Table 1 Number of deaths and malignancy in patients with SLE treated with azathioprine

Azathioprine (years of treatment)	n	Died No (%)	Lost to follow up No (%)	Malignancy No (%)
<1	38	5 (13)	0	0
1–4	55	10 (18)	2 (4)	5 (9)
5–9	40	11 (28)	0	3 (8)
≥10	15	1 (7)	0	0

between 1 and 4 years and 3 for between 5 and 9 years. The two patients lost to follow up had been receiving azathioprine treatment for 3 and 4 years at that time.

We have been unable to locate any publications examining azathioprine related complications in the treatment of patients with SLE. In rheumatoid arthritis and in Sjögren's syndrome, however, it has been linked with lymphoma development.[1 3 4]

We conclude that although azathioprine seems to be a safe second line agent for the treatment of patients with SLE larger and longer term studies are needed to confirm these findings.

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Bone mineral density in patients with systemic sclerosis

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Generalised radiological osteopenia has been seen to occur in a significant percentage of patients with systemic sclerosis (SSc).[1 2] Bone mineral content was found to be reduced at the radius,[3–5] lumbar spine, and the total body.[5] No data are available on quantitative ultrasound (QUS) evaluation of bone in patients with SSc.

PATIENTS AND METHODS

In this study, bone mineral density (BMD) and stiffness index (SI) were measured in patients with SSc not treated with steroids to investigate the presence of systemic osteoporosis.

Forty seven women (mean age 53.9 years (range 32–77)) affected with SSc were investigated: 20 were premenopausal (preSSc) and 27 postmenopausal (postSSc). All the patients satisfied the preliminary American Rheumatology Association criteria indicated in the classification of progressive SSc.

The control group consisted of 50 healthy female subjects: 23 premenopausal (prenorm) and 27 postmenopausal (postnorm). The exclusion criteria were treatment with corticosteroids, immunosuppressant drugs, hormone replacement therapy, thyroxine, and bone regulating drugs and the presence of demineralising diseases.

A detailed history was taken of each patient, with particular reference to age, menopausal status, disease duration, current or previous treatments, and current or previous diseases; their height and weight were measured and related by the body mass index ratio. There were no significant differences between groups. The following serological markers were determined: antinuclear antibodies, anticentromere antibodies, anti-extractable nuclear antigen, including anti-Scl70, -Sm, -RNP, -SSB, -SSA, and Jo-1.

Examinations were also carried out to determine the extent of any internal organ involvement. The patients were divided into three groups based on the extent of cutaneous involvement[6]: limited, intermediate, and diffuse. BMD (total body, lumbar spine, and femur neck) was evaluated by fan beam *x* ray Lunar Expert, version 1.72. The SI (derived from broadband ultrasound absorptiometry and speed of sound) was evaluated by quantitative ultrasonometry of the heel using the Lunar Achilles Plus. T scores (the difference between the BMD of the patients and that of young healthy adults corrected for the standard deviation) were used in dual *x* ray absorptiometry and QUS.

RESULTS

The results of this study show that bone mass was reduced in patients with SSc. BMD, expressed in g/cm^2, was significantly less in the SSc subgroups than in controls (lumbar spine BMD: 1.309 prenorm *v* 1.159 preSSc, $p<0.05$; 1.193 postnorm *v* 0.952 postSSc, $p<0.01$; neck femur BMD: 1.010 prenorm *v* 0.938 preSSc, $p<0.05$; 0.904 postnorm *v* 0.816 postSSc, $p<0.01$; stiffness: 100.0 prenorm *v* 72.0 preSSc, $p<0.05$; 91.0 postnorm *v* 78.2 postSSc, $p<0.05$). T scores were lower in the SSc subgroups than in controls. The reduction in bone mass was more marked in the lumbar spine and heel. It is known that these two sites are, respectively, partially and completely trabecular. SSc related osteoporosis thus seems to have the typical characteristics of postmenopausal osteoporosis.

Many studies suggest that QUS is useful in investigating bone quality.[7] In our patients the prevalent impairment of stiffness at the heel also provided an additional indication for the presence of a qualitative alteration in the trabecular microarchitecture.

BMD was not significantly different in patients with normal or altered indices of inflammation and in patients with absence or presence of specific autoantibodies. BMD and SI were reduced in women with the diffuse form of skin involvement and in women with one or more internal organs affected (table 1). A previous study reported that bone mass was related to the extent of skin involvement but did not evaluate the extent of visceral involvement.[5] Many authors

Table 1 Bone mineral density (g/cm^2) in women with SSc categorised according to the extent of disease

	Cutaneous disease Mean (SD)			Internal organs affected Mean (SD)	
	Limited (n = 15)	Intermediate (n = 14)	Diffuse (n = 18)	Absent) (n = 21	Present (n = 26)
Total body	1.104 (0.088)	1.085 (0.089)	1.021* (0.077)	1.099 (0.084)	1.024* (0.070)
Lumbar spine	1.038 (0.161)	1.025 (0.141)	0.945* (0.133)	1.032 (0.139)	0.950* (0.144)
Femur neck	0.831 (0.112)	0.886 (0.119)	0.787** (0.102)	0.881 (0.139)	0.790* (0.148)
Os calcis	89 (13.7)	87 (13.7)	63* (10.9)	88 (12.5)	65* (11.2)

*$p<0.05$ (SSc *v* control); **$p<0.01$ (SSc *v* control).

suggest that the extent of skin involvement is directly related to the extent of visceral involvement and to the severity of the disease.[8–10]

In the patients as a whole, a logistical model was prepared in which the presence of osteoporosis (a T score below −2.5) in at least one skeletal site was the dependent variable. In this model the age of the subject, years since menopause, and body mass index were all significantly associated with osteoporosis.

In conclusion our data suggest that bone mass, bone density, and bone quality are altered in patients with SSc with the diffuse form of skin disease and/or at least one internal organ affected.

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