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Collaborative National Quality and Efficacy Registry (CONQUER) for Scleroderma: outcomes from a multicenter US-based systemic sclerosis registry

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Abstract

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Compliance with ethical standards The study was conducted in compliance with the ethical rules for human subject research as outlined in the 1975 Declaration of Helsinki. The CONQUER scleroderma registry is IRB approved at each of the individual institutions. All subjects gave written informed consent for collection of specimens and data.

The Collaborative National Quality and Efficacy Registry (CONQUER) for Scleroderma is a multicenter US-based longitudinal study of patients with systemic sclerosis (SSc) within 5 years of first non-Raynaud's symptom. The data collection methodology incorporates successful models from other SSc registries. The cohort is designed to provide linked bio-specimen and clinical outcomes data on a longitudinal cohort of SSc patients for validation of hypothesis-driven research and to provide a platform for studying patient-reported outcomes in scleroderma. The CONQUER registry was developed using the guidelines of the International Society for Biological Repositories, and was an iterative process between physicians with an expertise in SSc, patient stakeholders, and information technology experts. Enrollment commenced in June 2018. During the first 6 months of the CONQUER Scleroderma study, 151 SSc patients with less than 5 years of disease duration (from first non-Raynaud's symptom) have been recruited. The mean age is 51 ± 14 years, 83% are female, and 60% of patients have diffuse disease. Survey completion rates are above 88% for all patient-reported outcome surveys. Bio-specimen collection rates are over 97%, and disease severity score completion rates are over 98%. Pulmonary function test data is available on 91% of patients, and echocardiography is available 80%. The CONQUER scleroderma study provides a unique and growing resource for studying scleroderma in a longitudinal, US-based population.

Keywords

Bio-specimens; Cohort study; Patient-reported outcomes; Prospective study; Registry; Systemic sclerosis

Introduction

Systemic sclerosis (SSc) is a rare autoimmune disease with a prevalence between 4 and 489 cases per million, and incidence between 0.6 and 122 per million per year depending on the geographic region studied [1]. Due to its rarity, single-center studies are typically too small in scope to harness the power of novel genomic technologies in order to identify biomarkers that predict disease prognosis and potential molecular drivers of pathogenesis [2, 3]. As science has evolved in SSc, it has become clear that developing a United States (US)–based multicenter longitudinal cohort of patients with SSc is imperative to provide a validation cohort for ongoing research. To date several large international collaborative registries have investigated outcomes in SSc patients. Seminal work on disease progression, standardized patient assessment, sociodemographic factors, and morbidity and mortality have been reported by the European League Against Rheumatism Scleroderma Trial and Research (EUSTAR) cohort [4–8], Canadian Scleroderma Research Group (CSRG) [9–11], Australian Scleroderma Interest Group (ASIG) [12], and German Network for Systemic Scleroderma (DNSS) [13]. Data harmonization to allow meta-analysis between these multinational groups has successfully been achieved through the International Systemic Sclerosis Inception Cohort (INSYNC) [14]. In 2012, the Prospective Registry of Early Systemic Sclerosis (PRESS) was established to standardize assessment and treatment of patients with diffuse skin involvement of less than 2 years' duration [15], but the scope of this study was limited to patients with early diffuse disease. In 2013, the Scleroderma-Patient Intervention Network (SPIN) further revolutionized the field by providing a platform for SSc patients in

research [16]. Building on these advances, the Collaborative National Quality and Efficacy Registry (CONQUER) was launched in June 2018 in partnership with the Scleroderma Research Foundation (SRF). The goal of the CONQUER scleroderma study is to incorporate successful models from other SSc registries into the design of this longitudinal validation cohort, with a focus on minimizing missing data, prioritizing bio-specimen integrity, and collecting data on patient-reported outcomes (PROs).

In this report, we present preliminary data from the CONQUER scleroderma registry focusing on data quality, the characteristics of this dataset, and the registry's potential for SSc clinical and translational discovery work.

Methods

The CONQUER scleroderma registry is IRB approved at each of the individual institutions. All subjects gave written informed consent for collection of specimens and data. Enrollment started in June 2018. Data lock was in April 2019.

Registry development and design

Through a series of face-to-face study design meetings, hands-on investigator training sessions, and ongoing monthly steering committee calls, the CONQUER scleroderma registry team harnessed the expertise of a group of SSc physicians to achieve consensus on critical data collection elements. This was a collaborative and iterative process. Additionally, the study team engaged input from patient stakeholders to ensure that collection of meaningful PRO data were incorporated into the registry design. Finally, the study team engaged a Data Coordinating Center (DCC) to design rules to ensure data quality [17]. The DCC consists of project management, data management, statistical personnel, and leadership. During this development phase, the team developed a governance structure with several subcommittees to ensure that the CONQUER scleroderma study prioritizes sustainability and transparency as a critical aspect of this long-term study [18].

Patient recruitment

All CONQUER patients are over 18 years old and fulfill the 2013 ACR/EULAR Classification Criteria for SSc and have a disease duration less than 5 years from onset of the first non-Raynaud's symptom. The registry includes 12 scleroderma centers geographically distributed throughout the US including California, Texas, Utah, Illinois, Michigan, Massachusetts, Maryland, New York, South Carolina, and Washington, D.C. The DCC is based at the University of Utah, and the Bio-specimen repository is housed at the University of Texas Health Science Center at Houston.

Eligible subjects are consented to enroll in the study during routine clinical visits and give permission for collection of longitudinal clinical outcomes data and collection of bio-specimens for use in research as outlined below. All subjects additionally complete PRO questionnaires, which are typically completed online but may be completed on paper with assistance of the study team if the patients prefer.

Data quality and consistency

The platform for CONQUER data capture is Research Electronic Data Capture (REDCap), which was developed at Vanderbilt University in 2004 and is a HIPAA-compliant, browser-based, metadata-driven electronic data capture software solution and workflow methodology for designing clinical and translational research databases [19]. The CONQUER REDCap database was developed by an information systems technician trained in Findable, Accessible, Interoperable, Reusable for humans and computers (FAIR) principles [20]. The CONQUER database has 748 data fields, with rules to ensure that data are complete and accurate. Rules identify duplicate or inconsistent data, check form completion, and identify missing data or data that are out of range. When a rule is violated, a query is generated to trigger the site research coordinator to provide source documents for data verification. The CONQUER database currently has more than 445 active rules. The selection of data elements was an iterative process between all stakeholders, which enhanced feasibility. All research coordinators entering data into the CONQUER database completed a series of online trainings. Bi-monthly trainings and updates are overseen by the DCC in order to minimize missing data and to ensure all security measurements for data quality are followed. The CONQUER Data Quality and Bio-repository Subcommittee meets monthly to audit the data for completeness.

Role of funding agency

The SRF sponsored the data coordination and management for this project. Data were collected through routine care provided in the clinical setting by SSc experts. The SRF actively sought patient feedback to ensure that minimizing patient burburden, while focusing on clinically important outcomes was at the cornerstone of the CONQUER database design.

Patient-reported outcome measures

Patient questionnaires are the foundation of meaningful patient outcomes research. Patients are important stakeholders in the research agenda for SSc. They contribute their personal perspective on certain disease features that evolve and symptoms that change over time as well as overall disease burden [21]. Further development in the area of disease-specific PROs in SSc is ongoing [22]. The CONQUER scleroderma registry currently captures the patient perspective through the use of seven different PROs listed in Table 1 with the rates of completion detailed. PRO questionnaires are completed at baseline and every 6 months, with the resource utilization questionnaire (RUQ) only being collected once per year.

The CONQUER database integrates user-friendly formats to allow patients to complete questionnaires online prior to, during or after their clinical visit. For patients who do not wish to complete PRO measures on-line they may complete them on paper, and study team assistance is available if needed (for example if the patient has digital contractures and trouble holding a pen or typing).

Bio-specimen collection

The CONQUER registry was developed using the best practice guidelines of the International Society for Biological Repositories (https://www.isber.org/page/BPR), and was an iterative process between physicians with an expertise in SSc, patient stakeholders, and

information technology experts. Blood samples are collected at the baseline, 6-month, and 12-month visits and yearly thereafter. Standardized protocols are used to collect samples for DNA, serum, plasma and whole blood RNA analysis. The whole blood RNA samples are collected into PAXgene (PreAnalytiX, Hombrechtikon, Switzerland) collection system, which stabilizes intracellular RNA at collection. Samples are shipped overnight to the CONQUER Bio-repository at the University of Texas-Houston. At the Bio-repository facility DNA is extracted from the buffy coat in the EDTA tubes. Serum and plasma samples are aliquoted according to standardized protocol. All samples are barcode labeled and stored at − 80 °C for future use. Sample volume, location and utilization is tracked in a custom-designed structured query language (SQL)–based sample tracking system.

Ethical issues

Ethical, Legal, and Social issues (ELSI) as well as privacy were the cornerstone of the database for CONQUER, as per professional guidelines for registry development [18]. The study was conducted in compliance with the ethical rules for human subject research as outlined in the 1975 Declaration of Helsinki. The CONQUER scleroderma registry is IRB approved at each of the individual institutions. All subjects gave written informed consent for collection of specimens and data.

Results

Demographic characteristics

At the time of data lock for this analysis, all sites had completed 6 months of active enrollment with 151 SSc patients enrolled. Enrollment commenced in June 2018. For the purposes of this analysis all patients enrolled prior to February 15, 2019, were included. The date of data lock was April 25, 2019, in order to allow for data entry on all subjects.

Table 2 outlines the baseline demographic characteristics of this cohort. The majority of the CONQUER participants are white (74.2%), non-Hispanic (84.1%), female (83.4%), aged 30–60 years (62.9%), married (67.5%), and employed either full-time or part-time (53%).

Clinical characteristics

In this cohort 59.6% of patients had diffuse scleroderma (Table 3). The most common first non-Raynaud’s symptoms reported were hand swelling/puffy hands (58.3%), skin tightening (12.6%), arthralgia/arthritis (8.6%), dyspnea (6.0%), digital ulcers (4.0%), gastroesophageal reflux (3.3%), and lower extremity swelling (2.0%). The majority of these patients were ANA (86.1%) and SSc-specific antibody (64.2%) positive (Anti-Centromere, Anti-SCL 70, or Anti-Polymerase III). A small proportion of patients did not have baseline autoantibody screens performed, but this was 6.6% of the entire cohort and these analyses will be performed on the stored bio-specimens in the future.

Clinical outcomes collected

Patients consent for the collection of data from studies performed during their routine clinical care including pulmonary function tests (PFTs), echocardiograms, 6-min walk testing, right heart catheterizations, and high-resolution chest CT scans. As outlined in Table

4, these data are not always available in all patients since they are only performed when indicated clinically, highlighting the challenges of an observational registry. PFTs were available for 90.7% of subjects, echocardiograms for 80.1% and high-resolution chest CTs for 62.9%.

Disease severity score completion rates were over 98% (modified Rodnan Skin Score, musculoskeletal assessment, vascular assessment, gastrointestinal severity assessment and cardiopulmonary assessment) for all subjects. As the CONQUER Scleroderma Study grows, we anticipate ongoing clinical data collection that will form a robust population for subsequent data analysis.

Patient-reported outcomes

Current completion rates for all surveys are between 88.7 and 92.7%. A major factor contributing to completion rates for PRO surveys is the length of the survey. In this study, the resource utilization survey is the longest and thus after consultation with patient stakeholders, it was placed as the last survey in the link. With this arrangement, we have demonstrated good completion rates for the PRO surveys. In Tables 5 and 6, we have analyzed which clinical features are associated with PRO non-completion and with method of PRO completion. At this early enrollment phase, there is no clinical feature that appears to influence PRO completion; however, patient age and disability status will be studied to see how these factors affect PRO completion longitudinally.

Bio-repository

At the time of data lock, 144 baseline blood samples (95.4% of cohort) had been stored in the CONQUER Bio-repository. A total of 123 samples (81.5%) were processed and stored within 36-h of the blood draw and 139 (92.1%) had a complete set of samples for DNA, serum, plasma, and whole blood.

Discussion

The CONQUER scleroderma study provides a unique multicenter US-based cohort for accelerating scleroderma research. One of the strengths of this cohort is the focus on inclusion of prospectively collected PRO data paired with clinical outcome data. Bio-specimens are collected according to standardized protocols, and collected specimens are processed and stored in a central repository. This will provide not only a valuable resource for future translational and clinical research in scleroderma but will also allow future research conducted through the registry to be anchored by validated patient centered outcome data.

One of the strengths of the cohort is the strong leadership of the study, and the enthusiasm and engagement of the investigators and patient partners. The investigative team is committed to discovery work in scleroderma, and the engagement of multiple geographically distributed sites will ensure that this cohort is representative of the diverse scleroderma population in the USA. The investigative team and DCC have regular meetings to track progress and ensure consistency, and through this rapid cycle feedback the team is able to ensure minimal missing data.

This work has several limitations which merit discussion. The CONQUER cohort is still in its infancy, and thus the cohort is currently small. However, this preliminary report demonstrates that the investigative team has been successful in recruiting and retaining patients in the study and in prospective collection of data and bio-specimens that are essential to success of the cohort. While this manuscript reports only the first 6 months of data, we anticipate ongoing analyses in the years to come.

The management of scleroderma is complex and evolving, and the CONQUER scleroderma study is a unique collaboration between the Scleroderma Research Foundation and multiple academic centers focused on building a robust repository of data and specimens which will grow as the field evolves. Through this work the team will be positioned to take advantage of cutting-edge new methodologies for advancing the understanding of molecular mechanisms of disease in scleroderma, and the database and Bio-repository will be fundamental to advancing research and improving patient care in this devastating disease. Finally, this multicenter registry has potential to serve as a platform for future adaptive trial design in scleroderma.

Conclusions

Rare disease clinical care registries are powerful tools for clinical and translational research when developed using standardized methods that adhere to a quality framework [18]. The CONQUER scleroderma registry has integrated the lessons learned and recommendations made from other SSc registries in order to develop a US validation cohort. While only in its infancy, the power of this registry lies within its investigators, study participants, patient partners, and the unique integration of clinical outcome data, patient outcome data and serial bio-specimens. Capturing PRO data while minimizing patient burden is a unique feature of the CONQUER registry, and integration of these unique features offers a novel and robust tool for future discovery in the field of scleroderma.

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Key Points

- The Collaborative National Quality and Efficacy Registry (CONQUER) for Scleroderma is a multicenter US-based longitudinal study of patients with systemic sclerosis (SSc) within 5 years of first non-Raynaud's symptom.
- The CONQUER scleroderma study provides a unique and growing resource for studying scleroderma in a longitudinal, US-based population.
- CONQUER is innovative in its design in that it is focused on prospective collection of paired clinical and patient outcome data with bio-specimens.

Table 1

Patient survey completion

Baseline form	Overall (*N* = 151)
Participant global assessment	138 (91.4%)
Scleroderma health assessment	140 (92.7%)
UCLA SCTC GIT 2.0 questionnaire	138 (91.4%)
PROMIS 29 survey	136 (90.1%)
Patient skin assessment	137 (90.7%)
Dyspnea survey	136 (90.1%)
Resource utilization questionnaire	134 (88.7%)

Table 2

Demographic characteristics

	Overall (*N* = 151)
Age at baseline visit	
Mean (SD)	50.6 (14.17)
Min–Max	19.8–77.8
Age at baseline visit category	
18–30 years	15 (9.9%)
30–60 years	95 (62.9%)
60+ years	41 (27.2%)
Gender	
Female	126 (83.4%)
Male	25 (16.6%)
Race	
White	112 (74.2%)
Black or African American	20 (13.2%)
Asian	11 (7.3%)
Other, multiple, or not reported	8 (5.3%)
Ethnicity	
Not Hispanic or Latino	127 (84.1%)
Hispanic or Latino	20 (13.2%)
Unknown or not reported	4 (2.6%)
Marital status	
Married	102 (67.5%)
Single	32 (21.2%)
Divorced, widowed or unknown	17 (11.3%)
Employment status	
Full-time	71 (47.0%)
Retired	23 (15.2%)
Homemaker	14 (9.3%)
Disabled, due to Scleroderma	13 (8.6%)
Unknown or not reported	12 (7.9%)
Part-time	9 (6.0%)
Student, unemployed, or disabled not due to scleroderma	9 (5.9%)
Smoking status	
Never	105 (69.5%)
Former	42 (27.8%)
Current	4 (2.6%)

Table 3

Clinical characteristics

	Overall (*N* = 151)
First non-Raynaud's symptom	
Hand swelling/puffy hands	88 (58.3%)
Skin tightening	19 (12.6%)
Arthralgia, arthritis	13 (8.6%)
Dyspnea	9 (6.0%)
Other[1]	22 (14.6%)
Patient ever had diffuse involvement	
Yes	90 (59.6%)
No	61 (40.4%)
ANA[2]	
Negative	11 (7.3%)
Positive	130 (86.1%)
Unavailable	10 (6.6%)
Anti-Centromere	
Negative	99 (65.6%)
Positive	13 (8.6%)
Unavailable	39 (25.8%)
Anti-SCL 70	
Negative	83 (55.0%)
Positive	51 (33.8%)
Unavailable	17 (11.3%)
Anti-Polymerase III	
Negative	77 (51.0%)
Positive	35 (23.2%)
Unavailable	39 (25.8%)
SSc-specific antibody positive (Anti Centromere, Anti SCL 70 or Anti Polymerase III positive)	
Yes	97 (64.2%)
No	44 (29.1%)
Unavailable	10 (6.6%)

[1] Other includes digital ulcer, reflux, leg swelling, carpal tunnel syndrome, GI symptoms (other than reflux) and other

[2] *ANA*, anti-nuclear antibody

Table 4

Clinical data, biospecimen collection and clinical assessment collection

Baseline form	**Overall (*N* = 151)**
Social History	151 (100.0%)
Medications	151 (100.0%)
Vitals	151 (100.0%)
Samples[1]	144 (95.4%)
Serum	144 (100.0%)
RNA	140 (97.2%)
EDTA	141 (97.9%)
Other[2]	6 (4.2%)
Pulmonary function test	137 (90.7%)
6-min walk test	19 (12.6%)
Echocardiogram	121 (80.1%)
Right heart catheterization	19 (12.6%)
Electrocardiogram	49 (32.5%)
High resolution CT	95 (62.9%)
Lab assessments	148 (98.0%)
ANA	143 (94.7%)
Autoantibodies	141 (93.4%)
Rodnan skin score	151 (100.0%)
Musculoskeletal assessment	148 (98.0%)
Vascular assessment	151 (100.0%)
Gastrointestinal severity assessment	150 (99.3%)
Cardio pulmonary assessment	149 (98.7%)

[1]Percentages of Serum, RNA, EDTA and Other are out of the number of patients that had samples collected

[2]Other samples could be skin or other specified sample

Table 5

Patient survey completion by demographic characteristics

	Enrolled (*N* = 151)		Completed all surveys (*N* = 133)	
	Completed all surveys[1]		Method of completion[2]	
	No N = 18 (11.9%)	Yes N = 133 (88.1%)	All in person *N* = 70 (52.6%)	At least 1 online[3] *N* = 63 (47.4%)
Age at baseline visit				
Mean (SD)	44.1 (12.38)	51.5 (14.20)	50.9 (14.51)	52.1 (13.95)
Min–Max	19.8–67.2	21.1–77.8	21.1–73.6	21.7–77.8
Age at baseline visit category				
18–30 years	4 (22.2%)	11 (8.3%)	8 (11.4%)	3 (4.8%)
30–60 years	12 (66.7%)	83 (62.4%)	40 (57.1%)	43 (68.3%)
60+ years	2 (11.1%)	39 (29.3%)	22 (31.4%)	17 (27.0%)
Gender				
Female	14 (77.8%)	112 (84.2%)	59 (84.3%)	53 (84.1%)
Male	4 (22.2%)	21 (15.8%)	11 (15.7%)	10 (15.9%)
Race				
White	13 (72.2%)	99 (74.4%)	52 (74.3%)	47 (74.6%)
Black or African American	3 (16.7%)	17 (12.8%)	9 (12.9%)	8 (12.7%)
Asian	2 (11.1%)	9 (6.8%)	4 (5.7%)	5 (7.9%)
Other, multiple, or not reported	0 (0.0%)	8 (6.0%)	5 (7.1%)	3 (4.8%)
Ethnicity				
Not Hispanic or Latino	13 (72.2%)	114 (85.7%)	57 (81.4%)	57 (90.5%)
Hispanic or Latino	3 (16.7%)	17 (12.8%)	12 (17.1%)	5 (7.9%)
Unknown or not reported	2 (11.1%)	2 (1.5%)	1 (1.4%)	1 (1.6%)
Marital status				
Married	13 (72.2%)	89 (66.9%)	44 (62.9%)	45 (71.4%)
Single	4 (22.2%)	28 (21.1%)	16 (22.9%)	12 (19.0%)
Divorced, widowed or unknown	1 (5.6%)	16 (12.0%)	10 (14.3%)	6 (9.5%)
Employment status				
Full-time	10 (55.6%)	61 (45.9%)	33 (47.1%)	28 (44.4%)
Retired	2 (11.1%)	21 (15.8%)	13 (18.6%)	8 (12.7%)
Disabled, due to scleroderma	2 (11.1%)	12 (9.0%)	7 (10.0%)	5 (7.9%)
Homemaker	1 (5.6%)	12 (9.0%)	4 (5.7%)	8 (12.7%)
Unknown or not reported	1 (5.6%)	11 (8.3%)	4 (5.7%)	7 (11.1%)
Part-time	0 (0.0%)	9 (6.8%)	4 (5.7%)	5 (7.9%)
Student, unemployed, or disabled not due to scleroderma	2 (11.1%)	7 (5.3%)	5 (7.1%)	2 (3.2%)
Smoking status				
Never	14 (77.8%)	91 (68.4%)	45 (64.3%)	46 (73.0%)
Former	3 (16.7%)	39 (29.3%)	24 (34.3%)	15 (23.8%)
Current	1 (5.6%)	3 (2.3%)	1 (1.4%)	2 (3.2%)

[1]Percentages of No and Yes are out of number of patients enrolled.

[2]Percentages of method are out of the number of patients who completed all surveys.

[3]Only 5 patients completed surveys online and in-person. For this reason this column includes anyone who completed at least 1 online

Table 6

Patient survey completion by clinical characteristics

	Enrolled (*N* = 151)		Completed all surveys (*N* = 133)	
	Completed all surveys[1]		Method of completion[2]	
	No *N* = 18 (11.9%)	Yes *N* = 133 (88.1%)	All in person *N* = 70 (52.6%)	At least 1 online[3] *N* = 63 (47.4%)
First non-Raynaud's symptom				
Hand swelling/puffy hands	9 (50.0%)	79 (59.4%)	37 (52.9%)	42 (66.7%)
Skin tightening	2 (11.1%)	17 (12.8%)	9 (12.9%)	8 (12.7%)
Arthralgia, arthritis	3 (16.7%)	10 (7.5%)	7 (10.0%)	3 (4.8%)
Dyspnea	2 (11.1%)	7 (5.3%)	4 (5.7%)	3 (4.8%)
Other[4]	2 (11.1%)	20 (15.0%)	13 (18.6%)	7 (11.1%)
Patient ever had diffuse involvement				
Yes	9 (50.0%)	81 (60.9%)	44 (62.9%)	37 (58.7%)
No	9 (50.0%)	52 (39.1%)	26 (37.1%)	26 (41.3%)
ANA[5]				
Negative	0 (0.0%)	11 (8.3%)	4 (5.7%)	7 (11.1%)
Positive	18 (100.0%)	112 (84.2%)	58 (82.9%)	54 (85.7%)
Unavailable	0 (0.0%)	10 (7.5%)	8 (11.4%)	2 (3.2%)
Anti-Centromere				
Negative	15 (83.3%)	84 (63.2%)	40 (57.1%)	44 (69.8%)
Positive	1 (5.6%)	12 (9.0%)	8 (11.4%)	4 (6.3%)
Unavailable	2 (11.1%)	37 (27.8%)	22 (31.4%)	15 (23.8%)
Anti-SCL 70				
Negative	9 (50.0%)	74 (55.6%)	35 (50.0%)	39 (61.9%)
Positive	9 (50.0%)	42 (31.6%)	26 (37.1%)	16 (25.4%)
Unavailable	0 (0.0%)	17 (12.8%)	9 (12.9%)	8 (12.7%)
Anti-Polymerase III				
Negative	14 (77.8%)	63 (47.4%)	36 (51.4%)	27 (42.9%)
Positive	4 (22.2%)	31 (23.3%)	9 (12.9%)	22 (34.9%)
Unavailable	0 (0.0%)	39 (29.3%)	25 (35.7%)	14 (22.2%)
SSc-specific antibody positive (Anti-Centromere, Anti-SCL 70 or Anti-Polymerase III positive)				
Yes	13 (72.2%)	84 (63.2%)	43 (61.4%)	41 (65.1%)
No	5 (27.8%)	39 (29.3%)	21 (30.0%)	18 (28.6%)
Autoantibodies not collected	0 (0.0%)	10 (7.5%)	6 (8.6%)	4 (6.3%)

[1] Percentages of No and Yes are out of number of patients enrolled

[2] Percentages of method are out of the number of patients who completed all surveys

[3] Only 5 patients completed surveys online and in-person. For this reason this column includes anyone who completed at least 1 online

[4] Other includes digital ulcer, reflux, leg swelling, carpal tunnel syndrome, GI symptoms (other than reflux), and other

[5] *ANA* anti-nuclear antibody