Anticentromere antibody, disease duration and history of surgical debridements predict calcinosis in patients with systemic sclerosis

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Background

Calcinosis (subcutaneous deposition of calcium salts, occurring predominantly over pressure points), is a characteristic feature of systemic sclerosis (SSc), occurring in 20-40% of patients [Figure 1]. It can also be associated with significant pain and disability.

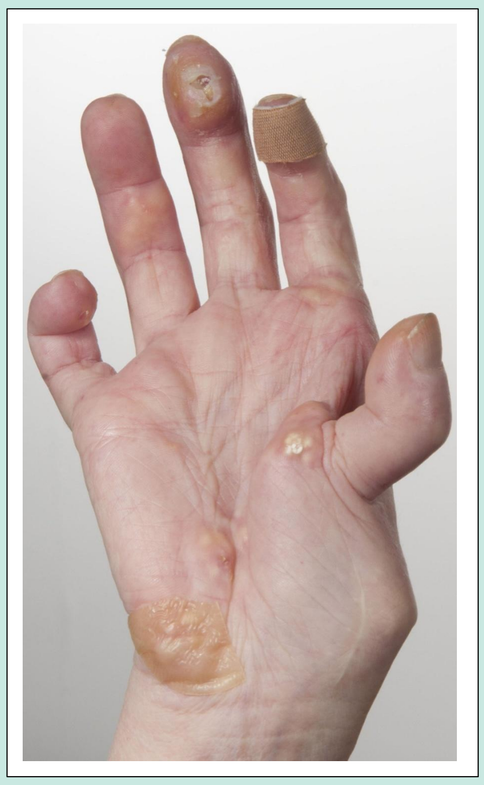

Figure 1: Calcinosis affecting the digits and hand

Aim

- To examine clinical and serological associates of SSc-related calcinosis, and whether it is possible to build a model to predict presence of calcinosis.

Methods

- This was a cross-sectional study of patients with SSc attending a tertiary referral centre. Clinical and demographic features were reviewed.

The variables examined were:

- age
- gender
- disease subtype
- duration of SSc
- previous intravenous prostanoid infusions
- surgical debridement and/or amputation
- autoantibody status (anticentromere and antitopoisomerase)
- pulmonary fibrosis
- pulmonary hypertension.

- Logistic regression was used to investigate associations between demographic and clinical factors and the odds of clinical calcinosis. Variables of interest were then combined in a multiple regression model to obtain adjusted odds ratios and confidence intervals.

Results

- 317 patients (86% female, median age 60 years, range 24-91)

- 94(30%) had clinically apparent calcinosis.

- Age distribution, and gender, were similar in those with and without calcinosis.

- Although a number of predictors suggested themselves during exploratory analysis of the data, only surgical debridements, anticentromere status and disease duration remained significant after adjusting for other variables [Table 1].

Characteristic	Calcinosis Present N = 94	Calcinosis Not Present N = 223	All patients N = 317
Age (years)	60.2 53.6 to 67.0 24.3 to 91.3	59.9 51.2 to 68.7 26.1 to 85.5	59.9 51.7 to 68.0 24.3 to 91.3
Sex (female)	86 (91.5)	186 (83.4)	272 (85.8)
Subtype (diffuse)	16 (17.0)	62 (27.8)	78 (24.6)
History of amputations	11 (11.7)	11 (4.9)	22 (6.9)
History of IV vasodilators	38 (40.4)	63 (28.3)	101 (31.9)
Debridements (Yes)*	29 (30.9)	19 (8.6)	48 (15.2)
Anticentomere positive	51 (54.3)	71 (31.8)	122 (38.5)
Pulmonary fibrosis	27 (28.7)	76 (34.1)	103 (32.5)
Hx digital iscaemia**	42 (44.7)	65 (29.1)	107 (34.4)
Organ involvement (pulmonary hyper)*	10 (10.6)	17 (7.7)	27 (8.5)
Scl70 positive*	8 (8.5)	41 (18.4)	49 (15.5)
Duration since 1st non-Raynaud's primary manifestation (years)*†	15.9 10.8 to 21.2 2.1 to 55.6	10.7 3.7 to 16.0 0.3 to 45.5	11.5 5.5 to 18.3 0.3 to 55.6

Table 1: Summary of the patients by calcinosis status. Median / IQR/ range for continuous variables, n (%) for categorical variables.

**Covariate information missing for 1 patient.*
***Covariate information missing for 6 patients.*

Table 2:

Factor	Adjusted Odds Ratio	P-value	95% Confidence Interval
Sex (female)	0.71	0.46	(0.29 , 1.76)
Subtype (diffuse)	1.16	0.70	(0.55, 2.46)
History of amputations	0.96	0.94	(0.35, 2.68)
History of IV vasodilators	1.20	0.56	(0.65, 2.21)
Debridements (yes)	3.39	0.001**	(1.61, 7.13)
Anticentomere positive	2.28	0.01**	(1.24, 4.21)
Scl70 positive	0.73	0.51	(0.29, 1.86)
Duration since 1st non-Raynaud's manifestation (years)	1.08	<0.001 ***	(1.04, 1.11)

Table 2: Adjusted odds ratios, 95% CIs and p-values from multiple logistic regression analysis

**p < 0.10 ** p < 0.05 ***p < 0.01*

Therefore:

- A patient who had had debridements was more likely to have calcinosis compared to one who had not (OR [95% CI]: 3.39 [1.61 to 7.13]) [Figure 2]

- a patient who had anticentromere positivity was more likely to have calcinosis compared to one who had not (OR [95% CI]: 2.28 [1.24 to 4.21]) [Figure 3]

- the odds of having calcinosis increased by 8% (CI, 4 to 11%) for each year since diagnosis.

The specificity of the model was high (correctly classifying a patient who did not have calcinosis 91% of the time), but the sensitivity was relatively low, correctly classifying a patient who did have calcinosis only 35% of the time.

Figure 2:

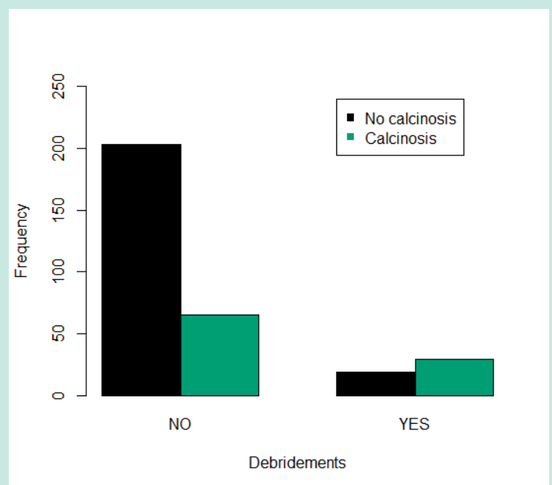

Figure 2: Calcinosis status of patients with and without debridements

Figure 3:

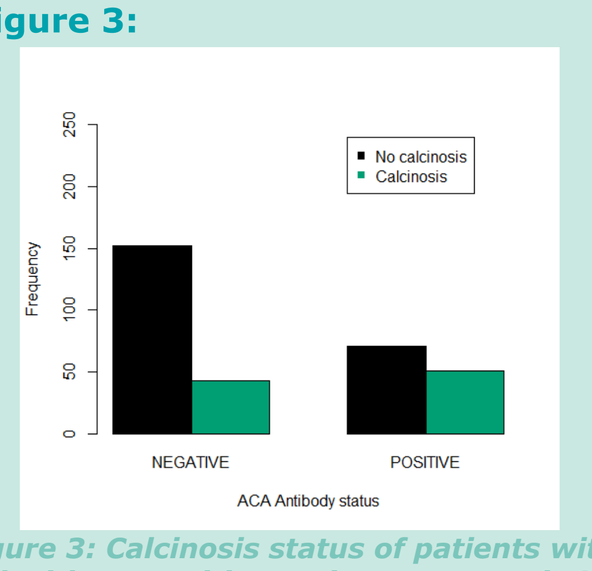

Figure 3: Calcinosis status of patients with and without positive anticentromere (ACA) antibody

Conclusions

- History of surgical debridement, positive anticentromere antibody and disease duration were predictors of calcinosis. The low sensitivity of a multiple regression model suggests there are other important predictors of calcinosis that have not been accounted for in this analysis.