Ankle brachial pressure index in systemic sclerosis: influence of disease subtype and anticentromere antibody

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Abstract

Objective. To test the hypothesis that patients with limited cutaneous systemic sclerosis (SSc) have a higher incidence of lower limb large vessel disease than patients with diffuse cutaneous disease, and that anticentromere antibody is a risk factor for lower limb large vessel disease.

Methods. Clinical and laboratory data from 119 patients with SSc (91 patients with limited cutaneous disease, 28 patients with diffuse cutaneous disease) who had bilateral ankle brachial pressure indices (ABPI) measured between March 1997 and January 2000 were reviewed retrospectively.

Results. There was no evidence of reduced ABPI in limited cutaneous disease (P = 0.65), average reduction 0.01 (95% confidence interval (CI) –0.04 to 0.07). There was some suggestion of reduced ABPI in anticentromere-positive patients (P = 0.12), average reduction 0.04 (95% CI –0.01 to +0.09).

Conclusions. The severity of large vessel macrovascular disease, as assessed by ABPI, is not dependent on disease subtype. Anticentromere antibody may be weakly associated with a reduction in ABPI.

Key words: Ankle brachial pressure index, Systemic sclerosis, Anticentromere antibody.
Hospital, Salford, who had had their ABPI checked between March 1997 and January 2000. The age, sex, drug treatment, smoking history, disease subtype, and anticentromere antibody status were documented. ABPI of both right and left lower limbs were measured. When ABPI had been checked more than once within the time frame of the study, the first value was considered. Any history of ischaemic stroke, intermittent claudication, and ischaemic heart disease was identified from the case notes.

**Non-invasive vascular assessment**

Peripheral circulation was assessed using a Hokanson CW 1 Doppler ultrasound machine with a 5 MHz probe. After a 5-min period of rest, the brachial artery pressure was measured in the supine position. The dorsalis pedis and posterior tibial pressures were then measured and ABPI calculated, using the highest value, by dividing ankle pressure by the brachial artery pressure. The normal value of ABPI is 1.0. Any value below 1.0 is abnormal and inversely proportional to the severity of peripheral vascular disease [11].

**Statistical analysis**

The lower ABPI in the left and right legs for each patient was used (two patients only had one measurement due to unilateral below knee amputation). Analysis of variance was used to compare groups, with adjustment for smoking where stated. ABPI values showed some non-normality due to a few particularly low values. However, when the effect of these extreme values was examined in a sensitivity analysis, the results were very robust.

**Results**

The demographic data of the 119 patients studied are given in Table 1. Seventy-one of these patients (50 of the 91 with limited and 21 of the 28 with diffuse cutaneous disease) were on vasodilator therapy. Five of the patients had intermittent claudication. All had limited cutaneous disease and four were anticentromere antibody positive, and one had had an ischaemic stroke (this patient was anticentromere negative). In addition, two of these five patients had had unilateral below knee amputations. Four patients had ischaemic heart disease—two with limited cutaneous disease (one anticentromere antibody positive) and two with diffuse cutaneous disease (one anticentromere antibody positive). Three patients had had an ischaemic stroke—two with limited cutaneous disease (one anticentromere antibody positive) and one with diffuse cutaneous disease.

Fourteen (12%) patients (11 patients with LCSSc and three patients with DCSSc) had an ABPI of less than 1.0 (either right or left lower limb).

**Age and smoking**

There was no association between age and ABPI ($r_s = -0.04$, $P = 0.65$). The median ABPI in smokers was 1.05 (range 0.36–1.33) and in non-smokers was 1.12 (range 0.75–1.38). Smoking was associated with a reduced ABPI ($P = 0.001$). The average reduction was 0.11 [95% confidence interval (CI) 0.05–0.17].

**LCSSc vs DCSSc (Fig. 1a)**

The median ABPI in patients with LCSSc was 1.1 (range 0.36–1.38) and in patients with DCSSc it was 1.1 (range 0.86–1.29). The analysis of LCSSc vs DCSSc was adjusted for the effect of smoking. There was no evidence of reduced ABPI in LCSSc ($P = 0.65$), average reduction 0.01 (95% CI $-0.04$ to $+0.07$).

**Effect of anticentromere antibody (Fig. 1b)**

The median ABPI in patients who were anticentromere antibody positive was 1.07 (0.36–1.38) compared with 1.11 (0.66–1.36) in those who were anticentromere antibody negative. After adjusting for the effect of smoking, there was some suggestion of reduced ABPI in anticentromere antibody-positive patients ($P = 0.12$), average reduction 0.04 (95% CI $-0.01$ to $+0.09$).

**Discussion**

Our study suggests that ABPI is not reduced in patients with LCSSc when compared with those with DCSSc. These findings therefore refute our original hypothesis that patients with limited cutaneous disease are at higher risk of lower limb large vessel disease than those with diffuse cutaneous disease.

From the findings of the present study we conclude that anticentromere antibody may be weakly associated with severity of large vessel disease, although differences in ABPI between patients who were anticentromere antibody positive and negative were not statistically significant. Anticentromere antibody positivity has been previously linked with severity of vascular disease [7, 8, 12] and interestingly not all of the six anticentromere-positive patients reported by Takahashi et al. [12] had definite SSc. However, from our previous work we believe that the higher prevalence of digital vascular problems in patients with limited cutaneous disease may relate largely to their more severe microvascular disease [9, 10]. Although the numbers with symptomatic large vessel disease were small, it is worth noting that four of

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**Table 1. Demographic data**

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 119)</th>
<th>LCSSc (n = 91)</th>
<th>DCSSc (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52 (26–83)</td>
<td>51 (26–83)</td>
<td>50 (28–75)</td>
</tr>
<tr>
<td>Male/female (%) males</td>
<td>21/98 (18)</td>
<td>12/79 (13)</td>
<td>9/19 (32)</td>
</tr>
<tr>
<td>No. of smokers (%)</td>
<td>23 (19)</td>
<td>17 (19)</td>
<td>6 (21)</td>
</tr>
<tr>
<td>Duration of Raynaud’s phenomenon (yr)</td>
<td>13 (0–66)</td>
<td>14 (0–66)</td>
<td>8 (0–55)</td>
</tr>
<tr>
<td>No. anticentromere antibody positive (%)</td>
<td>45 (38)</td>
<td>42 (46)</td>
<td>3 (11)</td>
</tr>
</tbody>
</table>

*Median (range).*
the five patients with intermittent claudication, two of the four patients with ischaemic heart disease, and one of the three patients with ischaemic stroke were anticentromere antibody positive, as compared with 38% of our overall cohort of 119 patients. Therefore, anticentromere antibody was over-represented in the symptomatic group, at least in those with intermittent claudication or ischaemic heart disease. Also, both the patients who had had below knee amputations were anticentromere antibody positive.

As anticipated, patients who smoked had lower ABPI than those who did not, but analyses of disease subtype and anticentromere antibody status were adjusted for smoking.

Previous studies which have systematically examined the macrovasculature of patients with SSC did not set out to compare patients on the basis of their disease subtype [4–6]. Youssef et al. [6] only studied patients with LCSSc. Our study suggests that disease subtype does not have a major influence on lower limb macrovascular disease. Our study was a retrospective study, and we are very aware that we did not have information on other risk factors for large vessel disease such as blood glucose and cholesterol. However, we have no reason to believe that blood glucose or cholesterol would be likely to differ between patients with limited or diffuse cutaneous disease.

Our study was purely a comparison of LCSSc and DCSSc, and it was not our purpose to make comparisons with a control population. While our prevalence of lower limb large vessel disease (12% of patients had an ABPI of less than 1.0) might appear low in comparison with other studies [4–6], it is not possible to draw conclusions about this without conducting a much more comprehensive study including a control population from northwest England, and this was outwith the scope of the current study. Similarly, it is not possible to compare the incidence of symptomatic macrovascular disease between studies because in our study this was identified purely by case note review, whereas Veale et al. [4] administered a claudication questionnaire in addition to reviewing the case notes. It is likely that in our population the prevalence of symptomatic large vessel disease has been underestimated.

Whether lower limb large vessel disease in SSC is atherosclerotic is currently an open question [5]. However, the possibility of less usual causes, such as vasculitis [13] or an antiphospholipid syndrome [14], should always be considered. Fortunately the necessity for lower limb amputation occurs rarely in patients with SSC [15] and only two of our patients had had below knee amputations.

In conclusion, the prevalence of lower limb macrovascular disease is likely to be similar in both subtypes of SSC. There may be a weak association with anticentromere antibody. The key point for the clinician is that digital ischaemia and ulceration in the patient with SSC may be due to large vessel as well as to small vessel disease and optimal management of the patient needs to take this into account.

References


