15 **INCREASED SERUM LEVELS AND TISSUE EXPRESSION OF MMP-12 IN PATIENTS WITH SYSTEMIC SCLEROSIS: CORRELATION WITH SEVERITY OF SKIN AND PULMONARY FIBROSIS AND VASCULAR DAMAGE**

M Manetti,^{1,2} S Guiducci,² E Romano,² S Bellando-Randone,² M L Conforti,² L Ibbamanneschi,¹ M Matucci-Cerinic² ¹Department of Anatomy, Histology and Forensic Medicine, University of Florence, Florence, Italy; ²Department of Biomedicine, Division of Rheumatology, University of Florence, Florence, Italy

10.1136/annrheumdis-2011-201235.15

Background and objective Systemic sclerosis (SSc) is a life-threatening connective tissue disease characterised by widespread vasculopathy, lack of angiogenesis and fibrosis of the skin, lung and other internal organs. Increasing evidence indicates that matrix metalloproteinase-12 (MMP-12) plays an important role in pulmonary inflammation and fibrosis. MMP-12 also suppresses angiogenesis through different mechanisms. In this study, the authors evaluated serum levels of MMP-12 and their correlation with clinical features in patients with SSc.

Methods Sera were obtained from 72 SSc patients and 42 healthy volunteers. SSc patients were assessed for disease subset (limited cutaneous SSc (lcSSc)/diffuse cutaneous SSc (dcSSc)), disease stage (early/late SSc), extent of skin sclerosis (modified Rodnan skin thickness score (mRSS)), autoantibodies, interstitial lung disease (ILD), pulmonary arterial hypertension and peripheral vascular involvement (digital ulcers (DU), nailfold videocapillaroscopy). Serum MMP-12 levels were measured by ELISA. Immunohistochemical expression of MMP-12 was analysed in skin biopsies from SSc patients (n=20) and healthy subjects (n=13), and lung biopsies from three patients with SSc-related ILD and five controls.

Results Circulating levels of MMP-12 were significantly increased in SSc patients compared with controls ($p<0.0001$). Serum MMP-12 levels were significantly higher in both lcSSc and dcSSc than in controls (both $p<0.0001$), and a trend towards a significant elevation in dcSSc versus lcSSc was observed ($p=0.06$). MMP-12 was significantly increased in both early- and late-stage SSc compared with controls (both $p<0.0001$), and in late-stage versus early-stage SSc ($p<0.0001$). Patients with $mRSS>10$ had significantly elevated levels of MMP-12 compared with patients with $mRSS\leq 10$ ($p<0.0001$). Moreover, MMP-12 levels correlated positively with mRSS ($r=0.62$, $p=0.01$). MMP-12 levels were significantly raised in SSc patients with ILD compared with patients without ILD ($p=0.02$) and correlated inversely with % forced vital capacity ($r=-0.82$, $p=0.01$). Elevated levels of MMP-12 were also significantly associated with presence of DU ($p=0.004$). Circulating MMP-12 was significantly higher in patients with 'late' nailfold capillaroscopic pattern than in those with 'early' and those with 'active' patterns ($p<0.0001$ and $p=0.009$, respectively), as well as in 'active' versus 'early' patterns ($p=0.02$). In contrast to almost undetectable MMP-12 expression in healthy skin, MMP-12 was strongly expressed in keratinocytes, dermal endothelial cells, fibroblasts/myofibroblasts and inflammatory cells in SSc skin. Affected lung tissues from patients with SSc-related ILD showed strong MMP-12 expression in capillary vessels, inflammatory cells, alveolar macrophages and fibroblasts in the thickened alveolar septa, while faint expression was observed in normal lung tissues.

Conclusions MMP-12 levels are elevated in SSc patients and are associated with severity of skin and pulmonary fibrosis and peripheral vascular damage. Increased levels of MMP-12 might be a potential marker for SSc patients with increased risk for severe, life-threatening disease.