

# Localized scleroderma and related comorbidities: a single-centre cohort study

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## Abstract

**Background** Localized scleroderma, or morphea, is a rare autoimmune disease that affects the skin and underlying tissue. It is more common in girls and women than in boys and men. The incidence has two peaks: one in childhood and another in middle-age. Concomitant autoimmune diseases are frequently observed, whereas systemic sclerosis occurs rarely simultaneously.

**Objectives** To assess the clinical features, comorbidities and treatments of localized scleroderma in Southwest Finland.

**Methods** Patients diagnosed with localized scleroderma (International Classification of Diseases, 10th Revision code L94) treated between 1 January 2005 and 30 November 2020 were identified from the hospital discharge register of Turku University Hospital, Turku, Finland. Diagnoses were classified into five main types and their subtypes based on the European Dermatology Forum criteria. Basic demographic data, associated comorbidities, and treatments used and their efficacy were recorded.

**Results** A total of 155 people with morphea were included, with 125 female patients (80.6%) and 30 male patients (19.4%). The most common subtype was limited, plaque-type morphea ( $n=71$ ; 45.8%), followed by the generalized type ( $n=57$ ; 36.8%). Fifty-nine concomitant autoimmune diseases were identified in 45 patients (29.0%), most frequently autoimmune thyroid diseases ( $n=23$ ; 14.8%). Simultaneous systemic sclerosis was rare ( $n=3$ ; 1.9%). The most common malignancy was breast cancer ( $n=11$ ; 7.1%). Extracutaneous manifestations were more common in patients with paediatric-onset morphea ( $n=4/27$ ; 14.8%) vs. those with adult-onset disease ( $n=2/122$ ; 1.6%). The most commonly used systemic treatment was methotrexate ( $n=25$ ; 16.1%), which was beneficial for 64% of the treated patients ( $n=16$ ). Phototherapy was administered in 63 of 155 patients (40.6%) and was beneficial in 49 (78%).

**Conclusions** At our centre, patients with morphea often require systemic immunomodulatory treatment or phototherapy. The incidence of the generalized subtype and the occurrence of concomitant autoimmune diseases, particularly thyroid autoimmune diseases, is relatively high. No evidence of an increased risk of malignancy was found in these patients.

## Lay summary

Localized scleroderma is a rare skin disease that causes the skin to harden. It is also known as 'morphea' (pronounced 'mor-fee-ah'). It is an autoimmune disease. An autoimmune disease is a condition where the body's immune system mistakenly attacks its own healthy tissues, thinking they are harmful. Morphea ranges in severity. In severe cases, it can be disabling. It is more common in women and girls. It most commonly peaks in childhood and middle age. Worldwide, up to 3 people per 100 000 can develop the disease every year. Treatment includes skin creams and tablets, as well as light therapy. Patients with the disease can also have other autoimmune diseases. However, it is not linked to an increased risk of cancer.

Our study was done in Southwest Finland. We collected information on people with morphea from the hospital's electronic health records from 2005 to 2020. We wanted to assess the characteristics of the disease and whether patients had any other medical conditions, particularly other autoimmune diseases and cancer.

We found that about 2 in every 100 000 people in Finland developed the disease every year. The majority of patients were girls and women. A large number of patients had a subtype of the disease that required multiple treatments. Symptoms in areas other than skin were uncommon. However, musculoskeletal symptoms were more common in patients who developed the disease in childhood. Other autoimmune diseases were common. The most common cancer was breast cancer.

In conclusion, morphea is a rare disease in Finland. Having other autoimmune diseases, as well as morphea, is common. However, the risk of cancer in patients with the disease was not increased.

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**What is already known about this topic?**

- Morphoea is a rare autoimmune skin disease with varying severity.
- Treatment options vary and may include topical or oral medications, as well as phototherapy, depending on the specific subtype of disease.
- Concomitant autoimmune diseases are common.

**What does this study add?**

- Our results indicate that autoimmune diseases of the thyroid are the most common concomitant autoimmune diseases.
- We found no evidence of an increased risk of malignancies in patients with morphoea.
- A significant number of patients required multiple treatment approaches.
- The incidence of morphoea remained stable throughout the study period.

Localized scleroderma, or morphoea, is an autoimmune condition that affects the skin and underlying tissues. Estimated incidence rates range from 0.4 to 2.7 per 100 000 inhabitants.<sup>1–3</sup> There is a female-to-male ratio of 6 : 1.<sup>4</sup> Incidence peaks occur in childhood and middle age.<sup>3,5,6</sup> Patients with paediatric-onset disease have a higher risk of recurrence.<sup>5</sup> Concomitant autoimmune diseases are common.<sup>3,7</sup> Differential diagnoses include, in particular, extragenital lichen sclerosus (LS) and radiation dermatitis.<sup>8</sup>

Extracutaneous manifestations are common in paediatric-onset morphoea. In a large study of 750 children with localized scleroderma, extracutaneous involvement was seen in 22.4% of cases.<sup>9</sup> Of these patients, 18.4% presented with a single manifestation, while 4.0% exhibited multiple manifestations. Articular involvement, such as arthritis, occurred in 47.2% of patients with extracutaneous manifestations.<sup>9</sup>

In 2017, the European Dermatology Forum (EDF) proposed, and subsequently updated in 2024, a classification system for localized scleroderma based on German guidelines published in 2016.<sup>2,10</sup> According to EDF guidelines eosinophilic fasciitis is considered a separate entity. The five main categories of morphoea are of the limited, generalized, linear, deep and mixed type.<sup>2</sup> The aim of our study was to assess the clinical features and associated comorbidities of localized scleroderma and the efficacy of the various treatments in Southwest Finland.

## Patients and methods

### Patients

Adult and paediatric patients with a diagnostic International Classification of Diseases, 10th Revision (ICD-10) code L94 for localized scleroderma, appearing at least once in their medical records between 1 January 2005 and 30 November 2020, were identified from the hospital discharge register of Turku University Hospital, Turku, Finland, a tertiary care centre serving the approximately 480 000 inhabitants of Southwest Finland. The annual population data were obtained from Statistics Finland (<https://stat.fi>). The incidence was calculated based on the annual number of patients in relation to the population within the hospital's catchment area. Most visits took place at dermatology or

paediatric outpatient clinics. Patient records were reviewed retrospectively by two authors (N.H. and S.K.). Cases involving other connective tissue disorders, incorrect diagnoses or typographical errors were excluded.

Using the EDF classification criteria, diagnoses were categorized into five main types and their subtypes. Incidence rates were calculated for 4-year intervals from 2005 to 2020. Data on extracutaneous manifestations were collected, along with basic demographic data such as age at disease onset, sex distribution and systemic sclerosis (SSc)-related symptoms (e.g. Raynaud phenomenon). Information on skin biopsy results, autoantibody profiles, *Borrelia burgdorferi* antibody status, comorbidities and treatments was also collected. A titre cutoff value of 320 was used to determine antinuclear antibody (ANA) positivity. Treatment efficacy was evaluated by reviewing electronic health records, based on clinicians' judgement. All study data were collected and managed with REDCap electronic data capture tools hosted at the University of Turku.<sup>11,12</sup>

### Statistical analysis

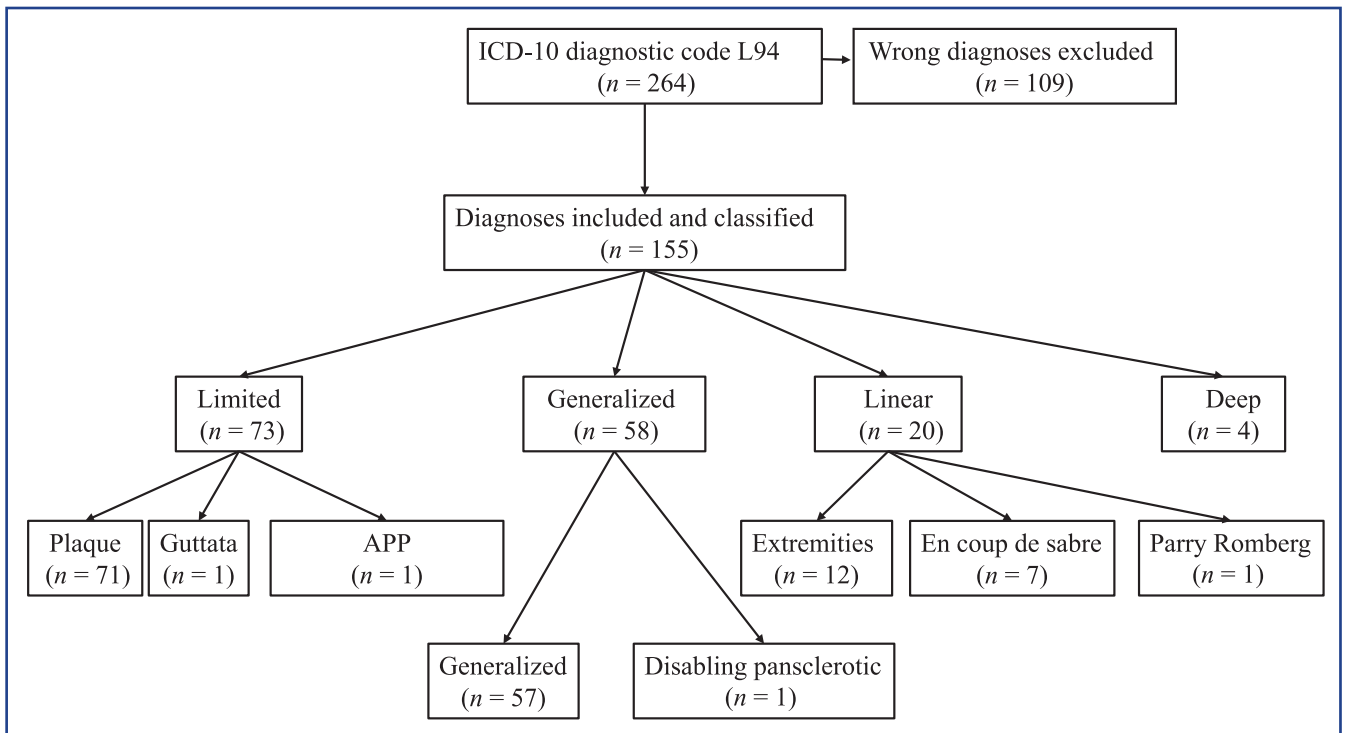
Statistical analyses are described in Appendix S1 (see [Supporting Information](#)).

## Results

### Demographics

A total of 155 patients with a diagnosis of morphoea were included. Figure 1 presents the distribution of the main disease types and their subtypes. The majority of patients ( $n=125$ ; 80.6%) were female, giving a female-to-male ratio of 4.2 : 1. The female predominance was more pronounced in patients with adult-onset disease vs. those with paediatric-onset morphoea, with female-to-male ratios of 4.5 : 1 and 3.3 : 1, respectively. The frequency of different subtypes differed between those with paediatric-onset vs. adult-onset disease [ $\chi^2(3)=50.85$ ;  $P<0.001$ ]. However, no individual subtype was statistically significantly more common in either group (Table S1; see [Supporting Information](#)).

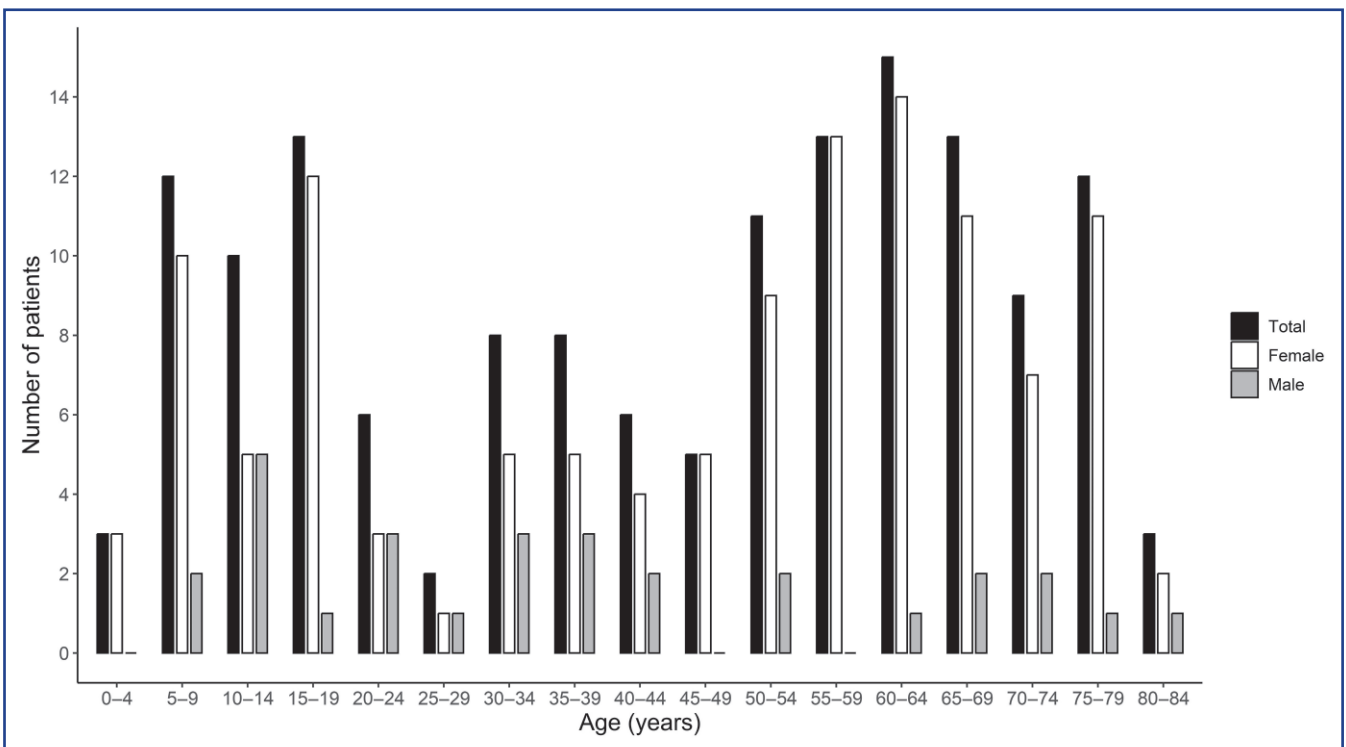
Median age at diagnosis was 50.0 years [interquartile range (IQR) 19.0–64.0]. For paediatric patients, the median age at diagnosis was 9.0 years (IQR 5.0–14.0), whereas for



**Figure 1** Subtypes of morphoea by confirmed cases. APP, atrophoderma of Pasini and Pierini; ICD-10, International Classification of Diseases, 10th Revision.

adults it was 56.5 years (IQR 37.0–67.0). The distribution of age at disease onset and sex is shown in Figure 2. Most patients ( $n=122$ ; 81.9%) had adult-onset morphoea, while

27 (18.1%) had paediatric-onset disease. For six patients, age at diagnosis was unavailable; of these, three diagnoses were made during childhood.



**Figure 2** Age distribution at disease onset for the whole study population, and for female and male patients separately. Age was categorized in 5-year intervals.

Histopathological findings from skin biopsies were available for 139 patients, with diagnoses based on current international criteria for morphea. In 16 patients without histological confirmation of disease, biopsies were not performed in 12 due to a clinically evident diagnosis. Six had generalized morphea, three limited and three linear. Diagnosis was made by a dermatologist in six cases, a rheumatologist in one and was undocumented in five. For four patients diagnosed at another hospital, biopsy status was unknown; two had linear and two had generalized morphea.

During the years 2005–20, the annual incidence of morphea varied from 0.43 and 2.32 per 100 000 inhabitants, with a mean (SD) annual incidence of 1.62 (4.8) per 100 000 inhabitants. When the mean annual incidence rates were grouped into 4-year periods (2005–08, 2009–12, 2013–16 and 2017–20), the incidence rates were 1.53, 1.39, 1.79 and 1.77 per 100 000 inhabitants, respectively. No statistically significant differences were found between these periods, and no increasing trend in incidence was identified.

## Autoimmune diseases

Fifty-nine concomitant autoimmune diseases were diagnosed in 45 patients (29.0%; Table 1). Autoimmune thyroid diseases were particularly common ( $n=23$ ). These were mainly diagnosed prior to the diagnosis of morphea ( $n=19/23$ ; 83%), whereas other autoimmune diseases could be diagnosed at any time (Table S2; see Supporting Information). LS was the second most frequent concomitant autoimmune disease ( $n=10$ ) (Table S3; see Supporting Information). All of these 10 patients had genital LS and 2 also presented with extragenital involvement. Both of these patients had limited morphea. In all cases, the diagnoses of morphea and LS were confirmed by skin biopsy. Nine female patients had rheumatoid arthritis (RA). Of these

**Table 1** Autoimmune diseases occurring simultaneously in 155 patients with localized scleroderma

| Autoimmune disease         | Number of patients (male/female) | Percentage of all patients ( $n=155$ ) |
|----------------------------|----------------------------------|--|
| Thyroid diseases           | 23 (0/23)                        | 14.8                                   |
| Autoimmune thyroiditis     | 21 (0/21)                        | 13.5                                   |
| Graves disease             | 2 (0/2)                          | 1.3                                    |
| Autoimmune skin diseases   | 17 (1/16)                        | 11.0                                   |
| Lichen sclerosus           | 10 (0/10)                        | 6.5                                    |
| Psoriasis                  | 2 (1/1)                          | 1.3                                    |
| Vitiligo                   | 2 (0/2)                          | 1.3                                    |
| Lichen planus              | 2 (0/2)                          | 1.3                                    |
| Frontal fibrosing alopecia | 1 (0/1)                          | 0.6                                    |
| Rheumatic diseases         | 16 (1/15)                        | 10.3                                   |
| Rheumatoid arthritis       | 9 (0/9)                          | 5.8                                    |
| Systemic sclerosis         | 3 (0/3)                          | 1.9                                    |
| SLE                        | 1 (0/1)                          | 0.6                                    |
| UCTD                       | 1 (0/1)                          | 0.6                                    |
| Sjögren syndrome           | 1 (0/1)                          | 0.6                                    |
| Ankylosing spondylitis     | 1 (1/0)                          | 0.6                                    |
| Coeliac disease            | 1 (0/1)                          | 0.6                                    |
| Autoimmune hepatitis       | 1 (0/1)                          | 0.6                                    |
| Inflammatory bowel disease | 1 (0/1)                          | 0.6                                    |

SLE, systemic lupus erythematosus; UCTD, undifferentiated connective tissue disease.

patients, four had seronegative and three had seropositive RA. Two patients with a prior diagnosis of RA from decades earlier lacked immunological data. Patients with concomitant autoimmune diseases were predominantly those with adult-onset morphea, although three cases of paediatric-onset morphea were also noted. The difference between concomitant autoimmune diseases in those with adult-onset vs. paediatric-onset morphea was statistically significant [ $\chi^2(1)=5.38$ ;  $P=0.02$ ]. Among patients with paediatric-onset disease, one was diagnosed with autoimmune hepatitis in childhood (at 13 years of age), while two others were diagnosed with autoimmune conditions (systemic lupus erythematosus and Sjögren syndrome, respectively) in adulthood. Of patients with concomitant autoimmune diseases, 43 were female and 2 were male, a difference that was statistically significant [ $\chi^2(1)=8.90$ ;  $P=0.003$ ]. Three patients (1.9%) had limited cutaneous systemic sclerosis (Appendix S2; see Supporting Information). Two of these patients had SSc diagnosed before developing morphea, and one was diagnosed afterwards. Two of the three patients with both conditions exhibited Raynaud phenomenon and abnormalities in nailfold capillaroscopy. Overall, 19 of 155 patients (12.3%) experienced Raynaud phenomenon. Nailfold capillaroscopy was performed for 17 patients, of whom 7 had Raynaud phenomenon (Appendix S3; see Supporting Information). Abnormalities were detected in three patients, all of whom had Raynaud phenomenon. The morphea types associated with concomitant autoimmune disease included 27 plaque-type ( $n=27/71$ ; 38%), 16 generalized type ( $n=16/58$ ; 28%), 1 guttata type ( $n=1/1$ ; 100%) and 1 en coup de sabre ( $n=1/7$ ; 14%). The difference between these groups was statistically significant [ $\chi^2(3)=10.11$ ;  $P=0.02$ ].

## Autoantibodies and *Borrelia burgdorferi*

Autoantibodies were analysed in 140 patients, of whom 86 (61.4%) tested negative for autoantibodies. ANA was detected in 44 of 140 patients (31.4%). The majority of patients who tested positive for ANA ( $n=28/44$ ; 64%) exhibited low titres ( $\leq 640$ ). ANA positivity was more common in children ( $n=13/27$ ; 48%) than in adults ( $n=31/122$ ; 25.4%) [ $\chi^2(1)=5.49$ ;  $P=0.02$ ]. Only two patients tested positive for antihistone antibody (AHA) or anti-DNA antibodies. Five patients were positive for anti-Sjögren syndrome-related antigen A autoantibodies (anti-SSA/Ro), two for rheumatoid factor or antiribonucleic protein, and one for antineutrophil cytoplasmic antibodies, anticentromere, anti-La antibodies (SSB), anti-Ku 72/86 or anti-PM-Scl-75 antibodies, with some patients having multiple autoantibodies. There were no statistically significant differences in the occurrence of any of these autoantibodies based on disease subtype, sex or the presence of concomitant thyroid autoimmune disease or LS.

Antibodies for *Borrelia burgdorferi* were analysed in 103 patients, with only 3 (2.9%) testing positive with low titres. In two patients, skin biopsies examined by polymerase chain reaction (PCR) to detect *B. burgdorferi* ruled out a local cutaneous infection as the cause of skin symptoms. One patient, who had a high titre of *B. burgdorferi* antibodies, was treated with antibiotics for erythema migrans prior to skin biopsy and PCR was negative. All three patients were

**Table 2** Malignancies occurring simultaneously in 155 patients with localized scleroderma

| Cancer type                         | Number of patients (male/female) | Percentage of all patients (n=155) |
|-------------------------------------|----------------------------------|------------------------------------|
| Breast cancer                       | 11 (0/11)                        | 7.1                                |
| Lung cancer                         | 2 (1/1)                          | 1.3                                |
| Gynaecological cancer               | 2 (0/2)                          | 1.3                                |
| Basal cell carcinoma                | 2 (0/2)                          | 1.3                                |
| Myeloma                             | 1 (0/1)                          | 0.6                                |
| Bladder cancer                      | 1 (1/0)                          | 0.6                                |
| GIST                                | 1 (0/1)                          | 0.6                                |
| Lymphoma                            | 1 (1/0)                          | 0.6                                |
| Hypernephroma                       | 1 (1/0)                          | 0.6                                |
| Thyroid cancer                      | 1 (1/0)                          | 0.6                                |
| Biliary tract cancer                | 1 (0/1)                          | 0.6                                |
| Colorectal cancer                   | 1 (0/1)                          | 0.6                                |
| Squamous cell carcinoma of the skin | 1 (1/0)                          | 0.6                                |
| Origin not known                    | 1 (0/1)                          | 0.6                                |

GIST, gastrointestinal stromal tumours.

treated with antibiotics, but none experienced improvement in their morphoea lesions.

### Malignancies

Twenty-seven cases of malignancy were identified in 23 of 155 patients (14.8%; Table 2). The median age at cancer diagnosis was 62 years (IQR 58.3–70.9). Four of these patients were men (13% of all male patients;  $n=4/30$ ) and 19 were female (15.2% of all female patients;  $n=19/125$ ); this difference was not statistically significant. Only one case of malignancy was found in a patient who had paediatric-onset morphoea: a metastatic adenocarcinoma, probably originating from the pancreas, diagnosed at age 58 years. The other 26 malignancies were diagnosed in patients who had adult-onset morphoea; this difference was also not statistically significant. Concomitant LS was associated with an increased risk of malignancy [ $\chi^2(1)=4.13$ ;  $P=0.04$ ], as 4 of the 10 patients with LS also had malignancies. The cancers found included breast cancer, colorectal cancer, cholangiocarcinoma and gastrointestinal stromal tumours, diagnosed between the age of 61 and 85 years.

Breast cancer was the most common malignancy ( $n=11$ ). The median age at breast cancer diagnosis was 62 years (IQR 54.3–67.6). All patients with breast cancer were women. Seven of them had plaque-type morphoea and four generalized morphoea. Seven of the breast cancer diagnoses were made within 4 years of the morphoea diagnosis. Breast cancer was most often diagnosed before the diagnosis of

morphoea, whereas other malignancies were mainly diagnosed after the morphoea diagnosis (see Table S2).

### Extracutaneous manifestations

Extracutaneous manifestations were found in six patients with musculoskeletal involvement (Table S4; see Supporting Information), including three with linear scleroderma (two with en coup de sabre and one of extremity subtype), one with plaque-type morphoea, one with generalized morphoea and one with deep morphoea. Magnetic resonance imaging (MRI) of the head was performed in five of the seven patients with en coup de sabre. Of these, two MRIs revealed soft tissue changes only, one showed inflammation in the fascia and two exhibited bony lesions. No patients exhibited brain tissue abnormalities. For one patient, diagnosed in the 1970s, MRI was not available, but the patient had undergone facial plastic surgery during childhood. Extracutaneous manifestations were more common in patients with paediatric-onset morphoea ( $n=4/27$ ; 14.8%) than in those with adult-onset disease ( $n=2/122$ ; 1.6%) [ $\chi^2(1)=13.67$ ;  $P<0.001$ ].

### Treatments

Topical therapy was the most commonly used treatment ( $n=136/155$ ; 87.7%) (Table 3). High-potency topical glucocorticoids were the most frequently used ( $n=122$ ; 78.7%). Additionally, 57 patients (36.8%) received topical calcineurin inhibitors, 11 (7.1%) used calcipotriol and 4 (2.6%) used calcitriol. Systemic immunomodulatory treatment was administered to 41 patients (26.5%), with methotrexate being the most common agent ( $n=25$ ; 16.1%) (Table 4). The median methotrexate dose was 10 mg once weekly for adult patients and 15 mg once weekly for paediatric patients. Other systemic agents included hydroxychloroquine ( $n=17$ ; 11.0%), systemic glucocorticoids ( $n=4$ ; 2.6%), leflunomide ( $n=1$ ; 0.6%), pentoxifylline ( $n=1$ ; 0.6%) and a combination of methotrexate and hydroxychloroquine ( $n=2$ ; 1.3%). One patient with disabling pansclerotic morphoea received multiple immunomodulatory agents. Systemic treatment was most commonly used in patients with linear and deep morphoea subtypes [ $\chi^2(3)=17.60$ ;  $P=0.001$ ]. The types of treatments initiated did not differ between patients with paediatric- or adult-onset disease (see Table S1).

Of the 63 patients (40.6%) treated with phototherapy, 25 (39.7%) also received systemic immunomodulatory agents, but these treatments were administered at different times and not concurrently. The most commonly used phototherapy modality was ultraviolet (UV)A1 ( $n=54/63$ ;

**Table 3** Different treatments and their combinations by the subtype of morphoea<sup>a</sup>

| Morphoea subtype       | Systemic | Topical | Phototherapy | Systemic + topical | Systemic + phototherapy | Topical + phototherapy | Systemic, topical + phototherapy |
|------------------------|----------|---------|--------------|--------------------|-------------------------|------------------------|----------------------------------|
| Limited ( $n=66$ )     | 1 (2)    | 44 (67) | 1 (2)        | 5 (8)              | 0 (0)                   | 11 (17)                | 4 (6)                            |
| Generalized ( $n=56$ ) | 0 (0)    | 16 (29) | 0 (0)        | 5 (9)              | 2 (4)                   | 21 (38)                | 12 (21)                          |
| Linear ( $n=18$ )      | 2 (11)   | 2 (11)  | 0 (0)        | 3 (17)             | 0 (0)                   | 5 (28)                 | 6 (33)                           |
| Deep ( $n=3$ )         | 0 (0)    | 1 (33)  | 0 (0)        | 1 (33)             | 1 (33)                  | 0 (0)                  | 0 (0)                            |

Data are presented as  $n$  (%). <sup>a</sup>Data were unavailable for 12 patients.

**Table 4** Efficacy of systemic treatments and phototherapy

| Treatment  | Improved | Stable  | Progressive | Intolerant | Missing |
|--|----------|---------|-------------|------------|---------|
| Any treatment ( <i>n</i> =113)                   | 45 (40)  | 31 (27) | 22 (19)     | 12 (11)    | 26 (23) |
| Any systemic medication ( <i>n</i> =50)          | 13 (26)  | 14 (28) | 8 (16)      | 4 (8)      | 11 (22) |
| Methotrexate ( <i>n</i> =25)                     | 7 (28)   | 9 (36)  | 2 (8)       | 2 (8)      | 5 (20)  |
| Glucocorticoids ( <i>n</i> =4)                   | 1 (25)   | 1 (25)  | 1 (25)      | –          | 1 (25)  |
| Hydroxychloroquine ( <i>n</i> =17)               | 2 (12)   | 3 (18)  | 5 (29)      | 2 (12)     | 5 (29)  |
| Methotrexate + hydroxychloroquine ( <i>n</i> =2) | 2 (100)  | –       | –           | –          | –       |
| Leflunomide ( <i>n</i> =1)                       | 1 (100)  | –       | –           | –          | –       |
| Pentoxifylline ( <i>n</i> =1)                    | –        | 1 (100) | –           | –          | –       |
| Phototherapy ( <i>n</i> =63)                     | 32 (51)  | 17 (27) | 6 (10)      | 4 (6)      | 4 (6)   |

Data are presented as *n* (%). Efficacy of treatment was assessed by clinicians' judgement.

85.7%), followed by psoralen+UVA in five patients (7.9%) and UV311 phototherapy in four (6.3%). Phototherapy was most frequently used in patients with the generalized subtype of morphoea [ $\chi^2(3)=20.21$ ;  $P<0.001$ ].

## Discussion

At our centre, patients with morphoea required systemic immunomodulatory treatment or phototherapy, and had a higher proportion of generalized morphoea than previously reported.<sup>4,13</sup> This may be because patients with milder forms of the disease were not referred to a tertiary care centre in Southwest Finland. The incidence, age at disease onset and sex distribution found in our study were comparable with previous reports.<sup>1–3,7</sup> The female preponderance was particularly pronounced in cases of adult-onset morphoea, with the peak incidence occurring between the age of 60 and 64 years. Extracutaneous manifestations occurred in 14.8% of patients with paediatric-onset morphoea, consistent with previous reports (22.4%),<sup>9</sup> but were rare in adult-onset disease (1.6%).

The annual incidence of morphoea remained stable over the 16-year follow-up period in our cohort. In contrast, studies from the USA have reported an increasing trend, with the most recent annual incidence estimate reaching 10 per 100 000 inhabitants.<sup>1,14</sup>

The occurrence of concomitant autoimmune diseases was relatively high, with 29% of patients (*n*=45/155) having one or more autoimmune conditions concurrently. Autoimmune thyroid diseases, LS and RA were particularly common. Comorbidity was more prevalent among adult patients, with 34.4% (*n*=42/122) of those with adult-onset disease having at least one autoimmune condition vs. only 11% (*n*=3/27) in those with paediatric-onset morphoea. In a hospital-based Finnish study of 455 female patients with LS and an age- and sex-matched population, the relative risk for concomitant morphoea was 60.0.<sup>15</sup>

In a large US study,<sup>7</sup> 29% of adults had concomitant autoimmune diseases, which is comparable to our findings. However, autoimmune diseases were more common in patients with paediatric-onset disease in our study than the 3% reported in the US study. Additionally, in contrast to the US study, most autoimmune diseases in our cohort occurred in adulthood in patients with paediatric-onset disease. The most frequently observed autoimmune diseases in the US study were psoriasis and alopecia areata, with no

reported cases of concurrent SSc and only one patient had autoimmune thyroiditis.

The concurrent occurrence of SSc and morphoea is rare,<sup>16</sup> with reported rates ranging from 2.4% to 7.4%.<sup>17</sup> In our study, two of the three patients with both diseases exhibited Raynaud phenomenon and nailfold capillaroscopy abnormalities, a combination that has been previously reported.<sup>18</sup> Only one patient tested positive for ANA, and none had SSc-specific autoantibodies. The pathogenesis of morphoea and SSc involves different mechanisms,<sup>18</sup> and although both affect the skin, they are considered distinct diseases.

ANA was detected less frequently in our patients with morphoea than in people with SSc, where 85–99% of patients test positive for ANA.<sup>19</sup> Previously, up to 50% of patients with morphoea have been found to harbour three main autoantibodies: ANA, AHA or anti-ssDNA.<sup>20</sup> The occurrence of other autoantibodies is typically <10% each. In our study, only 31.4% of patients (*n*=44/140) tested positive for ANA; the occurrence of other antibodies was even rarer.

*Borrelia burgdorferi* antibody or PCR testing of skin biopsies was conducted in 66.5% of patients, with only 3.9% yielding positive results. The high rate of antibody testing reflects our centre's location in an area endemic for the disease.<sup>21,22</sup> However, the occurrence of positive findings remained low. Routine testing for *Borrelia* is not recommended.<sup>2,3</sup>

Breast cancer was the most common malignancy, accounting for 11 cases (40.7% of all cancers and 57.9% of all cancers in females). The median age at breast cancer diagnosis was 62 years, consistent with the age at diagnosis reported in the general population according to the Finnish Cancer Registry (<https://cancerregistry.fi>). Most cases of morphoea in these patients were diagnosed within 4 years of breast cancer diagnosis, with morphoea being distinguished from radiation-induced morphoea. A recent study identified breast cancer as the most common malignancy preceding a morphoea diagnosis, occurring in 10 of 12 cases.<sup>23</sup> Notably, no cases of malignant melanoma were observed in our study, despite evidence suggesting an increased risk in patients with morphoea.<sup>24</sup> The number of malignancies was higher in patients with morphoea and LS; however, we lacked data solely on patients with LS. Therefore, it remains unclear whether the elevated cancer risk is attributable to LS alone. Finnish studies have indicated an increased risk of urogenital cancers in patients with LS.<sup>25,26</sup> As our study did not include data on the background population, we could

not assess the relative risk of malignancies within our study cohort.

In several cases, data on the efficacy of topical treatments were unavailable, as these patients were usually not followed at our centre. Topical glucocorticoids and calcineurin inhibitors were commonly used. However, in this study, we only assessed the efficacy of systemic immunomodulatory treatments and phototherapy. Methotrexate was the most frequently used systemic agent and appeared to have the best efficacy. Previous studies have indicated that, compared with systemic glucocorticoids, methotrexate is effective in children and generally well tolerated.<sup>3</sup> None of the patients received mycophenolate mofetil, which has been reported in a small series to be beneficial.<sup>27</sup> Unlike previous studies,<sup>28</sup> the efficacy of hydroxychloroquine in our cohort was modest. Phototherapy, particularly UVA1 phototherapy, appeared to be effective.

The strength of our study is that all patient records were reviewed by clinicians rather than relying solely on ICD codes. Our hospital serves as a tertiary care centre in the region, providing specialized level treatment and diagnostic tools, including skin biopsies and autoantibody analyses. Furthermore, we have comprehensive data on comorbidities, as all malignancies in these patients were treated in our hospital.

Our study data were collected retrospectively, and some records were unclear or incomplete. Patients treated solely with topical therapies were not followed at our centre, resulting in a lack of data on their treatment efficacy. Owing to inaccuracies in the records, the exact durations of systemic therapies and phototherapy could not be accurately determined. It is possible that not all patients with limited morphea were referred to our centre. Treatment efficacy assessments were based on clinicians' judgement. Additionally, we could not evaluate the risk of concomitant autoimmune diseases or malignancies in patients with morphea, as we lacked data on the background population. Also, patient-reported outcome measures were not available.

Our results provide real-world data on morphea patients from a single European centre. Patients frequently required multiple treatments, and the occurrence of concomitant autoimmune diseases, particularly thyroid diseases, was relatively high. No evidence of an increased risk of malignancy was observed.

### Author contributions

Saara Kortelainen (Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing [equal]), Niina Hieta (Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing [equal]), Tiia Rissanen (Data curation, Formal analysis, Methodology, Software, Writing – review & editing [equal]), Johanna Palta (Conceptualization [equal], Formal analysis, Methodology, Writing – review & editing [supporting]), Laura Pirilä (Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Supervision, Writing – review & editing [equal]) and Veli-Matti Kähäri (Conceptualization, Formal analysis, Funding acquisition, Methodology, Supervision, Writing – review & editing [equal]).

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### Conflicts of interest

The authors declare no conflicts of interest.

### Data availability

The data underlying this article cannot be shared publicly due to patient data protection regulations.

### Ethics statement

Permission for this study was obtained from the hospital district of Southwest Finland (T287/2021-1).

### Patient consent

This study was a noninterventional retrospective study without direct patient contact and, according to Finnish legislation, no patient consent was needed.

### AI disclosure

During the preparation of this work the authors used ChatGPT-4o in order to revise the language during the final editing of the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

### Supporting Information

Additional [Supporting Information](#) may be found in the online version of this article at the publisher's website.

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**76.9%**

(N=52)<sup>†</sup>

of patients with PsO achieved **PASI 100 at 5 years<sup>3</sup>**

**51.5%**

(n=222/431)

**50.6%**

(n=135/267)

and

of biologic-naïve and TNFi-IR PsA patients achieved **ACR 50 at Week 104/100**, respectively<sup>†1,4-6</sup>

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These data are from different clinical trials and cannot be directly compared.

Co-primary endpoints PASI 90 and IGA 0/1 at Week 16 were met.\*\*Secondary endpoints. †N= mNRI, missing data were imputed with mNRI (patients with missing data following treatment discontinuation due to lack of efficacy or a TRAE were counted as non-responders; multiple imputation methodology was used for other missing data). <sup>4</sup>43.9% (n=189/431), and 43.4% (n=116/267) of biologic-naïve and TNFi-IR PsA patients achieved the primary endpoint of ACR 50 at Week 16 in BE OPTIMAL and BE COMPLETE, respectively (vs 10.0% [n=28/281] and 6.8% [n=9/133] placebo, p<0.0001); 54.5% (n=235/431) and 51.7% (n=138/267) maintained it at Week 52 (NRI).<sup>4-6</sup> **ACR 50**, >50% response in the American College of Rheumatology criteria; **AS**, ankylosing spondylitis; **CRP**, C-reactive protein; **DMARD**, disease-modifying antirheumatic drug; **HS**, hidradenitis suppurativa; **IGA**, Investigator's Global Assessment; **(m)NRI**, (modified) non-responder imputation; **MRI**, magnetic resonance imaging; **nr-axSpA**, non-radiographic axial spondyloarthritis; **NSAID**, non-steroidal anti-inflammatory drug; **PASI 75/90/100**, ≥75/90/100% improvement from baseline in Psoriasis Area and Severity Index; **PsA**, psoriatic arthritis; **PsD**, psoriatic disease; **PsO**, psoriasis; **TNFi-IR**, tumour necrosis factor- $\alpha$  inhibitor – inadequate responder; **TRAE**, treatment-related adverse event.

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