Ankle Brachial Pressure Index Measurement And Its Correlation To Claudication In Patients With Scleroderma

L Bichile, A Ravan, A Sonawale, V Chewoolkar

Citation

Abstract
Systemic sclerosis (SSc) is a generalized disorder of connective tissue characterized clinically by thickening and fibrosis of skin (scleroderma). Raynaud's phenomenon and microcirculatory abnormalities are well recognized manifestations of this disease. Macrovascular disease has a significant impact on the course of the disease and a major cause of morbidity in the form of claudication, loss of digit or limb or cardiovascular events. In our study of 62 patients, 47(75.80%) patients had symptomatic peripheral vascular disease (PVD) measured by Edinburgh claudication score where as prevalence of objective PVD in these patients as measured by ankle brachial pressure index (ABPI) was seen only in 31(50%) of the patients. An ABPI value of less than 0.9 was more closely associated with clinical claudication than the ABPI value of 1 in our study. 20 out of the 30 patients with a positive anticardiolipin antibody had an ABPI of <1 (p value = 0.0312) which is considered as significant. 12(65%) of the 19 dyslipidemic patients had an ABPI of <1 indicating a correlation between ABPI and dyslipidemia. Thus ABPI is a simple non invasive reproducible tool to assess PVD in patients with scleroderma.

INTRODUCTION
Systemic sclerosis (SSc) is a generalized disorder of connective tissue characterized clinically by thickening and fibrosis of skin (scleroderma) and by distinctive forms of involvement of internal organs like heart, lungs, kidneys and gastrointestinal tract. CREST syndrome, one of the form of SSc, which manifests as calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia. Raynaud's phenomenon and microcirculatory abnormalities are well recognized. Characteristic features include endothelial dysfunction, and hemorrhheological abnormalities. Interestingly, similar abnormalities are seen in patients with macrovascular disease secondary to atherosclerosis. If premature atherosclerosis is a feature of SSc, this would have significant implications in terms of patient treatment as it may contribute to their premature mortality. Systemic sclerosis is often of tragic consequences to the patient. Morbidity and mortality are substantial and directly related to the extent and severity of organ involvement. Although much is available for supportive care of individuals in systemic sclerosis, there are no therapies known to modify the natural history of the disease.

MATERIALS AND METHODS
This is a monocentric, prospective study involving one point assessment of ABPI and claudication in 62 patients of Systemic sclerosis. Ethics Committee approval was obtained [Protocol no. EC/36/2006, approved on 2nd August 2006 (Ref. letter no. EC/OUT/544/2006)] before commencement of the study. 62 outdoor and indoor patients of either sex, above 18 years of age, attending the Rheumatology Clinic of K.E.M. Hospital were enrolled after obtaining a written informed consent.

INCLUSION CRITERIA
Patients between 18-60 years fulfilling the ACR (American College of Rheumatology) criteria, for SSc (diffuse cutaneous and limited cutaneous disease) were enrolled.

EXCLUSION CRITERIA
1. Patients with features of overlap syndrome.
2. Patients with rheumatological conditions other than scleroderma.
3. Patients below 18 years of age
4. Patients with exposure to vinyl chloride, chemotherapeutic agents, vibration injuries.
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STUDY PARAMETERS
Patient underwent clinical examination, immunological and laboratory work up. Ankle brachial pressure index was measured in all of them. Edinburgh claudication score questionnaire was administered. Patients underwent estimation of IgM and IgG anti cardiolipin antibodies (ACLA) [NR 8-11MPLU/ml & 8-11 GPLU/ml respectively] along with routine hematological, biochemical and lipid profile.

MEASUREMENT OF ABPI
ABPI was measured by mini Doppler (EMCO D500 MINIDOP, EMCO MEDITEK). ABPI is calculated as the posterior tibial artery pressure in mm Hg divided by the brachial artery pressure. The normal ABPI is 1.0 and any value <1.0 was considered to be abnormal, 8 with the severity of arterial disease being inversely proportional to the ABPI. 9

ASSESSMENT OF CLAUDICATION
Grading of claudication was calculated as per the Edinburgh claudication questionnaire. 10 The data was tabulated taking into consideration the values of ABPI, lipids, ACLA and clinical status of the patient, whether claudicant or non-claudicant.

We compared the following observations:
- ABPI and claudication
- ACLA and claudication
- ABPI and lipid levels.

Fischer's Exact Test was used to find the correlation between the above stated parameters using 'Graph Pasd InStat' online module.

RESULTS
62 patients [58 females (93.84%), 4 males (6.16%)] of with average age 31.7 years fulfilling ACR criteria were enrolled (Graph 1).

Graph 1: Age distribution of patients with scleroderma

47 patients were symptomatic for claudication on Edinburgh claudication score. Objective prevalence of PVD as assessed by ABPI was seen in only 50% (31/62) of these patients. ABPI values were <1 in 32 patients and >1 in 30 patients. 8 patients had ABPI value <0.9 and 7 of these were symptomatic with claudication, thus indicating that a value <0.9 is associated with clinical claudication than ABPI value of 1 in our study. No statistically significant correlation between the ABPI and claudication was found (p value 0.2753).

In 46 patients, ACLA levels were available. ACLA (IgM and IgG) levels were increased in 30/46 patients. 20/30 patients with high ACLA levels had an ABPI of <1 (P value = 0.0312). Thus ACLA levels correlated with lower ABPI value and claudication.

Figure 1

Figure 2

Table 1: Relationship between ACLA and ABPI

<table>
<thead>
<tr>
<th>ABPI</th>
<th>ACLA positive</th>
<th>ACLA negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>&lt;1</td>
<td>10</td>
<td>21</td>
</tr>
</tbody>
</table>

Figure 3

Table 2: Relationship between dyslipidemia and ABPI

<table>
<thead>
<tr>
<th>Dyslipidemic</th>
<th>Non Dyslipidemic</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABPI &gt;1</td>
<td>22 (65.5%)</td>
<td>31 (50%)</td>
</tr>
<tr>
<td>ABPI &lt;1</td>
<td>7 (21.25%)</td>
<td>9 (15%)</td>
</tr>
</tbody>
</table>

19/56 were dyslipidemic and 12 of the 19 had ABPI <1. This shows that a significant number of dyslipidemic patients had
ABPI<1.

**Figure 4**

Table 3: Disease duration v/s claudication

<table>
<thead>
<tr>
<th>Disease duration (years)</th>
<th>Claudicant</th>
<th>None-claudicant</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>5-9.9</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>10-14.9</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>15-19</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>20-24.9</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>≥25</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

There was no significant correlation between the disease duration and the presence of claudication (P value = 0.3431). This can be attributed to different stages of disease, disease duration and treatment at the time of enrollment.

**DISCUSSION**

Scleroderma manifests as skin thickening, which is a result of the fibrosis of connective tissue of the skin. The fibrosis also includes small and large arteries. Fibrosis leads to the narrowing of the arteries thus resulting in obliteration, which ultimately causes claudication in these patients. Study by Veale DJ et al has demonstrated a 22% prevalence of symptomatic peripheral arterial obstructive disease in scleroderma patients. Screening of these patients may allow identification of “at risk” patients at an early stage and allow therapeutic intervention to attenuate the high rate of cardiovascular mortality in these patients. Peripheral vascular disease is often accompanied by altered ABPI value, which is a non-invasive test and also a marker of the progression of the disease. A study has shown that ABPI is more sensitive in detection of the PVD. Hence ABPI value can be useful in the measurement of the vascular disease progression in SSc patients.

A cohort study by Bryan C et al demonstrated a fourfold increase in mortality rate (using standardized mortality ratio) in patients with SSc compared with their unaffected counterparts. Twenty nine percent of deaths were attributable to cardiovascular causes. This was almost five times greater than the 4.5% prevalence of symptomatic peripheral vascular disease seen in the general population as detected by the WHO claudication Questionnaire, which is similar to Edinburgh Questionnaire. Stafford et al identified excess ulnar artery disease in SSc. Mckenna et al showed that the low ratio of ankle to brachial blood pressures carries a very poor prognosis and should prompt investigation and treatment of atherosclerotic disease in other vascular systems. The Edinburgh Claudication Grading Questionnaire which is a method of the subjective evaluation of the disease has a specificity of 95%. Evaluation of our patients by this questionnaire revealed that there is a high prevalence of peripheral vascular disease amongst patients of scleroderma. In our study 75.8% of the patients had symptomatic PVD.

There is a relation between claudication and ACLA value. ACLA is one of the antiphospholipid antibodies known to contribute to peripheral vascular disease due to availability of beta 2 GP1 receptors. We found that the lower values of the ABPI correlate directly with the ACLA value. 80% patients with the positive ACLA had ABPI less than 1. Hence ABPI is proved to be the good early diagnostic measure for the measurement of the PVD SSc patients.

Low ABPI values correlate directly with peripheral ischemia. This was evident in 8 of our patients who had an ABPI value of less than 0.9. Further 7 (87%) of them were claudicant establishing a correlation between low ABPI and symptomatic claudication. Thus ABPI can serve as an early diagnostic tool for the measurement of the peripheral vasculopathies including scleroderma, saving the loss of the limb and digits (Figure 1 & 2).

**Figure 5**

Figure 1: Foot amputation in patient with scleroderma with peripheral vascular disease.
SSc is associated with rise in the serum lipid level due to the rise in anti-lipoprotein lipase antibodies and hypothyroidism. Studies have shown that there is increase susceptibility to oxidation of low-density lipoproteins isolated from patients with SSc, which further contributes to atherosclerosis and associated symptoms.

CAVEATS
This study considers one point assessment of ABPI in patients of scleroderma. As the patients were at different stages of disease, they had a wide range of ABPI from 0.63 to 1.30. Patients were also on different groups of drugs like calcium channel blockers, angiotensin converting enzyme inhibitors, statins and antplatelet agents like aspirin and clopidogrel. This could have led to variability in the ABPI values as well as claudication score. Further studies would be needed with the group of patient being classified into the types of SSc which are ‘diffuse’ and ‘limited cutaneous’. Also there is need for studies with the possible exclusion of confounding factors like diabetes, hypertension, smoking and use of vasodilators. Study should also include controls amongst the general population as control to generalize the statement on occurrence of PVD in SSc patients.

CONCLUSIONS
- Peripheral vascular disease exists in scleroderma.
- Macrovascular affection leads to claudication.
- ABPI is a simple, non invasive & reproducible tool to assess PVD in patients with scleroderma.
- No statistically significant correlation between the ABPI and claudication was observed in our study.
- Dyslipidemia and positive ACLA status contributes to symptomatic peripheral vascular disease.
- Periodic assessment of ABPI would throw light on therapeutic efficacy in symptomatic vascular disease.

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References
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