The risks of smoking in patients with spondyloarthritides

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The smoking prevalence in Europe varies from 14% in Sweden to nearly 38% in Greece.[1] In the USA it is now approximately 20%, with large differences between states and according to social class and ethnic background.[2] The proportions of men and women smoking is rather variable, but the relative risk of cardiovascular diseases seems to be higher in women.[3] Smoking prevalence decreases with higher educational level and higher family income. Smoking is a major risk factor for lung, cardiovascular and other diseases.[4 5] Smokers double their risk of having a heart attack compared with non-smokers[4] and many people die from diseases related to smoking.

The effects of nicotine, like those of other drugs with the potential for abuse and dependence, are centrally mediated. The impact of nicotine on the central nervous system is neuroregulatory in nature, affecting biochemical and physiological functions in a manner that reinforces drug-taking behaviour. Dose-dependent neurotransmitter and neuroendocrine effects occur as plasma nicotine levels rise when a cigarette is smoked.[6] Smokers have increased blood cholesterol levels. Smoking may also stimulate the blood clotting system in the blood, and the cardiovascular risk in smoking women using contraceptives is increased.

Cardiovascular diseases occur more frequently in people with elevated C-reactive protein.[7] The link between cardiovascular and rheumatic diseases is well established, and the increased mortality of patients with rheumatoid arthritis (RA)[8] is caused by cardiovascular deaths. It was shown that mortality is significantly reduced by continuous therapy with methotrexate,[9] and that the risk of myocardial infarction can be significantly reduced by successful anti-tumour necrosis factor therapy.[10]

Smoking also has an unfavourable influence on other outcomes of rheumatic diseases, and more intensive therapy is required for RA patients who smoke.[11] The interaction between genetic and environmental factors is of pathogenic importance for RA.[12] The presence of anticitrullinated protein antibodies is a risk factor for developing RA—especially in men who smoke.[13] Of interest, nicotine must be inhaled to confer risk—smokeless tobacco did not increase the risk of chronic inflammatory diseases.[14] It is largely unclear how inhaled nicotine does this.

Two independent studies[15 16] show an increased risk of smoking in patients with axial spondyloarthritis and psoriatic arthritis (PsA). Recently three independent studies[15–17] have shown an increased risk of severe disease in patients with axial spondyloarthritis and psoriatic arthritis (PsA) who are or were smokers. The results of these studies point largely in the same direction but one recent study on PsA came to a different result.[18] However, earlier studies[19] had also reported an increased risk conferred by smoking. The cardiovascular risk profile of patients with ankylosing spondylitis (AS) has recently been described in a meta-analysis.[20] Having spondyloarthritis was found strongly to predict early coronary artery bypass grafting.[21] A number of studies has shown that smoking is associated with poor outcome in patients with established AS.[22–26] For the first time, a clear negative effect of smoking is now reported in 647 patients with early inflammatory back pain and possible spondyloarthritis.[15] In that study, smoking was associated with an earlier onset of back pain, higher disease activity, worse functional status and quality of life, more frequent inflammation of the sacroiliac joints and spine as assessed by MRI, and more frequent structural lesions of the sacroilliac joints and spine as assessed by radiographs using the modified SASSS. As those patients had a short disease duration not much damage had occurred as yet.

Psoriasis is a chronic skin disease that affects 2–3% of the population. PsA, a frequent inflammatory joint condition that belongs largely to the spectrum of spondyloarthritis, affects approximately 20–25% of patients with psoriasis. The prevalence of the metabolic syndrome is high among individuals with psoriasis.[27] Past association studies in patients with psoriasis[28] and PsA[29] have suggested a worsening effect of smoking on the disease. Now, the association between smoking status, duration and intensity of smoking and incidence of PsA has been studied in 94 874 participants from the Nurses' Health Study II over a 14-year time period.[16] During 1 303 970 person-years of follow-up, 157 incident PsA cases were identified. Among total participants, smoking was associated with an elevated risk of PsA. Compared with never smokers, the relative risk was 1.5 for past smokers and 3.1 for current smokers. With increasing smoking duration or pack-years, the risk of PsA, especially for the more severe phenotypes increased. This confirms earlier studies with similar results[30] indicating comparable mechanisms in PsA and in RA.

Taken together, the interactions between environmental factors and the onset, the course and outcomes of rheumatic diseases are getting increasingly complex, and it is becoming increasingly clear how detrimental the influence of smoking is on most of these diseases. The role of rheumatologists is to inform their patients about these facts and the risks associated, and to encourage patients to quit smoking. Except in RA, the pathogenetic basis of the influence of smoking has remained largely unclear to date.

The benefits of quitting smoking begin as soon as an individual stops, and there are evaluated programmes to help give up smoking.[31] However, the advantages of the cessation of smoking in patients with rheumatic diseases have not been prospectively assessed as yet.

Of note, in patients with Crohn's disease cessation of smoking is thought to have an effect size similar to a medical intervention with azathioprine.[32] Of interest, smoking causes opposing effects on ulcerative colitis and Crohn's disease. The odds ratio of developing ulcerative colitis for smokers compared with lifetime non-smokers is thus 0.41, while smokers with Crohn's disease have a more aggressive course of the disease.[32]

European League Against Rheumatism recommendations for cardiovascular risk management in patients with arthritis have recently been published.[33] According to these the rheumatologist is in charge of identifying the risk of cardiovascular disease in patients with inflammatory rheumatic diseases. Who is in charge of treating that risk needs to be decided within each healthcare system. In any case, a close

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cooperation between the general practitioner and the rheumatologist seems warranted to achieve best patient care.

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