When there's smoke there's...scleroderma: evidence that patients with scleroderma should stop smoking

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Abstract There is no treatment for the autoimmune disease scleroderma (systemic sclerosis, SSc), a multisystem disorder characterized by vascular damage and fibrosis. In particular, SSc can severely affect the lung, resulting in pulmonary arterial hypertension and fibrosis. Smoking is well-known to affect pulmonary health, and a recent report (Hudson et al., *Arthritis Rheum*, [in press](#) Oct 8) provides convincing evidence that stopping smoking improves disease outcome in SSc patients. This commentary discusses this recent publication which suggests that physicians should encourage SSc patients to stop smoking immediately.

Keywords Scleroderma · Smoking · Lung fibrosis · Cardiovascular disease

Scleroderma (systemic sclerosis, SSc), a multi-system disease of unknown etiology, is characterized by immune system activation and by vascular disease, including Raynaud's phenomenon and pulmonary arterial hypertension, and organ fibrosis, from which patients often die if there is lung involvement (Khanna and Denton 2010). Treatment regimens for SSc are extremely limited (Khanna and Denton 2010), thus alterations in patient behavior may help manage disease progression and outcome.

Smoking is well-known to affect the cardiovascular system and also to promote fibrosis, including in the lung (Camici and Crea 2007; Vassallo and Ryu 2008; Leask 2010). Patients who have SSc are often told not to smoke, but clear statistical evidence supporting the notion that

stopping smoking improves the progression and outcome of SSc with lung involvement have been lacking; indeed, contradictory results have been obtained (Greenwald et al. 1987; Broholm et al. 2008; Quadrelli et al. 2009). Discrepancies have likely occurred due to small sample size, or to using simple exposure variables (for example, self-described ever, never or pack-year smoking) that may have resulted in so-called 'healthy smoker bias' in which an individual who smokes *a priori* have lungs that are more resistant to the effects of smoking (Becklake and Lalloo 1990).

A recent study appears to have addressed this controversy by employing more detailed statistical modeling of smoking history and a large population-based cohort to assess the question whether cigarette smoking worsens the vascular, gastrointestinal and respiratory outcomes in SSc (Hudson et al., [in press](#)). The Canadian Scleroderma Research Group patient registry was used for this study, which examined 606 SSc patients, with a mean age of 55 (+12) years. Patients had SSc for an average duration of 11 (+9) years, and, of these, 36% had diffuse disease. Considering 1 606 patients, 16% were current, 42% past and 42% never smokers. The mean amount of cigarettes smoked was considered; current smokers had smoked for 25 (+17) pack-years whereas past smokers had smoked for 17 (+18) pack-years and had stopped smoking approximately 16 (+12) years prior to their initial visit to the registry. Various parameters relating to vascular, gastrointestinal and respiratory outcomes were assessed. Data was analyzed using a Comprehensive Smoking Index (CSI) which integrates parameters related smoking intensity, duration and time since cessation into a single covariate permitting the simultaneous modeling of current, past and never smoking patients with a wide range of smoking behaviors.

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Smoking was associated with a significant increase in the frequency and severity of vascular and gastrointestinal symptoms, as well as an increase in breathlessness and decrease in forced expiratory volume in one second and forced vital capacity. Although not quite achieving statistical significance, there was a strong trend towards worsening carbon monoxide diffusion capacity with smoking. Increased severity of Raynaud's was found mainly in current smokers; once the patient stops smoking, the effect disappears. Conversely, acid reflux was more severe in smokers, but symptoms did not subside until after ~11 years had passed. For carbon monoxide diffusion capacity, the effect of smoking was cumulative and virtually permanent.

Overall, these data provide robust statistical support for the notion that smoking has a deleterious effect on SSc. These effects can be long-lasting, but stopping smoking cessation could be beneficial with respect to several other outcomes, notably Raynaud's. The authors concluded that physicians caring for SSc patients should encourage patients to stop smoking as soon as possible.

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