Progressive Skin Fibrosis, Internal Organ Involvement and All - Cause Mortality in an Early Systemic Sclerosis US Multicenter Registry

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Kate Homer[1], Benjamin Brennan[1], Shervin Assassi[2], Elana Bernstein[3], Flavia Castelino[4], Robyn Domsic[5], Jessica Gordon[6], Faye Hant[7], Monique Hinchcliff[8], Ami Shah[9], Victoria K. Shanmugam[10], Virginia Steen[11], Veronica J. Berrocal[1], Melanie Hemmrich[12], Tracy Frech[13], and Dinesh Khanna[1]

[1.] University of Michigan 2.University of Texas, Houston 3. Columbia University 4. Harvard University 4. University of Pittsburgh 6. Hospital for Special Surgery 7. Medical University of South Carolina 8. Northwestern University 9. John Hopkins University 10. George Washington University 11. Georgetown 12. Bayer AG 13. University of Utah

INTRODUCTION

Prospective Registry of Early Diffuse Cutaneous Systemic Sclerosis

- Early diffuse cutaneous systemic sclerosis (dcSSc) carries a high morbidity and mortality, predominantly due to internal organ involvement.[1]
- Ongoing international cohorts have predominantly included prevalent patients with both limited cutaneous and dcSSc.
- The Prospective Registry of Early Systemic Sclerosis (PRESS) is an ongoing observational registry of early dcSSc that is being conducted at 12 different Scleroderma Centers.
- The purpose of the registry to understand the current management of dcSSc and trends in morbidity and mortality in current era.
- Data is entered in the RedCap and housed at the University of Michigan.

OBJECTIVE

Time to Event Visceral Organ Involvement and All-Cause Mortality

- The purpose of this study was to investigate the time to event of new onset of visceral organ involvement and all-cause mortality in early dcSSc participants in an ongoing US multicenter registry (PRESS).

METHOD

- Inclusion criteria include a diagnosis of dcSSc and a disease duration of ≤ 2 years calculated from the date of onset of first non-Raynaud's phenomenon.
- Organ involvement was defined as new involvement or worsening during follow up visits—
- 1) absolute increase in mRSS of ≥5 units or ≥ 25%
- 2) an absolute decline of FVC % of ≥ 10%; 3) Pulmonary Hypertension on right heart catheterization;
- 4) LVEF of ≤ 45% on echo;
- 5) scleroderma renal crisis; or
- 6) all-cause mortality.

- We reported number of participants experiencing organ involvement during the course of the study via frequency tables and characterized the distribution of events through plots of the cumulative proportion of participants experiencing each event by time.
- Confidence intervals in the cumulative proportion plots were derived via bootstrap method.

RESULTS

- The cohort consisted of 239 participants at baseline with median follow-up of 414 days (IQR=112-922 days).
- The baseline mean age was 50.1 years
- 71.1% were female
- 76.2% were white
- Mean baseline mRSS was 21.31
- Mean disease duration was 1.21 years
- Mean HAQ-DI score was 0.82 (Table 1.)
- During the first year of the study, 82.0% were on immunomodulatory therapy.
- At any time during the course of the study, 83.3% were on immunomodulatory therapy.[2] (Table 2.)

RESULTS

Table 1: PRESS Demographic Characteristics (n=239)

Age (years), mean (SD)	50.1 (14)
Female, n (%)	170 (71.1)
Hispanic or Latino, n (%)	23 (9.6)
White, n (%)	182 (76.2)
Black or African American, n (%)	40 (16.7)
Other, n (%)	17 (7.1)
Disease duration (years), mean (SD)	1.21 (0.69)
MRSS (n=231), mean (SD)	21.31 (10.25)
HAQ-DI (n=204), mean (SD)	0.82 (0.64)
FVC (n=201), mean (SD)	79.99 (18.91)
DLCO (n=192), mean (SD)	69.53 (25.48)

*Disease duration calculated from date of first non-Raynaud's Phenomenon sign or symptom

Table 2: Immunomodulatory therapy among PRESS participants at any time during the course of the study

Mycophenolate Mofetil	63.2%
Methotrexate	20.9%
Cyclophosphamide	5.0%
D-penicillamine	3.4%
Hydroxychloroquine	16.3%
Azathioprine	2.1%
Any immunomodulatory therapy*	83.3%

*Percentage is greater than 83.3% as some participants were on multiple therapies at a single time-point and/or during the study).[2]

Table 3: Organ involvement among PRESS participants at any time during the course of the study

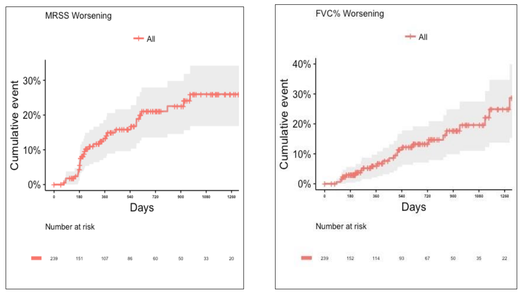
Absolute increase in mRSS of ≥5 units or ≥ 25% (n=231), n (%)	31 (13.4)
Absolute decline of FVC % of ≥ 10% (n=192), n (%)	27 (14.1)
Pulmonary Hypertension on right heart catheterization (n=239), n (%)	5 (2.1)
LVEF of ≤ 45% on echo (n=199), n (%)	4 (2.0)
Scleroderma renal crisis (n=239), n (%)	12 (5.0)
All-cause mortality (n=239), n (%)	14 (5.9)

RESULTS

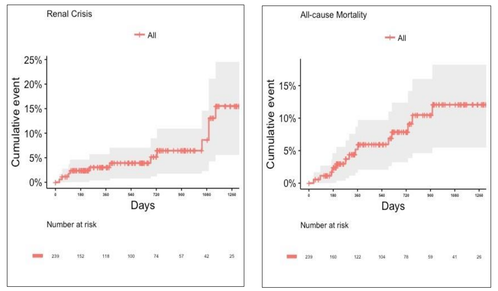
Table 4: Cause of death among PRESS participants who died during the course of the study (n=14)

SSc related, n(%)	12 (85.7)
Progressive ILD	2 (16.7)
Severe GI dysmotility	2 (16.7)
Significant PAH	1 (8.3)
Cardiac arrhythmia	4 (33.3)
Cardiac toxicity due to CYC	1 (8.3)
Scleroderma renal crisis, Severe GI dysmotility, and severe PH	1 (8.3)
Unknown	1 (8.3)
Non-SSc related	2 (14.3)
Esophageal cancer	2 (100.0)

Figure 1: Cumulative Progressive Skin Fibrosis, Internal Organ Involvement and All-Cause Mortality Event Percentages with Confidence Intervals*



RESULTS



*Shading represents confidence intervals.

CONCLUSION

- Despite 83.3% on immunomodulatory therapy during the course of the study, a high proportion of early dcSSc patients experience worsening of mRSS and lung function and mortality within 2 years of dcSSc diagnosis.
- There are ongoing vascular-predominant complications over the course of the disease, consistent with published literature.[3]
- This data supports an ongoing need to identify novel therapies for dcSSc.

REFERENCES

1. Denton CP, Khanna D. The Lancet. 2017.
2. RB Blank, Gordon JK, et al. ACR/ARHP Annual meeting. 2018.
3. Nihtyanova SI, et al. Arthritis & rheumatology. 2014

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