Comorbidities of Psoriatic Arthritis — Metabolic Syndrome and Prevention: A Report from the GRAPPA 2010 Annual Meeting

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ABSTRACT. Psoriatic arthritis (PsA) is associated with serious comorbidities such as increased cardiovascular risk, hypertension, depression, and reduced quality of life. Patients with psoriasis have been observed to have an increased incidence of metabolic syndrome compared with the general population; recently, this has also been observed in patients with PsA. This review focuses on the comorbidities associated with PsA, with an emphasis on risks of coronary artery disease and metabolic syndrome. We also discuss the development of a comprehensive approach for the management of comorbidities of PsA. The review summarizes a presentation at the 2010 annual meeting of GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis). (J Rheumatol 2012;39:437–40; doi:3899/jrheum.111244)

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TOTAL CARE
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PREVENTION

Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease associated with psoriasis; in addition to the involvement of the cutaneous system, it often involves extraarticular sites that may be neglected in clinical practice.

Recent reports suggest that patients with PsA have an increased risk for cardiovascular disease (CVD) and mortality, as well as metabolic syndrome and its components. The simplest explanation for increased cardiovascular risk is the prevalence of traditional risk factors such as age, gender, smoking, and history of diabetes. However, this is not the case with psoriatic disease, where many studies have found that up to 30%–50% of patients with atherosclerosis do not have these risk factors. Therefore, treatment regimens for PsA patients must be tailored to comorbidities associated with PsA, including metabolic abnormalities. The objective of this review is to discuss the constellation of comorbid conditions associated with PsA, with an emphasis on atherosclerosis and metabolic syndrome.

Relationship Between Systemic Inflammation, Obesity, and Atherosclerosis
Psoriatic disease is uniquely associated with obesity, insulin resistance, and hypertension, which are capable of inducing inflammatory cascades on the endothelial lining to initiate the process of atherosclerosis. Although no physiological mechanism for this association has been identified to date, the observation that psoriatic disease is a risk factor for coronary artery disease (CAD) provides a unique opportunity to study the contributing role of systemic inflammation to atherosclerosis.

The influence of obesity on psoriatic disease appears to stem from a complex interaction of inflammatory and metabolic factors. Under normal conditions, the endothelial cells of the arterial wall resist adhesion and aggregation of leukocytes and promote fibrinolysis. When activated by stimuli such as obesity, insulin resistance, hypertension, or inflammation, the endothelial cells express adhesion molecules that selectively recruit various classes of leukocytes.

Adipocytokines are cytokines associated with adipose tissue including TNF-α; the most widely studied are leptin, adiponectin, resistin, and visfatin. Other Comorbidities in PsA
PsA is associated with inflammatory bowel disease.
uvecitis, valvular heart disease, fatigue, osteoporosis, and comorbidities secondary to therapy or to chronic pain, disability (Table 1) and reduced quality of life.

Individual components of metabolic syndrome such as obesity, hypertension, insulin resistance, and dyslipidemia have been reported by several studies in patients with PsA. The leading cause of death in 428 Canadian patients with PsA was cardiovascular diseases (36.2%) in a followup study of patients with PsA (n = 648), a significantly higher prevalence of angina, myocardial infarction, and hypertension was observed. In a cross-sectional comparative study of patients with PsA (n = 3066), the prevalences of ischemic heart disease, congestive heart failure, atherosclerosis, type II diabetes mellitus (T2DM), hyperlipidemia, and hypertension were significantly higher in patients with PsA than in controls (p < 0.05). In a study of 47 patients with PsA and 100 healthy controls, PsA patients had significantly higher levels of hypertension, hyperlipidemia, erythrocyte sedimentation rate, CRP, and fibrinogen. A nationwide Danish registry study found that the cardiovascular risk from severe psoriasis or PsA is of similar magnitude to that of DM.

Recently, we observed an increased prevalence of metabolic syndrome in patients with PsA (61/105 patients; 58.1%) compared to 35.2% reported for the Third National Health and Nutrition Examination Survey (NHANES III) data. Of the patients with metabolic syndrome, 15 (24.6%) had CAD, 24 (39.3%) had T2DM, and 11 (18.0%) had chronic kidney disease.

Can We Prevent Metabolic Syndrome and Cardiovascular Comorbidities of PsA?

It is essential to monitor risk factors of CAD and provide necessary care to prevent the progress of atherosclerosis in patients with PsA. Standard care includes avoiding tobacco, lowering blood pressure to below 140/90 mm Hg, lowering serum cholesterol to below 200 mg/dl (more specifically LDL cholesterol to below 100 mg/dl), weight reduction, a healthy diet, and ≥ 30 min/day of physical activity, all of which have been recommended for the general population. Healthy diet, weight reduction, and ≥ 30 min/day of physical activity should be recommended for PsA patients as well.

In patients with PsA, the severity of skin inflammation may be an indicator of increased cardiovascular disease; thus, early diagnosis and treatment targeting the inflammatory cascades associated with PsA may halt disease progression and reduce mortality and morbidities.

Reports suggest that treatment with disease-modifying antirheumatic drugs (DMARD), such as methotrexate, appear to provide a substantial benefit in reducing risk of vascular disease in psoriasis and RA. However, although methotrexate is beneficial for RA-associated metabolic syndrome and appears to reduce atherosclerosis, it has not been shown to reduce inflammation in PsA. Further, prolonged treatment with DMARD may increase the risks of infectious and malignant diseases.

Similarly, the use of biologics has inherent risks for mycobacterial infection, deep fungal infection, lymphoma, and other malignancies. The cardioprotective role of TNF blockers provides a new dimension for the treatment of RA, PsA, and AS because of their prominent antiinflammatory action. Recent publications demonstrated an improvement of arterial stiffness with etanercept in patients with RA and with infliximab in patients with AS. Data from the British Biologics Registry suggest RA patients who responded to anti-TNF agents may have reduced risks for myocardial infarction. These data may justify usefulness of biologics in reducing/preventing the cardiovascular comorbidities associated with psoriatic disease, but randomized controlled trials are needed for confirmation.

Conclusion: The Concept of Total Care

Given the increased prevalence of comorbidities in patients with psoriatic disease, it is essential to approach the disease as a potentially multisystem disorder. An ideal treatment regimen for PsA would provide comprehensive and effective care similar to the proposed Total Care Program for psoriasis. Table 3 provides an outline of a comprehensive program that includes exemplary care of joints and skin and of the comorbidities associated with PsA.

<table>
<thead>
<tr>
<th>Comorbidities in psoriatic arthritis.</th>
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<tbody>
<tr>
<td>• Inflammatory bowel disease</td>
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<td>• Uveitis</td>
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<td>• Valvular heart disease</td>
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<td>• Coronary artery disease</td>
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<td>• Metabolic syndrome</td>
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<td>• Fatigue</td>
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<td>• Depression</td>
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<td>• Osteoporosis</td>
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<td>• Comorbidities secondary to therapy</td>
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<td>• Comorbidities secondary to chronic pain/disability: anxiety, economic, and psychosexual problems</td>
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REFERENCES

Table 2. The 10 recommendations for cardiovascular (CV) risk management in rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS).

1. RA should be regarded as a condition associated with higher risk for CV disease. This may also apply to AS and PsA, although the evidence base is less.
2. Adequate control of disease activity is necessary to lower the CV risk.
3. CV risk assessment using national guidelines is recommended for all patients with RA and should be considered annually for all patients with AS and PsA. Risk assessments should be repeated when antirheumatic treatment has been changed.
4. Risk score models should be adapted for patients with RA by introducing a 1.5 multiplication factor. This multiplication factor should be used when the patient with RA meets 2 of the following 3 criteria:
   • Disease duration more than 10 years
   • RF or anti-CCP positivity
   • Presence of certain extraarticular manifestations
5. TC/HDL cholesterol ratio should be used when the SCORE model is used.
6. Intervention should be carried out according to national guidelines.
7. Statins, ACE inhibitors, and/or AT-II blockers are preferred treatment options.
8. The role of coxibs and most NSAID in CV risk is not well established and needs further investigation. Hence, we should be very cautious about prescribing them, especially for patients with a documented CV disease or in the presence of CV risk factors.
9. Corticosteroids: use the lowest dose possible.
10. Recommend smoking cessation.

ACE: angiotensin-converting enzyme; anti-CCP: anti-cyclic citrullinated peptide; AT-II: angiotensin II; coxibs: cyclooxygenase-2 inhibitors; HDL: high-density lipoprotein; NSAID: nonsteroidal antiinflammatory drugs; RF: rheumatoid factor; SCORE: Systematic Coronary Risk Evaluation; TC: total cholesterol.


Table 3. The concept of total care.

• Perform complete evaluation: systemic and cutaneous
• Educate both parents and child
• Emphasize healthy lifestyle changes
• Perform aggressive therapy of inflammatory arthritis with disease-modifying antirheumatic drugs and biologics
• Identify/prevent/treat:
  Comorbidities of psoriatic arthritis (see Table 1)
  Comorbidities from therapy (infection/malignancies)
• Emphasize wellness program: exercise, diet, de-addiction, relaxation
• Build self-esteem: suggest support group, counseling


