CCP (cyclic citrullinated peptide) positive, extra-articular manifestations).<sup>7</sup> More recently,

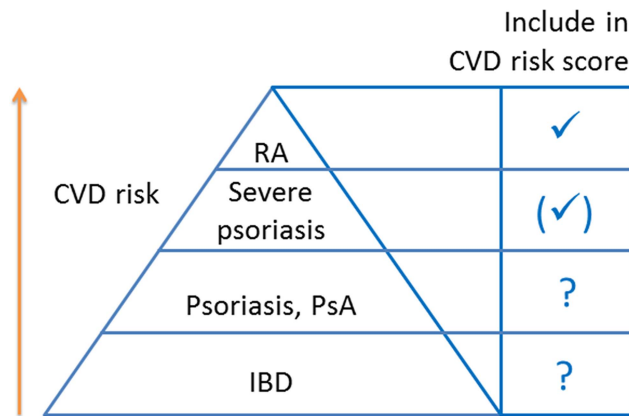
the JBS3 risk score introduced in the UK for cardiovascular risk screening placed RA as an independent risk multiplier irrespective of other risk factors and specific criteria.<sup>8</sup> The JBS3 risk score is based on data derived from the QRISK2 score model, which showed clear evidence of elevated cardiovascular risk in RA independent of all other risk factors (including continuously measured lipids and blood pressure) with adjusted HRs of 1.50 in women and 1.38 for men with RA,<sup>9</sup> risk levels broadly consistent with findings by Ogdie *et al*.<sup>1</sup>

If we turn to the evidence presented by Ogdie *et al* for cardiovascular risk in patients with psoriasis, a risk multiplier for all such patients is hard to justify, as relative risk appears lower compared with RA. Nevertheless, by use of DMARD treatment, the study identified a group of patients with psoriasis with a markedly increased cardiovascular risk (and death from cardiovascular disease) broadly comparable to that of patients with RA. Similar findings for severe psoriasis have been reported in other cohorts,<sup>10 11</sup> although this is the first study to provide a simultaneous comparison to risk levels in RA. The inclusion of severe psoriasis as an independent cardiovascular risk factor could reasonably be considered in the forthcoming update of the EULAR recommendations on cardiovascular risk, along with the optimal/pragmatic criteria for demarcating such patients.

If we turn next to PsA, here, despite the large cohort assembled in this analysis, the absolute number of events among patients with PsA was low; hence it is currently difficult to conclude the need for a risk multiplier for such patients. Further studies in PsA are clearly needed, including, if possible, the determination of the relative contributions of the skin disorder versus arthralgia to vascular risk. A similar uncertainty is also true for conditions associated with inflammation in other tissues such as in inflammatory bowel disease, where the evidence likewise suggests a slightly higher risk of cardiovascular disease, especially in patients with continued flares, although how this finding is factored into clinical management is also currently unclear.<sup>12 13</sup> The extent to which such risks are fully independent of established risk scores is also unclear. Nevertheless, these findings collectively reiterate the observation that conditions associated with ongoing inflammation in a variety of tissues appear to be associated with accelerated vascular risk, albeit with potentially different magnitudes (figure 1).

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**Figure 1** Cardiovascular disease (CVD) risk in inflammatory conditions and CVD risk? This simple conceptual figure is not meant to be definitive but illustrates that several inflammatory conditions are associated with CVD. From available evidence, it is clear that rheumatoid arthritis (RA) presents an independent risk factor for CVD and requires a risk multiplier as introduced in the JBS3 guidelines. The present study suggests relative risk levels may be similarly elevated in patients with psoriasis receiving disease-modifying antirheumatic drugs, which makes a case to risk-score patients with severe psoriasis in a similar way to those with RA. Future guidelines will look at this. It is also clear that more evidence is needed for patients with psoriatic arthritis (PsA).

Finally, in each of these conditions, we lack clinical trials to show that modulation of inflammation lessens cardiovascular risk, although current observational data with their inherent limitations point in this direction. It is hard to design appropriate cardiovascular disease end-point trials to test the inflammation–cardiovascular disease hypothesis in autoimmune conditions. Healthcare professionals will nevertheless continue to target such disease activity as best they can in line with current guidelines, not least because optimising articular and cutaneous well-being is a priori a critical aim of treatment paradigms. What is now clearly also needed is education programmes for rheumatologists and dermatologists to help them better manage cardiovascular and metabolic risks in their patients. Such education, which does not need to be onerous, will help lessen cardiovascular risks further in their patients.

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