Systemic sclerosis and breast implants: associations between anti-RNA polymerase III antibodies and implant complications

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ABSTRACT

Objective. *To assess the potential association between systemic sclerosis (SSc) and breast implants, with particular attention to the temporal relationship with disease onset, autoantibody status, and implant-related complications.*

Methods. *We conducted a retrospective cohort study of all patients evaluated for SSc at a tertiary referral centre between 1998 and 2026. Patients with breast implants were identified through electronic health record searches. Demographic, clinical, immunological, and implant-related data were collected.*

Results. *Among 3138 patients with SSc in the whole cohort, sixty-five patients with SSc and breast implants were identified. Of these, 58 had undergone implantation prior to SSc onset, with a median interval of 8.6 years. A higher prevalence of anti-RNA polymerase III antibodies (ARA) was observed (32.8%).*

Implant-related complications occurred in 41.7% of patients, most commonly rupture and lymphadenopathy, and frequently preceded SSc onset (29.2%). Compared with ARA-negative patients, ARA-positive patients were more likely to have implant-related complications (OR 4.32, 95% CI 1.26–14.84; p=0.032) and to have undergone explantation (OR 3.49, 95% CI 1.05–11.57; p=0.043) prior to SSc onset. No synchronous cancer was identified among ARA-positive patients.

Conclusion. *In this retrospective cohort of patients with SSc, breast implants and implant-related complications frequently preceded disease onset and were associated with ARA positivity. These findings indicate a temporal and clinical association but do not establish causality. Further multicentre prospective studies are required to confirm these observations.*

Introduction

Systemic sclerosis (SSc) is a rare connective tissue disease characterised by inflammation, vasculopathy and fibrosis of the skin and internal organs (1). Its aetiology is complex and involves both genetic susceptibility and environmental exposures. Among these, silica exposure is the most consistently reported, with case-control studies showing an increased risk (2).

Amorphous silica compounds are widely used in medical-grade materials, including silicone breast implants (3). Since the introduction of cosmetic breast implants, potential associations with autoimmune diseases, particularly SSc, have been suggested (4).

Previous case reports and case series have described a higher prevalence of anti-RNA polymerase III antibodies (ARA) in affected patients (5). ARA positivity has also been linked to implant rupture, independent of its established paraneoplastic association (6, 7). However, evidence from larger observational studies remains inconclusive. A meta-analysis reported no significant association between breast implants and SSc (8), and several case–control studies have yielded similar negative findings (9).

Given these conflicting findings, the relationship between SSc and breast implants remains uncertain. The aim of this study was to reassess this association, with particular focus on temporal relationships, autoantibody status, and implant-related complications.

Material and methods

All patients with SSc evaluated at the

Centre for Rheumatology between 1998 and January 2026 were included. Patients with breast implants were identified through systematic searches of clinical correspondence using the search terms "breast implant", "breast augmentation", and "breast prosthesis". Electronic clinical records were also screened using ICD codes for breast implants and CT reports were searched using the Boolean terms ("systemic sclerosis" OR "scleroderma" OR "SSc") AND ("breast implant" OR "breast augmentation" OR "breast prosthesis"). A separate subgroup of patients evaluated at the same centre who did not fulfil systemic sclerosis classification criteria was analysed separately and not included in the primary cohort.

Data were extracted from clinical records, and additional information was obtained by telephone contact with patients. The following variables were collected: sex; age at SSc onset, and breast implantation; skin subset; autoantibody profile; baseline skin score; overlap syndromes; major organ involvement [as defined in previous SMART cohort studies (10)]; treatment at diagnosis; implant characteristics (laterality, indication, type, placement, and complications); and outcomes, including cancer and mortality.

The study was approved by the London-Fulham NHS Research Ethics Committee (IRAS ID 279682), and all patients provided written informed consent.

The primary objective was to assess the potential association between SSc and breast implants. Patients with and without breast implants were compared across clinical and immunological variables. In addition, a subgroup analysis restricted to ARA-positive patients evaluated breast implant status and cancer phenotype, including synchronous (within 1-2 years of SSc diagnosis) and non-synchronous cancer, as well as absence of both breast implants and cancer. Together, these analyses aimed to further define the phenotype of SSc associated with breast implants. Categorical variables are presented as counts and percentages, and continuous variables as median and interquartile range (IQR). Group comparisons were performed using Fisher's exact test for categorical variables. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Statistical analyses were conducted using R software (version 4.5.2).

Results

In our cohort of 3,138 patients with SSc, 2,605 were female (83.0%), and 65 of them (2.5%) had a history of breast implantation. Among these, 58 underwent implantation prior to SSc onset, whereas 7 received implants after diagnosis.

Patients implanted prior to SSc onset

Among patients implanted prior to SSc onset, all were women and 29.3% had a history of smoking. The distribution of SSc subtypes was similar, with 51.7% limited cutaneous disease and 48.3% diffuse (Table I).

Breast implantation was performed at a median age of 32.8 years (IQR 23.3–40.6), whereas SSc was diagnosed at 45.3 years (IQR 36.4–55.2), corresponding to a median interval of 8.6 years (IQR 6.1–16.5).

Regarding immunological characteristics, ARA were the most frequent (32.8%), followed by anti-centromere antibodies (25.9%) and anti–Scl-70 antibodies (19.0%). Other specificities were rare, and 5.2% of patients were ANA/ENA-negative. Additional data on overlap syndromes, organ involvement, and treatment are presented in Table I.

Implant characteristics and complications

Most implants were bilateral (92.7% of 55), placed for cosmetic indications (93.0% of 57), and silicone-based (92.1% of 38). Submuscular placement was the most common surgical approach (71.9% of 32) (Table I). A small number of patients (n=3) reported systemic symptoms shortly after implantation, including alopecia, sicca symptoms and gastrointestinal complaints.

Among the 48 patients with available data on complications, 20 (41.7%) developed implant-related complications. The most frequent complications were implant rupture (35.4%) and axillary lymphadenopathy (16.7%), as well as infection (6.3%). Other adverse effects, including capsular induration, breast lumps, and calcifications, were infrequent.

Most complications (29.2%) occurred prior to SSc onset. Implant rupture preceded SSc in 27.1% of patients, with a median interval of 5 years (IQR 1.5–12.3) before diagnosis. Similarly, axillary lymphadenopathy was diagnosed before SSc onset in 12.5% of patients, most often concurrently with implant rupture.

Explantation was performed in 50.0% of patients, including 35.4% prior to SSc onset. In these patients, the median interval between explantation and SSc diagnosis was 6.3 years (IQR 3.9–11.5). Reimplantation occurred in 25.0% of patients, predominantly before disease onset (22.9%). Only one patient reported improvement in SSc symptoms following explantation.

Overall, 39.6% of patients experienced at least one event (rupture, lymphadenopathy, or explantation) prior to SSc onset.

Cancer history

Ten patients (17.2%) had a history of malignancy (only one synchronous cancer), including six with breast cancer. Among patients with breast cancers, four underwent reconstructive surgery, while two had implants prior to cancer.

Association with ARA positivity

In ARA-positive patients, implant surgery preceded the onset of systemic sclerosis by a median of 11.7 years (IQR 7.7–20).

Compared with the ARA-negative within patients with breast implants before SSc, ARA positivity was associated with scleroderma renal crisis (OR 13.6, 95% CI 1.5–127.5; p=0.006).

Additionally, ARA positivity was associated with implant-related complications (OR 4.32, 95% CI 1.26–14.84; p=0.032) and explantation (OR 3.49, 95% CI 1.05–11.57; p=0.043) prior to SSc onset. Implant rupture showed a similar trend but did not reach statistical significance (Table II).

Table I. Characteristics of patients with breast implants before systemic sclerosis onset.

Variable	Value (n=58)
Patient characteristics	
Female, n (%)	58 (100.0)
Smoking history, n (%)	17 (29.3)
Systemic sclerosis characteristics	
Subtype	
LSSc, n (%)	30 (51.7)
DSSc, n (%)	28 (48.3)
Antibody specificity	
Anti-RNA polymerase III, n (%)	19 (32.8)
Anticentromere, n (%)	15 (25.9)
Anti-topoisomerase I, n (%)	11 (19.0)
Other SSc-related antibodies (PM/Scl, U3-RNP, Ro) (n=2 each), n (%)	2 (3.4)
mRSS at diagnosis	
LSSc (n=29), median [IQR]	2 [0.5–4.5]
DSSc (n=24), median [IQR]	16 [12.5–21.0]
Overlap syndrome	
Polymyositis, n (%)	4 (6.9)
Rheumatoid arthritis, n (%)	3 (5.2)
Eosinophilic fasciitis, myositis, and Sjögren's disease (n=1 each), n (%)	1 (1.7)
Organ involvement	
ILD, n (%)	21 (36.2)
Time from SSc onset to ILD, years, median [IQR] (n=11)	0.3 [0.0–2.5]
SRC, n (%)	7 (12.0)
Time from SSc onset to SRC, years, median [IQR] (n=5)	0.5 [0.2–0.8]
PH, n (%)	5 (8.6)
Time from SSc onset to PH, years, median [IQR] (n=3)	5.1 [1.5–7.0]
Cardiac involvement, n (%)	2 (3.4)
Treatment at diagnosis (individual drugs)	
MMF, n (%)	29 (52.6)
HCQ, n (%)	13 (22.8)
GC and MTX (n=8 each), n (%)	8 (14.0)
ATG, AZA, CYC, and TCZ (n=1 each), n (%)	1 (1.8)
Treatment combinations at diagnosis	
MMF in monotherapy, n (%)	16 (28.1)
HCQ + MMF, n (%)	7 (12.3)
HCQ in monotherapy, n (%)	6 (10.5)
GC + MMF, n (%)	4 (7.0)
MTX in monotherapy, n (%)	4 (7.0)
Breast implant characteristics	
Time from implants to SSc onset, years, median [IQR] (n=48)	8.7 [6.1–16.5]
Laterality (n=55)	
Bilateral, n (%)	51 (92.7)
Unilateral, n (%)	4 (7.3)
Indication (n=57)	
Cosmetic, n (%)	53 (93.0)
Reconstruction, n (%)	4 (7.0)
Type (n=38)	
Silicone, n (%)	35 (92.1)
Saline, n (%)	3 (7.9)
Placement (n=32)	
Submuscular, n (%)	23 (71.9)
Subglandular, n (%)	9 (28.1)
Implant complication (n=48), n (%)	20 (41.7)
Explant (n=48), n (%)	24 (50.0)
Reimplant (n=48), n (%)	12 (25.0)
Outcomes	
Malignancy, n (%)	10 (17.2)
Death, n (%)	10 (17.2)

Data are presented as n (%) unless otherwise indicated.
ATG: antithymocyte globulin; AZA: azathioprine; CYC: cyclophosphamide; GC: glucocorticoids; dSSc: diffuse cutaneous systemic sclerosis; HCQ: hydroxychloroquine; ILD: interstitial lung disease; lSSc: limited cutaneous systemic sclerosis; MMF: mycophenolate mofetil; mRSS: modified Rodnan skin score; MTX: methotrexate; PH: pulmonary hypertension; SRC: scleroderma renal crisis; SSc: systemic sclerosis; TCZ: tocilizumab.

When considering all events irrespective of timing, these associations remained significant, and implant rupture also reached statistical significance (OR 3.49, 95% CI 1.05–11.57; p=0.043) (Supplementary Table S1).
No synchronous cancer was identified in ARA-positive patients with breast implants.
No significant differences were observed in age, other organ involvement, implant characteristics, or mortality (data not shown).

Subgroup analyses (overall SSc cohort)
Considering all patients in the entire cohort, compared with patients without breast implants, those with implants had higher frequencies of diffuse SSc (48.3% *vs*. 32.6%, p=0.016), as well as higher prevalence of ARA positivity (32.8% *vs*. 9.3%, p<0.001) and scleroderma renal crisis (12.1% *vs*. 3.8%, p=0.007) (Table III).
Breast implant surgery was more frequent among ARA-positive patients compared with patients with other autoantibody specificities (19/309 (6.1%) *vs*. 39/2829 (1.4%), p<0.001).
Among ARA-positive patients in the overall cohort, we compared four groups: patients with breast implants prior to SSc (n=19), synchronous cancer (n=8), non-synchronous cancer (n=32), and patients without breast implants or cancer (n=250). Patients with breast implants were diagnosed with SSc at a younger age compared with synchronous cancer (44.2 (IQR 35.6–52.0) vs 57.5 (IQR 52.1–65.3), p=0.011). No other differences were found among clinical and immunological variables (Supplementary Table S2).

Patients implanted after SSc onset
Among patients implanted after SSc (n=7), most had diffused skin disease (57.1%), with anti-Scl-70 (42.9%) and ARA (28.6%) the most frequent antibodies; 71.4% had a history of breast cancer.
In an additional subgroup of patients evaluated at the same Centre for Rheumatology who did not meet classification criteria for SSc (11), ten patients had a breast implant before developing

Table II. Implant complications in anti-RNA polymerase III-positive *vs*. negative patients.

Outcome	ARA positive (n=19)	Negative patients (n = 29)	OR (95% CI)	*p*-value
Before systemic sclerosis onset				
Rupture, n (%)	8 (42.1)	5 (17.2)	3.49 (0.93–13.20)	0.070
Axillary lymphadenopathy, n (%)	3 (15.8)	3 (10.3)	1.63 (0.31–8.70)	0.540
Infection, n (%)	2 (10.5)	0 (0.0)	8.43 (0.40–177.00)	0.110
Any complication, n (%)	9 (47.4)	5 (17.2)	4.32 (1.26–14.84)	0.032
Explant, n (%)	10 (52.6)	7 (24.1)	3.49 (1.05–11.57)	0.043
Reimplant, n (%)	6 (31.6)	5 (17.2)	2.21 (0.57–8.67)	0.230

Data are presented as n (%).
Only patients with breast implants and documented implant-related complications preceding the onset of systemic sclerosis were included in the analysis.
Any complication includes rupture, axillary lymphadenopathy and/or infection.
Data on implant complications were unavailable for 10 patients.
Odds ratios were calculated from 2×2 contingency tables.

Table III. Characteristics of patients with systemic sclerosis according to breast implant status.

Variable	Implant (n = 58)	Non-implant (n = 3080)	*p*-value
SSc onset age, years, median [IQR]	45.3 [36.4–55.2] (n=57)	46.3 [35.7–56.0] (n=2652)	0.994
Systemic sclerosis subtype			
LSSc, n (%)	30 (51.7)	2083 (67.6)	0.015
DSSc, n (%)	28 (48.3)	997 (32.4)	0.015
Antibody specificity			
Anti-RNA polymerase III, n (%)	19 (32.8)	269 (8.7)	<0.001
Anticentromere, n (%)	15 (25.9)	938 (30.5)	0.564
Anti-topoisomerase I, n (%)	11 (19.0)	658 (21.4)	0.748
PM-Scl antibody, n (%)	2 (3.4)	98 (3.2)	0.708
U3-RNP antibody, n (%)	2 (3.4)	111 (3.6)	1.000
Overlap syndrome, n (%)	10 (17.2)	765 (24.8)	0.219
Organ involvement			
ILD, n (%)	21 (36.2)	996 (32.3)	0.560
SRC, n (%)	7 (12.0)	111 (3.6)	0.020
PH, n (%)	5 (8.6)	237 (7.7)	0.802
Cardiac involvement, n (%)	2 (3.4)	122 (4.0)	1.000

Data are presented as n (%) unless otherwise indicated.
dcSSc: diffuse cutaneous systemic sclerosis; ILD: interstitial lung disease; lcSSc: limited cutaneous systemic sclerosis; PH: pulmonary hypertension; SRC: scleroderma renal crisis; SSc: systemic sclerosis.

autoimmune manifestations (median 7.1 years (IQR 5.4–8.2)), including undifferentiated connective tissue disease (UCTD) with interstitial lung disease (50%) and autoimmune Raynaud's phenomenon (50%). During follow-up, two ruptures (one case pre-onset) and four explantations (two cases pre-onset) were documented in this subgroup.

Discussion

In this single-centre cohort of patients with SSc and breast implants, we identified a long interval between implantation and disease onset, an enrichment of ARA positivity, and a higher frequency of implant-related complications and explantation preceding SSc in ARA-positive patients.

SSc is now recognised as a multifactorial disease resulting from the interaction between genetic susceptibility and environmental exposures (12). Silicone-based medical devices have been considered biologically inert; however, experimental data suggest that silicone may act as an immunological adjuvant and induce immune activation even in asymptomatic individuals (12-14). Although breast implant technology has evolved, associations with autoimmune diseases continue to be reported (15).

The epidemiological evidence linking breast implants and SSc remains limited, largely based on case reports and small series, while observational studies are often constrained by short follow-up, limiting assessment of long latency periods (17, 18).

The prevalence of breast implants in our SSc cohort (2.1%) appears comparable to that reported in European general population-based registries. For example, frequencies range from 1.6% to 6.4% in Sweden and approximately 4.1% in Italy (14, 15). However, data on prevalence in the United Kingdom are limited. Overall, these findings do not suggest an increased prevalence of breast implants among patients with SSc compared with the general population, consistent with previous large observational studies (18).

In our cohort, the median interval between implant surgery and SSc onset is consistent with reported latency in other studies (median of 10 years [IQR 5–20]) (4, 5, 7, 9, 16-21). Similarly, silica exposure has been associated with long latency periods prior to SSc development (2).

We observed a high prevalence of ARA positivity (32.8%) among patients with breast implants, markedly higher than that reported in general SSc cohorts, including a United Kingdom cohort (11.0%) and a recent meta-analysis (9.0%) (22, 23). Importantly, the overall prevalence of ARA positivity in our entire SSc cohort was comparable to these published estimates (Table III), suggesting that this difference is not explained by baseline variation in ARA prevalence within the cohort.

Similar findings have been reported in smaller studies, including a Japanese case series (4/6 patients were ARA positive, 66.7%) and Italian cohorts (5/12 patients, 41.7%). However, these earlier studies were often limited by incomplete immunological characterisation (5-7). Overall, these data indicate a consistent signal of increased ARA positivity among patients with breast implants.

Most implants in our study were placed for cosmetic indications. Consistent with this, prior studies have reported a predominance of cosmetic procedures

(4, 7, 17-19), whereas an Italian multicentre study reported a higher proportion of reconstructive surgeries (8/12, 66.7%) (6).

Most implants were silicone-based, with the exception of one patient with saline implants. However, even saline implants are typically enclosed in a silicone elastomer shell (24).

A high proportion of patients reported implant-related complications (41.7%), most commonly rupture (35.4%) and axillary lymphadenopathy (16.7%). An Italian multicentre study reported a high rupture rate (8/12, 66.7%) particularly among ARA-positive patients (4/5 ARA-positive patients had a rupture), although the temporal relationship with SSc onset was not reported (6). In contrast, a Japanese series described frequent calcifications and lymphadenopathy (67.0% and 33.0%, respectively) but no ruptures (5).

Other case reports show heterogeneous findings. Rupture has been described both before and after SSc onset, sometimes followed by explantation and reimplantation, without consistent clinical improvement (4, 19, 20). In a comparative study, rupture was observed in SSc cases (1/2 patients) but not in controls with implants only (22). Another study found a higher prevalence of rupture among ANA-positive patients, particularly in those with connective tissue diseases (25).

Overall, these data suggest a high frequency of implant rupture among patients with SSc; however, whether such events contribute to disease development remains uncertain and requires consideration of temporal relationships. In our cohort, most complications (29.2%) occurred prior to SSc onset. However, approximately 60% of patients did not have documented complications or explantation before SSc onset, raising the possibility of subclinical or undetected events. Silent implant rupture is well described, and clinical manifestations may precede diagnosis by several years (26).

Importantly, ARA-positive patients showed a higher frequency of implant-related complications and explantation prior to SSc onset. Implant rupture was also associated when considering all events irrespective of timing. These findings support an association between implant-related events and an ARA-positive SSc phenotype, although causality cannot be inferred.

Interestingly, none of the ARA-positive patients had synchronous cancer, supporting the concept that ARA positivity may be independently associated with breast implants.

Among ARA-positive patients, those with breast implants were diagnosed with SSc at a younger age than those with synchronous cancer. These findings are consistent with known population data on the typical age of breast implantation (mean 34 years) and breast cancer onset (peak 60-64 years) (27-30). This observation raises the hypothesis that differences in timing of exposure may contribute to differences in age at SSc onset.

At a mechanistic level, somatic RNA polymerase III subunit A mutations have been identified in patients with SSc and breast cancer (31). It is possible that similar mechanisms could occur in peri-implant tissues, leading to enhanced antigen exposure and immune activation. We hypothesise that implant-related complications may increase antigen exposure; however, this remains speculative and requires further investigation.

Accordingly, two ARA-associated scenarios can be described: SSc developing several years after breast implantation and SSc occurring synchronously with malignancy.

Several limitations must be acknowledged. This is an observational study, and causality cannot be established. Incomplete data and possible underreporting of complications may have influenced the results. Additionally, as a tertiary referral centre, our cohort may be subject to selection bias toward more severe cases. Importantly, our findings do not demonstrate an increased risk of SSc associated with breast implants but instead identify reproducible association between ARA positivity, breast implant exposure, and prior implant-related events that should be confirmed in future prospective multicentre studies.

Overall, these findings are hypothesis-generating and support a model in which genetic susceptibility and environmental exposures, such as breast implants or malignancy, may interact in the development of an ARA-associated SSc phenotype.

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