The response rate was 100%. The female: male ratio was 63:41, 49 of these patients were aged >60 years, 43 were between 41 and 60 years and the remainder were aged 20–40 years. Our audit cycle confirms that sharing information with patients and involving them in their care has a positive impact on their understanding and management of disease (90%). Dictating the clinic letters in their presence may also improve the understanding and mutual trust between patients and specialists.

Our study suggests that 96% of patients would prefer to receive copies of clinic letters as this contributes to a better understanding and perhaps enhances the ability to self-manage their disease. They also felt that the quality of communication was particularly satisfying as the consultants took notice of their views and values. Ninety-eight per cent of patients also felt that highlighting the management decision as an agreed plan was particularly useful, as they knew what the expected course of action would be.

In this study, 75% of patients understood the content of the letters fully and 25% partially. The latter is possibly related to the use of medical terminology. However, by dictating the letter in their presence, the patients were given the opportunity to question anything that they did not understand. Previous studies have shown that sensitive issues were often avoided from being mentioned in the letters, but such issues do not arise when letters are dictated in the patients’ presence as consent is easily obtainable.

This survey confirms that patients prefer not only to be informed about their illness and treatment in a passive way, but also very much like to be involved in their management decisions as an active player. This form of triangular communication may also generate better understanding and mutual trust between the patients and doctors. This combined approach to care is being emphasized by the NHS at all times, and should be encouraged, propagated and practised by all in the health care industry. By involving patients in their care and dictating and providing copies of clinic letters, we engage patients in a seemingly indirect educational process besides the application of evidence-based medicine, which shows our commitment to good clinical practice according to the DH guidelines.

**Rheumatology key message**

- Engaging patients in clinic letter dictation enhances understanding and compliance.

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**References**


**Osteopontin in the development of systemic sclerosis—relation to disease activity and organ manifestation**

SIR, SSc is characterized by an interplay between early immunological activation and vascular damage, resulting in the generation of activated fibrogenic fibroblasts and, ultimately, excessive synthesis of extracellular matrix with deposition of increased amounts of structurally normal collagen. The organ involvement in SSc ranges from skin-limited to multi-organ fibrosis. Depending on the degree of skin involvement, SSc is frequently categorized as lcSSc or dcSSc type.

Osteopontin (OPN) is a pleiotropic cytokine involved in the recruitment and retention of macrophages and T cells to sites of inflammation. Classical mediators of acute inflammation (TNF-α, IL-1β) as well as fibrogenic cytokines (angiostatin II, TGF-β) strongly induce OPN expression. OPN has been implicated as a key factor in the development of interstitial fibrosis.

Due to its chemotactic and pro-fibrotic properties, we analysed circulating levels of OPN in patients with SSc and varying degrees of organ involvement by a commercially available ELISA. Plasma of a total of 70 patients with SSc was analysed. Twenty age-matched healthy volunteers and 59 patients with idiopathic pulmonary hypertension served as controls. All patients were recruited from the Department of Immunology and Rheumatology and the Department of Dermatology at Hanover Medical School and Charite University Berlin, Germany, between 2008 and 2009. The study was carried out in accordance with the
Declaration of Helsinki and approved by the institutional review board of Hanover Medical School. Written informed consent was obtained.

Plasma OPN concentrations are elevated 4-fold in patients with SSC \( [n = 70; 89.1(52.4) \text{ ng/ml}] \) compared with healthy controls \( [n = 21; 23.8(3.7) \text{ ng/ml}; P < 0.0001] \) and 1.4-fold compared with patients with idiopathic pulmonary hypertension \( [n = 59; 63.4(44.2) \text{ ng/ml}; P = 0.003] \). In the group of SSC patients, plasma OPN concentrations correlate significantly with CRP \( (r = 0.3; P = 0.02) \). OPN levels showed a weak, but significant association with disease duration \( (r = 0.27; P = 0.03) \).

Patients with or without the presence of sclerodactyly \( (P = 0.2) \), oesophageal involvement \( (P = 0.1) \) and cutaneous calcinosis \( (P = 0.2) \) did not differ with regard to circulating levels of OPN. Similarly, the presence or absence of autoantibodies such as anti-topoisomerase antibody \( (P = 0.6) \) and centromer B antibodies \( (P = 0.08) \) did not have an effect on OPN levels. Patients with a diffuse form of scleroderma showed significantly elevated levels of OPN compared with patients presenting with a limited form \( (P = 0.001) \). Moreover, OPN levels correlated weakly with the modified Rodnan skin score \( (r = 0.3; P = 0.05) \).

Plasma OPN levels in patients with pulmonary fibrosis \( (n = 29) \) are significantly elevated compared with patients without pulmonary fibrosis \( (P < 0.0001; \text{Fig. 1A}) \). The same was true for patients with pulmonary hypertension \( (n = 6) \) compared with patients without \( (P = 0.001) \).

We calculated receiver operating characteristic (ROC) curves to address the diagnostic value of OPN as a novel disease marker for SSC and its complication pulmonary fibrosis. When patients with pulmonary fibrosis were compared with patients without, an OPN cut-off value of \( >65.1 \text{ ng/ml} \) resulted in a specificity of 57.1%, a sensitivity of 90.3%, and a likelihood ratio of 2.1 in diagnosing patients with pulmonary fibrosis [area under the curve 0.8 (0.05); 95% CI 0.7, 0.9; \( P < 0.0001 \); \text{Fig. 1B}].

In the present study, we investigated for the first time circulating plasma levels of OPN in patients with SSC and varying degrees of organ involvement. The pro-fibrotic role of OPN has been described in various experimental studies \([4, 5]\). As part of the inflammatory response, OPN leads to the recruitment and retention of macrophages and T cells \([3]\). Ultimately, this results in interstitial fibrosis. The increased level of OPN would support a role for OPN in an autocrine feedback loop, which could potentiate the disease process by promoting the further accumulation of T cells and macrophages to the site of inflammation. Thus, OPN might be central to the perpetuation of disease activity by influencing the availability of the disease-promoting cells in SSC. Moreover, recombinant OPN induced a significant increase of migration and proliferation of fibroblasts \([6]\), another important pathophysiological mechanism in SSC. It was also shown that OPN expression in skin fibroblasts is responsible for inflammation-associated fibrosis [7]. Delivery of OPN antisense oligodeoxynucleotides into mouse skin wounds leads to accelerated healing and reduced granulation tissue formation and scarring [7]. Macrophage-derived platelet derived growth factor-BB seems to be responsible for the OPN expression in wound fibroblasts [7].

In our study, OPN levels in patients with pulmonary fibrosis were significantly elevated compared with patients without. This finding is in line with a previous study, identifying OPN as one of the major genes that significantly distinguished idiopathic pulmonary fibrosis from healthy control lungs [6].

Our results may offer the possibility of using OPN inhibitors as a novel therapeutic target of T-cell chemotaxis, since monoclonal OPN antibodies have been used with great success in CIA [8]. In addition, the serial measurement of OPN in SSC should be studied to clarify whether the increase of OPN parallels or precedes the development of pulmonary fibrosis. Then, OPN measurement would be an attractive tool for early detection of this complication that responds better to treatment in the early stage.

**Rheumatology key message**

- OPN parallels the development of pulmonary fibrosis in SSC and might be an attractive biomarker of this complication.

**Fig. 1** (A) Plasma levels of OPN are elevated in patients with pulmonary fibrosis \( (P < 0.0001) \) compared with patients without. (B) ROC curve analysis identifies patients with pulmonary fibrosis with good sensitivity and specificity. LF: lung fibrosis.
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References


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Possible role of anti-TNF monoclonal antibodies in the treatment of Mycobacterium marinum infection

Sr, TNF plays a major role in mycobacterial defence. Mycobacterium marinum (M. marinum) infection typically presents with chronic inflammation of hands and feet [1, 2]. Its diagnosis is often delayed and antibiotic treatment is long-standing. Safe re-exposure to anti-TNF therapy after successful bacterial elimination was reported [3], yet addition of anti-TNF monoclonal antibodies to control inflammation seemed paradoxical so far.

A 44-year-old Caucasian farmer presented with dactyliitis of a toe. Local glucocorticoid injection induced a chronic fistula, which was surgically removed. Several months later carpal arthritis and tenosynovitis developed and the patient reported inflammatory back pain. Suspecting spondyloarthritides, NSAIDs and glucocorticoids were introduced, later co-medicated with MTX, yet proved insufficient. Assessment of latent tuberculosis before anti-TNF therapy showed a positive IFN-γ-release assay [IGRA; Quantiferon-TB Gold in Tube (QFT), Cellestis Ltd, Victoria, Australia; Fig. 1a] [4]. Isoniazid was introduced against latent tuberculosis. Etanercept was added 1 month later and within few weeks synovitis and back pain improved. Unexpectedly carpal tenosynovitis

fig. 1 (a) Laboratory findings regarding M. marinum infection. np: not performed; in: PCR reaction inhibited; INH: isoniazid; R: rifampin; E: ethambutol; C: clarithromycin.

(b) Histological findings of synovial tissue. Synovial tissue specimens of the carpus showing classical findings of M. marinum infection: granuloma formation, dense infiltrates of mononuclear cells and several giant cells (arrow).