

REFERENCES

- 1 Frances C, El Khoury S, Gompel A, Becherel PA, Chosidow O, Piette JC. Transient secondary amenorrhoea in women treated by thalidomide. *Eur J Dermatol* 2002;**12**:63–5.
- 2 Vegetti W, Marozzi A, Manfredini E, Testa G, Alagna F, Nicolosi A, et al. Premature ovarian failure. *Mol Cell Endocrinol* 2000;**161**:53–7.
- 3 Falsetti L, Scalchi S, Villani MT, Bugari G. Premature ovarian failure. *Gynecol Endocrinol* 1999;**13**:189–95.
- 4 Pasoto SG, Viana BST, Mendonca BB, Yoshinari NH, Bonfa H. Anti-corpus luteum antibody: a novel serological marker for ovarian dysfunction in systemic lupus erythematosus? *J Rheumatol* 1999;**26**:1087–93.
- 5 Taylor PV, Maloney MD, Campbell JM, Skerrow SM, Nip MM, Parmar R, et al. Auto-reactivity in women with endometriosis. *Br J Obstet Gynaecol* 1991;**98**:680–4.
- 6 Grimes DA, LeBolt SA, Grimes KR, Wingo PA. Systemic lupus erythematosus and reproductive function: a case-control study. *Am J Obstet Gynecol* 1985;**153**:179–86.
- 7 Kammerer-Doak DN, Magrina JF, Nemiro JS, Lidner TK. Benign gynecologic conditions associated with a CA-125 level >1000 U/mL. A case report. *J Reprod Med* 1996;**41**:179–82.
- 8 Van Kasteren YM, Schoemaker J. Premature ovarian failure: a systematic review on therapeutic interventions to restore ovarian function and achieve pregnancy. *Hum Reprod Update* 1999;**5**:483–92.
- 9 Kalantaridou SN, Nelson LM. Premature ovarian failure is not premature menopause. *Ann New York Acad Sci* 2000;**900**:393–402.
- 10 Check JH, Summers D, Nazari A, Choe J. Successful pregnancy following in vitro fertilization-embryo transfer despite imminent ovarian failure. *Clin Exp Obstet Gynecol* 2000;**27**:97–9.

Doppler ultrasound identifies increased resistive indices in SSc

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Cutaneous lesions in patients with systemic sclerosis (SSc) are characterised by fibrosis as well as by changes in the microvasculature. Various methods, including nailbed capillaroscopy, laser Doppler flow monitoring, thermography, and plethysmography, have been used to evaluate distal digital vascularisation and to assess the microvascular damage.^{1–4} In studies using Doppler flowmetry and iontophoresis, patients with SSc showed reduced vasodilatory reserve of the skin microvasculature in response to ischaemia.^{5–6} A new colour Doppler ultrasound (DU) technique of the nail bed appears to be able to detect and quantify early vascular damage in patients with connective tissue disease.⁷ However, none of these methods has been generally introduced and accepted in clinical routine.

METHODS

This study aimed at assessing the digital blood flow of patients with SSc by DU. We compared the resistive indices (RIs) of 14 healthy subjects and 19 patients with SSc. Patients with SSc were classified as affected by limited SSc or diffuse SSc according to the criteria proposed by LeRoy *et al.*⁸ The measurements were performed with an Ultramark 9 HDI duplex Doppler ultrasound (HDI; Advanced Technology Laboratories) after at least 15 minutes of thermal acclimatisation in our ultrasound laboratory. A 10 MHz probe was used for visualising digital vessels (Doppler filter 100 Hz, minimal flow velocity 10 cm/s). The outcome variable was the RI of the distal palmar arteries (arteriae digitales palmares propriae) of the thumb and the forefinger of the right and left hand (dig I and II). The arteries were identified by colour DU. The Doppler samples were obtained at the distal part of the digital artery, and the RI was determined by analysis of the spectral waveforms (fig 1). The RI was calculated according to the standard formula:

$$RI = (\text{peak}_{SV} - \text{end}_{DV}) / \text{peak}_{SV}$$

where SV = systolic velocity; DV = diastolic velocity.

The RI of each of the digital arteries was determined in duplicate, and the mean of the resulting eight measurements was used for statistical analysis. Measurements were incomplete in seven patients with SSc, because it was impossible to identify all four digital arteries. In these seven patients we used the available measurements for statistical analysis. Statistical analysis was performed using the Mann-Whitney rank test.

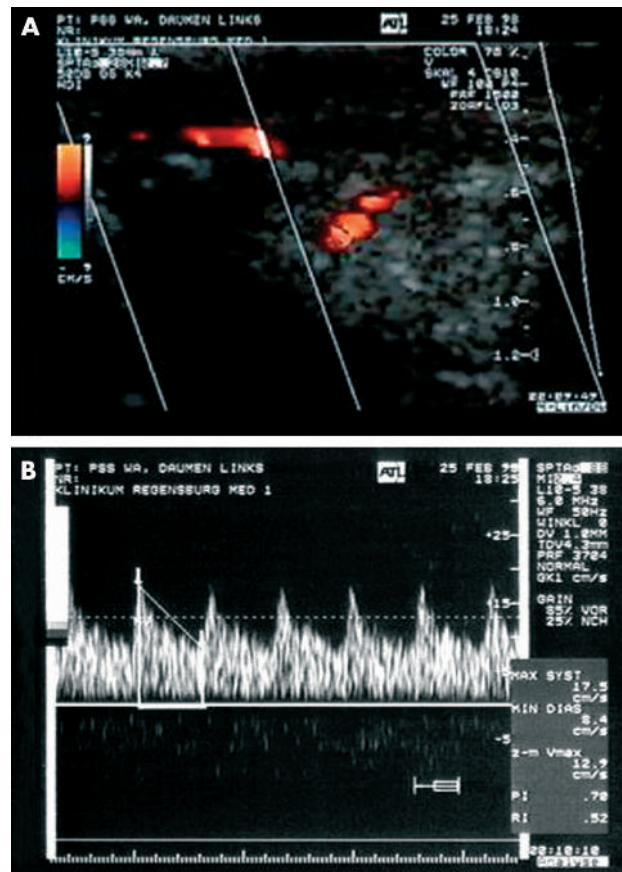


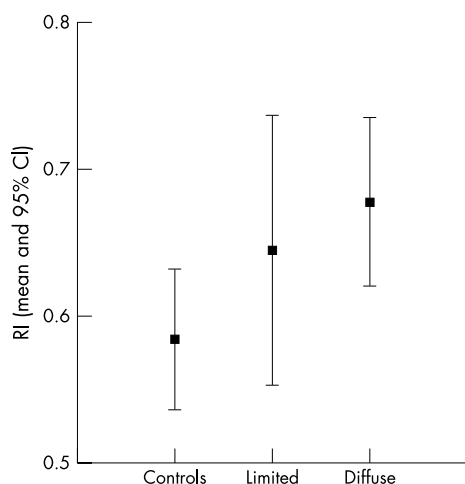
Figure 1 Picture of a colour Doppler ultrasound (A) and the associated spectral waveform (B) of the distal artery of the left thumb (patient with diffuse disease).

RESULTS

Table 1 shows the clinical characteristics of patients and controls. The mean of all measurements of all fingers showed a significantly higher RI for patients with SSc (limited and diffuse disease) (RI = 0.66) than for healthy controls (RI = 0.59; p = 0.01). However, there was a considerable overlap between the two groups. Individual digital analysis

Table 1 Patients characteristics

	SSc	Controls
Male	8	8
Female	11	6
Age (mean) years:		
Limited disease	50.3* (p=0.001)	30.9
Diffuse disease	44.2 (p=0.11)	
Raynaud's phenomenon	17	None
Unknown	1	None
Smoking	1	3
Unknown	1	None
Limited disease	10	—
Diffuse disease	9	—
Immunosuppressive drugs	3	None
Vasodilators	5	None

**Figure 2** Mean resistive indices and 95% confidence interval of all measurements of patients with limited disease (n = 10), diffuse disease (n = 9), and controls (n = 14).

showed that the mean of the RI of the left thumb ($p = 0.01$) and the right thumb ($p = 0.035$) were significantly higher in patients with SSc than in normal controls. In contrast, there was no significant difference between the right and left forefinger, and the RI of the individual fingers of the patients did not show a consistent correlation.

We analysed patients with diffuse and limited disease separately, and found no significant difference between healthy controls and patients with limited disease (fig 2). However, patients with diffuse disease showed a significantly

higher RI of the left thumb ($p = 0.005$), the right thumb ($p = 0.033$), the left forefinger ($p = 0.031$), the right forefinger ($p = 0.046$), and for the mean of all measurements ($p = 0.013$) in comparison with the healthy controls. In addition, no significant difference between the patients with limited and diffuse disease was found when calculating the mean of all measurements, but in individual digital analysis patients with diffuse disease showed a significantly higher RI of the right forefinger ($p = 0.04$).

In summary DU is an economic and simple non-invasive investigation technique, which may help to provide more information on the status of the digital microvasculature in patients with SSc. The increased RI values may reflect structural changes in digital arterial walls associated with a low vessel compliance, but, owing to the overlap of the RI between both groups, the diagnostic value of the RI measurements in the present group of patients was limited.

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REFERENCES

- Cafagna D**, Meloni F, Balbi M, Ponte E. Vascular manifestations in systemic sclerosis (scleroderma). *Minerva Med* 1989;**89**:153–61.
- La Civita L**, Rossi M, Vagheggini G, Storino FA, Credidio L, Pasero G, *et al*. Microvascular involvement in systemic sclerosis: laser Doppler evaluation of reactivity to acetylcholine and sodium nitroprusside by iontophoresis. *Ann Rheum Dis* 1998;**57**:52–5.
- Stafford L**, Englert H, Gover J, Bertouch J. Distribution of macrovascular disease in scleroderma. *Ann Rheum Dis* 1998;**57**:476–9.
- Herrick AL**, Clark S. Quantifying digital vascular disease in patients with primary Raynaud's phenomenon and systemic sclerosis. *Ann Rheum Dis* 1998;**57**:70–8.
- Wigley FM**, Wise RA, Mikdasi J, Schaefer S, Spence RJ. The post-occlusive hyperemic response in patients with systemic sclerosis. *Arthritis Rheum* 1990;**33**:1620–5.
- Goodfiel M**, Hume A, Rowell N. Reactive hyperemic responses in systemic sclerosis patients and healthy controls. *J Clin Invest Dermatol* 1989;**93**:368–71.
- Keberle M**, Tony HP, Jahns R, Hau M, Haerten R, Jenett M. Assessment of microvascular changes in Raynaud's phenomenon and connective tissue disease using colour doppler ultrasound. *Rheumatology (Oxford)* 2000;**39**:1206–13.
- LeRoy EC**, Black C, Fleischmajer R, Jablonska S, Krieg T, Medsger TA, *et al*. Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. *J Rheumatol* 1988;**15**:202–5.