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Neoplasm related mortality risk in Systemic Sclerosis: a nationwide study

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Abstract

Background The higher mortality rates in patients with Systemic sclerosis (SSc) are related to SSc activity, cardiovascular disease, and neoplasms, among other factors. Our objective was to assess the impact of solid organ neoplasms (SON) and hematological neoplasms (HN) on mortality among SSc patients.

Methods A retrospective, observational comparison of SON and HN-related deaths in SSc patients with those in the general Spanish population was conducted using data from the Spanish Hospital Discharge Database. Binary logistic regression was used to analyze the impact of SSc on mortality risk from each neoplasm.

Results During 2016–2019, 139,531 in-hospital deaths from neoplasms were certified in Spain (67 in patients with SSc). Malignancies accounted for 9.7% of all deaths in SSc patients, and disease activity for 11.5% ($p > 0.05$). Compared to the general Spanish population, patients with SSc had a higher death ratio from lung neoplasms (18.6 vs. 25.4%, OR = 2.228, 95% CI 1.260–3.937), gynecological neoplasms (3 vs. 13.4%, OR = 4.804, 95%CI 2.372–9.730), attributable to the increased risk of uterine tumors (0.9 vs. 4.5%, OR = 6.177, 95% CI 1.931–19.758) and ovarian carcinomas (1.3 vs. 4.5%, OR = 3.456, 95% CI 1.083–11.032), and from T/NK lineage lymphomas (0.3 vs. 3.0%, OR = 8.955 95% CI: 2.181–36.767).

Conclusion The detection of chronic comorbidities such as cancer is emerging as a noteworthy component of standard care for SSc patients. This can be addressed during their follow up or even in specific screening programs aimed at achieving better long-term quality of life and prognosis.

Keywords Systemic sclerosis, Neoplasm-related mortality risk, Lung cancer, Gynecological neoplasms, Lymphoma

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Background

Systemic sclerosis (SSc) is a complex inflammatory disease resulting from the combination of three phenomena: microvascular abnormalities, altered autoimmunity and the accumulation of collagen in skin and visceral organs [1]. Consequently, SSc has been associated with a wide clinical spectrum, including limited and diffused types, which have poor survival rates [2].

Although this disease has a low incidence and prevalence and its prognosis has improved in recent decades, it still has high morbidity and mortality [2]. Similar to other autoimmune diseases, the epidemiological data related to survival rates cannot be solely attributed to complications of SSc such as interstitial lung disease, pulmonary hypertension, cutaneous changes or gastrointestinal reflux [3]. In fact, cardiovascular diseases and neoplasms have been related to increased death rates in SSc patients as well as in Sjögren's syndrome and Systemic Lupus Erythematosus populations [4–6].

However, the link between SSc and cancer is controversial. In fact, several studies have shown conflicting results [6–8]. While Chatterjee et al. screened more than 500 SSc patients in the United States between 1973 and 2002 without finding an association with neoplasm development, a similar analysis in Australia including almost 450 SSc cases, reported a twofold global increased risk of cancer and a sixfold higher pulmonary tumor rate in this specific population [9, 10]. These differences have been mainly explained by study designs, demographic intrinsic characteristics, temporal links between SSc and cancer detection and SSc underdiagnosis. Nevertheless, recent evidence favors an association between both diseases, approximately 3–10% of tumor diagnoses being found in SSc patients [11–13]. Moreover, most of the previous studies analyzed the incidence or absolute cancer risk, rather than mortality from certain neoplasm types and lineages, which in turn requires a higher population size and comparison with the general population.

Therefore, our objective was to assess the impact of the different types of neoplasms on SSc patient mortality in a nation-wide analysis conducted in Spain, a country with a population of 47 million.

Materials and methods

We performed a descriptive analysis based on the Spanish National Hospital Discharge Database (SNHDD). This public access registry belongs to the Spanish Government and contains demographic, epidemiological and clinical data on hospital admissions throughout the country. Clinical information is described along 14–20 discharge diagnoses codified by the International Classification of Diseases (ICD). From 1997 to 2015, the ninth version of the ICD (ICD-9) coding list was used. From 2016 to date, the tenth version (ICD-10) is applied. Several groups, including ours, have performed epidemiological studies for other illnesses and have recognized the database's high value for producing estimates of current burden and time trends for different clinical conditions at national level [14–17].

Study population

In this study, we evaluated the impact of SSc on the risk of dying from each neoplasm group and lineage. For this purpose, we described the characteristics of all admissions of patients with SSc. Accordingly, the study population was all patients admitted from 2016 to 2019 with a diagnosis coded as ICD-10-CM M34 (Systemic Sclerosis) in any diagnostic position. Patients who presented systemic lupus erythematosus, Sjögren's syndrome, rheumatoid arthritis, sarcoidosis or dermatomyositis, according to the ICD-10-CM codes, were excluded, as these conditions might impact the neoplasm-related risk in the SSc population [6, 15, 16, 18, 19]. In a second step, we compared the risk of dying from each neoplasm with that of the general Spanish population. Therefore, all in-hospital deaths notified in Spain from 2016 to 2019 were retrieved from the SNHDD and were used as the control group for comparison with SSc patients.

Variables and neoplasm-related deaths

According to the database structure and design, the main diagnosis was the defining reason for admission and the cause of death if it occurred. Therefore, all main diagnoses of the deceased patients were decoded, analyzed, and clustered. Only those admissions and deaths attributable to neoplasms (ICD-10-CM codes C.00–D.49), other than SSc itself (M.34), were analyzed.

Following ICD-10-CM coding criteria, neoplasm related deaths were classified as malignant neoplasms, which include solid organ malignant neoplasms (C00-C80), hematological malignant neoplasms (C81-C96), in situ neoplasms (D00-D09), benign solid organ neoplasms (D10-D36 and D3A) and unknown or non-specified behavior neoplasms (D37-D49), in turn also including solid organ and hematological neoplasms. Myelodysplastic syndromes (MDS), based on their worse prognosis and mortality rate, were considered malignant hematological neoplasms. Finally, the main solid organ and hematological neoplasm lineages, and subsequent subclassifications, such as gastrointestinal, lung, breast, gynecological, urological, together with lymphoma, leukemia or MDS, among others, were considered and analyzed separately.

Statistical analysis

Categorical variables were reported as frequencies and percentages while continuous variables were presented as means and standard deviations. The significance of

Table 1 Patient characteristics

Admissions of patients with SSc (*N* = 10,192)	
Patient/admissions characteristics	
Female, *N* (%)	8,750 (85.9)
Age (years) (Mean, SD)	67.8 (15.4)
SSc activity-related admission, *N* (%)	1,728 (17.6)
Neoplasm-related admission, *N* (%)	588 (5.9)
Ethnicity, *N* (%)	
Arabic	73 (0.7)
Asian	13 (0.1)
Black African	46 (0.5)
Caucasian	8,293 (81.4)
Hindu	8 (0.1)
Latin/Hispanic	209 (2.1)
Unknown	1,550 (15.2)
Outcomes	
Deaths, *N* (%)	689 (6.8)
SSc-activity related	79 (11.5)
Neoplasm-related	67 (9.7)
Admission-length (days), (Mean, SD)	9.24 (12.4)
ICU admission, *N* (%)	507 (5.0)
ICU admission length (days), (Mean, SD)	6.7 (13.3)

SSc: Systemic Sclerosis, SD: Standard deviation, ICU: Intensive care unit

differences between the two groups was determined by the Chi-square or Student's *t*-test, as appropriate. In addition, we performed a binary logistic regression analysis for each neoplasm group and lineage to determine the impact of SSc on the risk of dying from each neoplasm group and lineage. Age, female sex, tobacco and alcohol consumption (according to ICD-10 CM codes F17 or Z72.0 and F10, K70 or I42.6, respectively) were included in the adjusted model. For all analyses, a significance level of 0.05 was set. Statistical analysis was performed using SPSS version 26.0 (IBM, Spain).

Ethics

The study complies with the Declaration of Helsinki and was approved by the local research ethics committee (Clinical Research Ethics Committee of Puerta de Hierro University Hospital, expedient number PI 80-21). The data were provided after all potential patient identifiers had been deleted and data were given anonymously. Due to the design of the study, and according to Spanish law, informed consent was not required.

Results

SSc patient characteristics

According to the Spanish National Registry, between 2016 and 2019, a total of 10,192 SSc patients were admitted; their demographic and clinical features are presented in Table 1. Overall, 8,750/10,192 (85.9%) were female, with a mean age of 67.8 years. Caucasian was the main ethnic group, representing 8,293/10,192 cases (81.4%). Disease activity was the major cause of admission in 1,728/10,192 (17.6%), while 588/10,192 (5.9%) of admissions were attributable to neoplasm. A total of 507/10,192 patients (5.0%) required admission to the Intensive Care Unit (ICU) and 689/10,192 (6.8%) ultimately died, 67/689 (9.7%) due to neoplasm and 79/689 (11.5%) related to SSc activity ($p > 0.05$), with an average age of 67.9 and 61.3 years, respectively ($p = 0.015$). The mean length of admission was 9.2 days.

Differences in neoplasm related deaths in SSc patients and the general Spanish population

The mean Spanish population between from 2016 to2019 was 46,704,229 inhabitants. During this period, 705,557 in-hospital deaths were identified, with 139,531/705,557 (19.8%) attributed to neoplasms (supplementary Table 1). Overall, 127,153/139,531 (91.1%) of these deaths were related to solid organ neoplasms (SON) and 12,378/139,531 (8.9%) involved hematological neoplasms (HN). As previously noted, a total of 67 SSc patients died from neoplasms during this period.

Table 2 compares neoplasm-related deaths in SSc patients with those in the general Spanish population.

Table 2 Differences in neoplasm-related deaths between SSc patients and the general Spanish population during 2016–2019

	Neoplasm-related deaths *N* (%)			**Mean age (years), (SD)**		
	Non-SSc	**SSc**	***p***	**Non-SSc**	**SSc**	***p***
Total	139,464	67	-	70.7 (13.5)	67.6 (12.5)	0.058
SON	127,091 (91.1)	62 (92.5)	0.832	70.6 (13.3)	67.7 (12.3)	0.09
HN	12,373 (8.9)	5 (7.5)	0.832	71.9 (15.5)	65.8 (16)	0.381
Malign neoplasm	136,815 (98.1)	67 (100)	0.641	70.6 (13.5)	67.6 (12.2)	0.067
Malign SON	124,841 (89.5)	62 (92.5)	0.550	70.5 (13.3)	67.8 (12.3)	0.100
Malign HN	12,002 (8.6)	5 (7.5)	1	71.7 (15.6)	65.8 (16)	0.401
Benign SON	727 (0.5)	0	1	72.3 (13.5)	-	-
UB neoplasm	1,698 (1.2)	0	1	78.7 (13.8)	-	-
UB SON	1,327 (1.0)	0	1	78.6 (14.7)	-	-
UB HN	371 (0.3)	0	1	79 (10.5)	-	-
In situ carcinoma	187 (0.1)	0	1	73.4 (12.4)	-	-

SSc: Systemic sclerosis, SD: Standard deviation, SON: Solid organ neoplasm, HN: Hematological neoplasm, UB: Uncertain behaviour

Both the proportion of SON and HN (91.1% vs. 92.5 and 8.9% vs. 7.5 respectively) and the mean age were similar (70.7 vs. 67.6, $p = 0.058$). No statistical differences were found in subsequent analysis regarding hematological neoplasms, solid organ tumor disease (categorized into malignant or benign neoplasms), uncertain-behaviour cancer, or in situ carcinoma.

Differences in neoplasm lineages

Despite finding no differences in SON or HN between SSc patients and the general Spanish population, the different neoplasm lineages were analyzed (Tables 3 and 4), by a binary logistic regression model (Figs. 1 and 2).

Regarding solid organ malignancies (Table 3; Fig. 1), SSc patients had lower risk and mortality rates related to digestive neoplasms (16.4% vs. 29.8% $p = 0.01$, OR = 0.509, 95% CI 0.266–0.977), but a fourfold higher risk of gynecological neoplasm mortality (3% vs. 13.4 $p < 0.001$, OR = 4.804 CI2.372-9.730), attributable to the increased risk of uterine tumors (0,9% vs. 4.5, OR = 6.177, CI 1.931–19.758) and ovarian carcinomas (1.3% vs. 4.5, OR = 3.456 CI1.083-11.032) compared to the general Spanish population. In addition, the regression model demonstrated a doubled risk of lung neoplasm deaths in the SSc group (18.6% vs. 25.4, OR = 2.228 CI 1.260–3.937).

Table 3 Solid organ neoplasm-related deaths differences between SSc patients and the general Spanish population by lineage

	Non-SSc	SSc	*p*	OR (95% CI)*
Solid organ neoplasm	127,091 (91.1)	62 (92.5)	0.832	1.292 (0.519-3.221)
Malign solid organ neoplasm	124,841 (89.5)	62 (92.5)	0.550	1.548 (0.621-3.860)
Digestive system	41,580 (29.8)	11 (16.4)	**0.019**	**0.509 (0.266-0.977)**
Esophagus	2,319 (1.7)	2 (3)	0.307	3.054 (0.742-12.577)
Stomach	6,426 (4.6)	3 (4.5)	1	1.031 (0.324-3.286)
Small bowel	459 (0.3)	0	1	-
Colo-rectal	15,059 (10.8)	4 (6)	0.241	0.583 (0.211-1.611)
HCC and others	3.817 (2.7)	0	1	-
Pancreas	8.709 (6.2)	2 (3)	0.443	0.413 (0.101-1.684)
Cholangiocarcinoma	4.485 (3.2)	0	0.281	-
Lung	25,886 (18.6)	17 (25.4)	0.157	**2.228 (1.260-3.937)**
Breast	3,631 (2.6)	1 (1.5)	1	0.256 (0.035-1.852)
Gynecological	4,130 (3.0)	9 (13.4)	<0.001	**4.804 (2.372-9.730)**
Vulva	280 (0.2)	1 (1.5)	0.126	8.325 (1.145-60.510)
Vagina	63 (0.1)	0	1	-
Cervix	649 (0.5)	2 (3)	0.039	2.937 (0.710-12.149)
Uterine	1,261 (0.9)	3 (4.5)	0.014	**6.177 (1.931-19.758)**
Ovarian	1.746 (1.3)	3 (4.5)	0.052	**3.456 (1.083-11.032)**
Other	131 (0.1)	0	1	-
Otorhinolaryngological	4.107 (2.9)	2 (3)	1	1.557 (0.379-6.398)
Endocrine	1,780 (1.3)	2 (3)	0.211	2.165 (0.529-8.865)
Neuroendocrine	1,289 (0.9)	2 (3.2)	0.135	3.202 (0.780-13.146)
Skin	1,025 (0.7)	1 (1.5)	0.390	2.174 (0.301-15.707)
Melanoma	532 (0.4)	0	1	-
Central nervous system	4,029 (2.9)	2 (3.2)	0.720	0.932 (0.226-3.833)
Urological	11,072 (7.9)	2 (3)	0.173	0.703 (0.169-2.920)
Prostate	3,290 (2.4)	0	0.412	-
Kidney	2,138 (1.5)	0	0.629	-
Bladder	5,147 (3.7)	2 (3)	1	1.507 (0.364-6.242)
Others	497 (0.4)	0	1	-
Others	4,212 (3.0)	4 (6)	0.144	1.874 (0.681-5.154)
MUO	23,390 (16.8)	11 (16.4)	1	0.774 (0.404-1.483)
BSON	727 (0.5)	0	0.596	-
UBSON	1,327 (1.0)	0	1	-
Carcinoma in situ	187 (9.1)	0	1	-

SD: Standard deviation, SSc: Systemic sclerosis, OR: Odds ratio, CI: Confidence interval, HCC: Hepatocarcinoma, MUO: Metastasis from unknown/unspecified origin, BSON: Benign solid organ neoplasm, UBSON: Unknown behavior solid organ neoplasm

* After adjustment for age, sex, alcohol and tobacco consumption

Bold text highlights statistical significance differences

Table 4 Hematological neoplasm-related deaths differences between SSc patients and the general Spanish population by lineage

	Neoplasm-related deaths *N* (%)			OR (95% CI)*
	Non-SSc	SSc	*p*	
Hematological	12,373 (8.9)	5 (7.5)	0.832	0.774 (0.310-1.928)
Malign hemotological	12,002 (8.6)	5 (7.5)	1	0.798 (0.320-1.989)
Lymphoma	4,245 (3)	3 (4.5)	0.460	1.379 (0.433-4.395)
Hodgkin Lymphoma	261 (0.2)	0	1	-
Non-Hodgkin Lymphoma	3,984 (2.9)	3 (4.5)	0.443	1.465 (0.460-4.668)
B cell lineage	3,545 (2.5)	1 (1.5)	1	0.534 (0.074-3.854)
T/NK cell lineage	439 (0.3)	2 (3.0)	**0.019**	**8.955 (2.181-36.767)**
Leukemia	4,630 (3.3)	1 (1.5)	0.728	1.940 (0.845-4.454)
Myeloid lineage	3,195 (2.3)	0	0.410	-
Lymphoid lineage	1,005 (0.7)	1 (1.5)	0.384	2.619 (0.641-0.585)
Multiple myeloma	2,165 (1.6)	0	0.630	-
Myelodisplastic syndrome	885 (0.6)	1 (1.5)	0.347	2.788 (0.384-20.240)
Others	77 (0.1)	0	1	-
Unknown behavior	371 (0,3)	0	1	-
Myeloproliferative disorders	243 (0.2)	0	1	-
Others	128 (0.1)	0	1	-

SD: Standard deviation, SSc: Systemic sclerosis, OR: Odds ratio, CI: Confidence interval

* After adjustment for age, sex, alcohol and tobacco consumption

Bold text highlights statistical significance differences

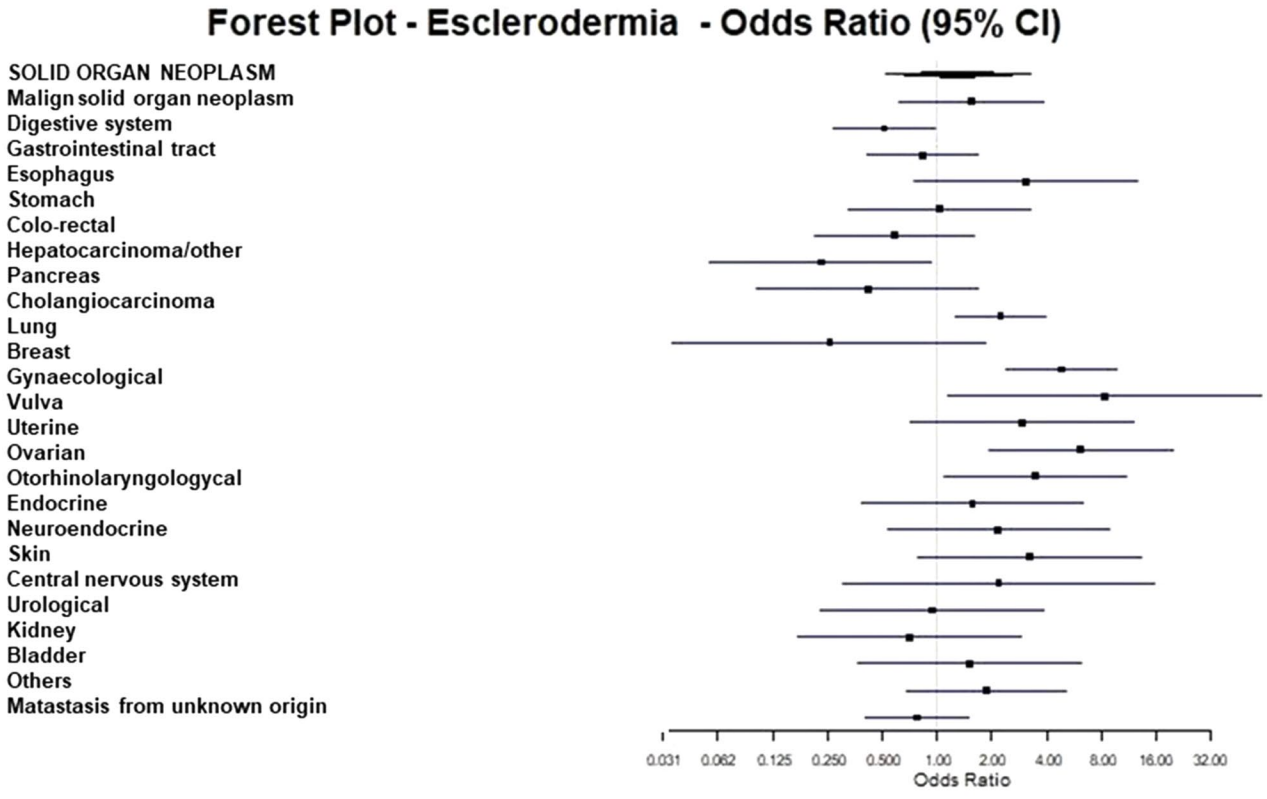

Fig. 1 Solid organ neoplasms related deaths for SSc patients. The figure represents the risk of dying from solid organ neoplasms for SSc patients, after adjustment by age, sex, alcohol and tobacco consumption, for each neoplasm lineage. The results are expressed in Odds ratio (dots) and 95% confidence interval (bars)

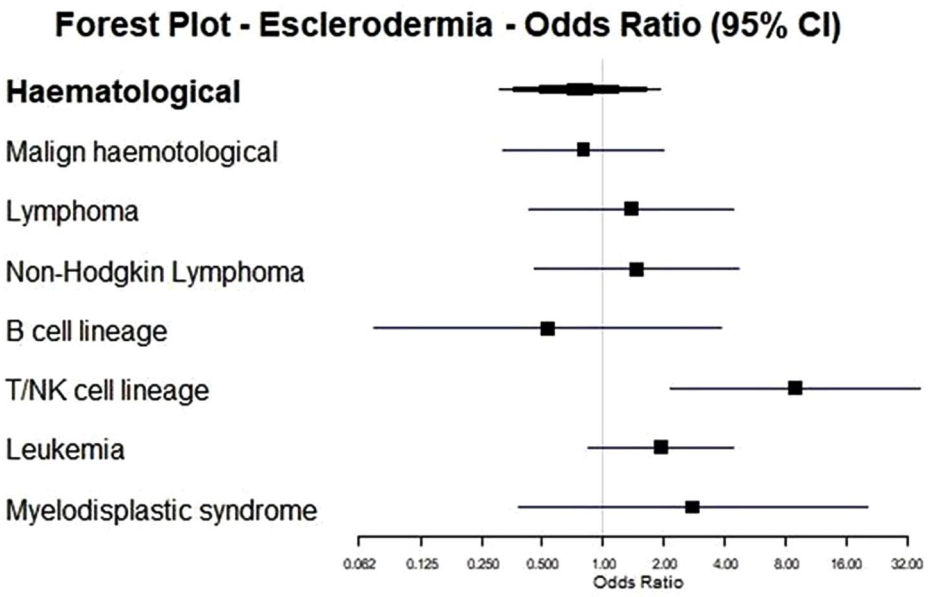

Fig. 2 Hematological neoplasms related deaths for SSc patients. The figure represents the risk of dying from hematological neoplasms for SSc patients, after adjustment by age, sex, alcohol and tobacco consumption, for each neoplasm lineage. The results are expressed in Odds ratio (dots) and 95% confidence interval (bars)

No increased neoplasm-related mortality rate was demonstrated in other malignancy types such as breast, otorhinolaryngological, endocrine, skin, urological or central nervous system cancer. An age-comparison model found no statistically significant differences compared to the general Spanish population or the malignancy lineage subgroups.

Higher mortality rates from HN (Table 4; Fig. 2) linked to T/NK cell lineage lymphomas were found in the SSc population compared to the general Spanish population (0.3% vs. 3.0%, $p = 0.019$, OR = 8.955 CI: 2.181–36.767). Nevertheless, B-cell lineage lymphoma and Hodgkin lymphoma-related deaths did not significantly differ between the SSc and the non-SSc groups. No statistical differences were reported in leukemia, multiple myeloma, myelodysplastic or myeloproliferative syndromes. Similarly, no age differences were found between the SSc patients and the general Spanish population.

Discussion

This natiowide analysis of a large sample of SSc cases identifies malignancies as an equally frequent cause of death as SSc activity itself. Moreover, the cancer subtype analysis revealed that, among solid organ malignancies, lung and gynecological neoplasm had a higher death ratio, as well as a higher mortality from T/NK lineage lymphomas.

In our study, neoplasms accounted for 9.7% of all deaths in SSc patients. These figures approach the upper limit of the reference levels described in previous literature. The Mayo Clinic conducted one of the first published analyses of cancer-related risk in SSc over 15 years (1959–1975) in a 2,141-patient population and observed a mortality proportion of 3.64% [20]. Later studies found even higher percentages, ranging between 3 and 11% [21–24]. The higher mortality rate from certain lineages observed in SSc patients may have multiple underlying causes including genetic, pathophysiological and environmental mechanisms, including chronic inflammation, fibrosis, immunosuppressant treatments, and even association with certain antibodies, (e.g., RNA polymerase III antibodies) [3, 25–31]. Herein, others have proposed that some SSc cases present as paraneoplastic phenomena that coincide with neoplasm diagnosis or clinical onset [3, 18, 32–34]. Finally, some authors suggest that the synergy between both inflammatory and tumor processes and their common risk factors may be responsible for the progression of SSc and the malignancy in a period of a few months or years as seen in the age comparison between SSC activity and neoplasm deaths in our population [31–33, 35].

As regards solid organ cancer, the mortality risk for lung neoplasm was double in the SSc group. Many studies have exhibited such a relationship, suggesting that areas of chronic inflammation, interstitial disease and fibrosis may be the main contributing factors [34, 36, 37]. Accumulated damage could eventually lead to tumorigenesis [38].

Furthermore, SSc patients had up to fivefold higher risk of gynecological neoplasm diagnosis and death rate

partly influenced by an elevated risk of uterine and ovarian cancer. Recently, several publications have described these tumor subtypes as paraneoplastic manifestations, with early-onset detection and even simultaneous diagnosis with SSc [39]. Consequently, these neoplasms may become chronic diseases with subsequently higher complication, recurrence and death rates [40]. Also, Gniadecki et al. reported that somatic hypermutation in fibrotic tissue occurs in cases with early progressive SSc, potentially associated with revise tumors.

In our population, SSc patients had lower risk and mortality rates associated with digestive neoplasms, probably related to a lower death risk from colorectal carcinoma. However, a detailed analysis of tumor localization did not find significant differences, presumably due to the small sample size and subsequently low statistical power. More evidence in this field is needed to reach conclusive statements. In this context, colorectal carcinoma represents the major gastrointestinal tract malignancy in the general population of our sample, likely due to the national health system (SNS) program which provides universal cancer screening (fecal occult blood test or endoscopic study) to every adult older than 50 years [41]. However, patients followed up by autoimmune diseases units and consequently, undergoing regular clinical and laboratory monitoring, will probably be diagnosed earlier with anemia or iron deficiency, and an endoscopic study will therefore detect a higher proportion of premalignant damage or even tumor lesions at earlier stages, resulting in a more favorable prognosis and less aggressive treatments.

Among hematological neoplasms, higher risk and mortality rates linked to T/NK cell lineage lymphomas were found in SSc population compared to the general Spanish population. In fact, the occurrence of lymphoproliferative malignancies is increased in the entire spectrum of systemic autoimmune disorders, systemic lupus erythematosus, sarcoidosis, Sjögren's syndrome, rheumatoid arthritis and inflammatory myopathies [6, 15, 16, 42–45]. This finding largely stems from aberrant immune system responses involving direct T and B cell activation [44, 46]. Although B cell lineage lymphomas have been the predominant hematological neoplasms related to autoimmune diseases, some authors have described mechanisms involved in T/NK disorders in these situations [47–49]. For example, cytokine storms involving molecules such as interleukin-18 (IL-18) have been reported in both autoimmune diseases and NK/T cell lymphomas. Similarly, modified expression of tumor suppressor genes (FOXO3 and PDRM1 as examples) has been considered significant in NK-cell neoplasm associated with autoimmunity. Nevertheless, more investigation is required in this field to validate this evidence, since our analysis is presumably the first description of a potential relationship and association with mortality risk [8].

Several limitations of this study cannot be ignored. Firstly, the lack of the availability of disease course (including diffuse or limited forms of the disease), the antibody profile, histopathological neoplasm information, and the therapeutic measures limits the establishment of potential causal relationships. Therefore, further research is needed to confirm not only association but causal relationship between SSc and certain neoplasms, as well as the temporal trends and chronology between the two conditions, in order to design a potential preventive strategy. In addition, the exclusive inclusion of hospital admissions may have influenced statistical power and selection bias, but because we analyzed deaths from neoplasm, which are difficult to misclassify, our findings remain clinically plausible. The results are compatible with existing scientific knowledge and the potential bias was minimized with an adjusted multivariate model. Finally, the prevalence of SSc could not be properly recorded in the databases, and only deaths could be compared, yielding an estimated proportion and death risk but not an absolute risk ratio. Altogether, we believe these limitations are the counterpart of analyzing a large population size and solid outcomes such as death. Accordingly, this study represents a large sample analysis in an uncommon disease, reaffirming previous data in this field and adding features such as age onset, mortality rates and cancer subtype.

To conclude, the detection of chronic comorbidities such as cancer is emerging as a noteworthy part of standard care for SSc patients. This analysis represents one of the largest studies in an SSc population focused on mortality rates and identifies lung and gynecological malignancies as potential threats to the SSc population. These risks can be addressed during follow-up or even in specific screening programs, with the objective of achieving better long-term quality of life and prognosis for these patients.

Abbreviations

HN	Hematological neoplasms
ICD	International Classification of Diseases
ICU	Intensive Care Unit
MDS	Myelodysplastic syndromes
SNHDD	Spanish Hospital Discharge Database
SON	Solid organ neoplasms
SSc	Systemic Sclerosis

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41927-025-00477-z.

Supplementary Material 1: Supplementary table 1. Neoplasm related deaths in the Spanish population in the period 2016–2019.

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None.

Author contributions
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Data availability
The data proceeds from a public registry from the Spanish National Hospital Discharge Database. All data are freely available. The database from the Spanish Ministry of Health can be accessed upon request. Data are anonymously given.

Declarations

Ethical approval
The study complies with the Declaration of Helsinki and was approved by the local research ethics committee (Clinical Research Ethics Committee of Puerta de Hierro University Hospital, expedient number PI 80-21).

Consent to participate
The data were provided after all potential patient identifiers had been deleted and data were given anonymously. Due to the design of the study, and according to Spanish law, informed consent was not required.

Consent for publication
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Competing interests
The authors declare no competing interests.

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