Disclosure of Interests: Elizabeth Hensor: None declared, Maria Grazia Lazzaroni Consultant of: Boehringer Ingelheim, Janssen, Grant/research support from: Boehringer Ingelheim, Michelle Wilson: None declared, Mark Gilthorpe: None declared, Francisco Del Gallo Speakers bureau: Boehringer Ingelheim, Jannsen, AstraZeneca, Consultant of: AstraZeneca, Boehringer Ingelheim, Capella, Chemomab, Janssen, Mitsubishi-Tanabe, Grant/research support from: Abbvie, AstraZeneca, Boehringer Ingelheim, Capella, Chemomab, Kymab, Janssen, Mitsubishi-Tanabe.

DOI: 10.1136/annrheumdis-2023-eular.3105

PO51290 INCREASED RISK OF MYOCARDIAL INFARCTION AND STROKE IN PATIENTS WITH SYSTEMIC SCLEROSIS: A NATIONWIDE COHORT STUDY

Epidemiology, Systemic sclerosis, Cardiovascular disease

Y. Eun¹, K. D. Han², J. K. Ahn¹.¹ Kangbuk Samsung Hospital, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); ²Soongsil University, Department of Statistics and Actuarial Science, Seoul, Korea, Rep. of (South Korea)

Background: Previous studies have suggested a link between systemic sclerosis (SSc) and cardiovascular disease, but large-scale data are still lacking due to the nature of rare autoimmune diseases.

Objectives: We aimed to compare the incidence of myocardial infarction (MI) and stroke in patients with SSc and age- and sex-matched controls in a nationwide population-based cohort in Korea.

Methods: We included patients with SSc defined by the ICD-10 code (M34) and rare and intractable disease code (V138) and 1.5 age- and sex-matched controls using the Korean National Health Insurance Database. The outcomes of the study were MI and stroke. Cox proportional hazard analysis and Kaplan-Meier curve were used to compare the incidence of outcomes between patients with SSc and controls.

Results: A total of 4700 patients with SSc and 23500 controls were included in the study. The mean follow-up period was 5.6 ± 2.8 years. Baseline, patients with SSc had higher prevalent rates of comorbidities such as hypertension, hyperlipidemia, and congestive heart failure than controls. Patients with SSc had a 3-fold higher risk of MI (adjusted hazard ratio [aHR] 3.01, 95% confidence interval [CI] 2.41–3.76) and a 1.7-fold higher risk of stroke (aHR 1.65, 95% CI 1.28–2.14) compared to controls. There were no differences in the association between SSc and MI or stroke by age, sex, or comorbidities.

Conclusion: This nationwide population-based cohort study revealed an association between SSc and increased risk of MI and stroke.

REFERENCES: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.6502

PO51291 PREDICTION OF MORTALITY IN SSC-ILD DEPENDS ON DEFINITION OF ILD PROGRESSION

Lungs, Systemic sclerosis, Prognostic factors

A. M. Hoffmann-Vold¹,°, L. Petelytska²,°, F. Hreiftein¹, I. Baruas¹, M. O. Becker³, H. J. Bjørkjeaker¹, C. Brurng⁴, C. Bruni², P. P. Diep⁵, R. Dobrots⁶, M. Durheim⁷, M. Elhai³, S. Jordan², E. Langball¹, O. Midvedt¹, C. Milha², M. Molver⁸, O. Dieterler⁹,¹ Oslo University Hospital, Rheumatology; Oslo, Norway; ²University Hospital Zurich, University of Zurich, Zurich, Switzerland; ³Hospital of Southern Norway, Rheumatology, Kristiansand, Norway; ⁴Oso University Hospital, Oslo Centre for Biostatistics and Epidemiology, Oslo, Norway; ⁵Oso University Hospital, Respiratory Medicine, Oslo, Norway

Background: Progression of interstitial lung disease (ILD) is a candidate for long-term mortality in patients with systemic sclerosis (SSc). Different definitions of progression have been proposed. Declining lung function is often used, whereas others include composite definitions such as the 2022 ATS/ERS/JSR/ALAT guidelines for progressive pulmonary fibrosis (PPF) and the INBUILD criteria for progressive fibrosing ILD (PF-ILD). These different definitions have not been compared in SSc-ILD.

Objectives: To estimate the prevalence of ILD progression applying different definitions and test their performance of predicting mortality.

Methods: We included all SSc patients from the Oslo and Zurich cohorts who had ILD on HRCT and serial assessments of disease progression defined as: (A) Absolute FVC decline ≥5% over 12 months (B) PPF guideline criteria with 2/3 criteria present over 12 months of (1) worsening of respiratory symptoms; (2) absolute decline in FVC >5% or in DLco >10% and (3) disease progression on HRCT

(C) INBUILD PF-ILD criteria within 24 months with (1) FVC decline ≥10%, (2) FVC decline ≥5–10% and worsening of respiratory symptoms or increased lung fibrosis on HRCT, or (3) worsening of respiratory symptoms and increased lung fibrosis.

We assessed the prevalence of ILD progression using these competing definitions and tested their performance of predicting mortality.

Results: We included all SSc patients from the Oslo and Zurich cohorts who had ILD on HRCT and serial assessments of disease progression defined as: (A) Absolute FVC decline ≥5% over 12 months (B) PPF guideline criteria with 2/3 criteria present over 12 months of (1) worsening of respiratory symptoms; (2) absolute decline in FVC >5% or in DLco >10% and (3) disease progression on HRCT

(C) INBUILD PF-ILD criteria within 24 months with (1) FVC decline ≥10%, (2) FVC decline ≥5–10% and worsening of respiratory symptoms or increased lung fibrosis on HRCT, or (3) worsening of respiratory symptoms and increased lung fibrosis.

We assessed the prevalence of ILD progression using these competing definitions and tested their performance of predicting mortality.

Results: In total, 231 SSc-ILD patients from Oslo and Zurich were included, with 71 (31%) showing FVC decline ≥5%, 43 (19%) fulfilling the PPF guideline and 89 (39%) the INBUILD PF-ILD criteria. Most progressive patients fulfilled ≥1 of the definitions of progression (107 (56%) while 124 (54%) did not progress (Figure 1). Patient characteristics did not differ between the definitions, except for more extensive ILD and ground glass on HRCT and more frequent oxygen desaturation among those fulfilling the PPF criteria (Table 1). The number of deaths [44 (47%) over mean 7.7 years (SD 3.9)] follow up were comparable in the different groups. The progression definitions performed differently in multivariable cox models adjusted for age, sex, disease duration, SSc subtype, extent of lung fibrosis, baseline FVC and treatment using FVC declines≥5% (HR1.87, 1.10-3.17

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2022-eular.3181

On 22 July by guest. Protected by copyright.

Downloaded from http://ard.bmj.com/ on July 22, 2023 by guest. Protected by copyright.
**References:** NIL.

**Acknowledgments:** NIL.

**Disclosure of Interests:** Anna-Maria Hoffmann-Vold Speakers bureau: Boehringer Ingelheim, Janssen, Medsca, Merck Sharp & Dohme and Roche. Consultant of: ARXX, Boehringer Ingelheim, Genentech, Janssen, Medsca, Merck Sharp & Dohme and Roche. Grant/research support from: Boehringer Ingelheim, Janssen, Liubov Petelytska: None declared, Cosimo Bruni Speakers bureau: Eli-Lilly, Consultant of: Boehringer Ingelheim, Grant/research support from: Gruppo Italiano Lotta alla Sclerodermia

**Conclusion:** The prevalence of ILD progression varies depending on which definition was applied. FVC decline alone and PF-ILD criteria predicted mortality significantly but not the 2022 PPF guideline criteria.

<table>
<thead>
<tr>
<th>FVC decline&gt;5%</th>
<th>PPF</th>
<th>PF-ILD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, n (%)</td>
<td>20 (28)</td>
<td>12 (28)</td>
</tr>
<tr>
<td>Age at onset, y (SD)</td>
<td>49 (14)</td>
<td>50 (13)</td>
</tr>
<tr>
<td>Disease duration&gt;3y, n (%)</td>
<td>43 (61)</td>
<td>24 (56)</td>
</tr>
<tr>
<td>dcSSc, n (%)</td>
<td>38 (54)</td>
<td>24 (56)</td>
</tr>
<tr>
<td>ATA, n (%)</td>
<td>7 (14)</td>
<td>4 (15)</td>
</tr>
<tr>
<td>CRP, n (%)</td>
<td>93 (19.6)</td>
<td>89 (19.5)</td>
</tr>
<tr>
<td>FVC, % (SD)</td>
<td>66 (16.3)</td>
<td>61 (16.2)</td>
</tr>
<tr>
<td>Functional class 3&amp;4, n (%)</td>
<td>9 (19)</td>
<td>6 (19)</td>
</tr>
<tr>
<td>ILD&gt;10%, n (%)</td>
<td>20 (43)</td>
<td>18 (40)</td>
</tr>
<tr>
<td>Ground glass, n (%)</td>
<td>28 (42)</td>
<td>23 (56)</td>
</tr>
<tr>
<td>G Desaturation, n (%)</td>
<td>6 (14)</td>
<td>7 (20)</td>
</tr>
<tr>
<td>Immunosuppressives, n (%)</td>
<td>23 (32)</td>
<td>21 (49)</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>32 (45)</td>
<td>20 (47)</td>
</tr>
</tbody>
</table>

**Figure 1:** Venn diagram of patients fulfilling the different definitions of ILD progression.

**REFERENCES:** NIL.

**Acknowledgments:** NIL.

**Disclosure of Interests:** Anna-Maria Hoffmann-Vold Speakers bureau: Boehringer Ingelheim, Janssen, Medsca, Merck Sharp & Dohme and Roche. Consultant of: ARXX, Boehringer Ingelheim, Genentech, Janssen, Medsca, Merck Sharp & Dohme and Roche. Grant/research support from: Boehringer Ingelheim, Janssen, Liubov Petelytska: None declared, Cosimo Bruni Speakers bureau: Eli-Lilly, Consultant of: Boehringer Ingelheim, Grant/research support from: Gruppo Italiano Lotta alla Sclerodermia (GILS), European Scleroderma Trials and Research Group (EUSTAR), Foundation for research in Rheumatology (FOREUM), Scleroderma Clinical Trials (GILS), European Scleroderma Trials and Research Group (EUSTAR), Foundation for research in Rheumatology (FOREUM), Scleroderma Clinical Trials

**Background:** Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by microvascular damage, dysregulation of innate and adaptive immunity, and fibrosis in many organs[1]. Observational studies have suggested associations between SSc and cardiovascular diseases (CVD)[2]. However, this association is easily disturbed by confusion and reverse causality. In the study, we used Mendelian randomization (MR) to conduct a study on bidirectional causality to examine the relationship between SSc and CVD.

**Objectives:** The study aims to evaluate the connection between SSc and CVD, and further to provide comprehensive CVD assessment and treatment for SSc patients.

**Methods:** Summary-level statistical data for SSc were derived from a large meta-analysis of GWAS, including 55,114 cases and 482,295 controls. The summary data for 12 CVD were retrieved from genome-wide association studies (GWAS). In this study, we conducted MR analysis using the random-effects inverse-variance (IVW) method as the primary approach. The weighted median approach can yield consistent causal estimates, assessing these genetic variants' horizontal pleiotropy and heterogeneity using the MR-Egger intercept test and additionally, we utilized the leave-one-out analysis to detect the robustness and consistency of the results.

**Results:** Atrial fibrillation(AF) increased the risk of SSc (IVW OR = 1.428, 95% CI = 1.101-1.854, p = 0.007), Meanwhile, MR-Egger and weighted median pointed toward a similar direction of effect (weighted median: OR = 1.374; 95% CI = 0.987-1.912; p = 0.063; MR-Egger: OR = 1.471, 95% CI = 0.905-2.391, p = 0.140). In the reverse MR, the results of IVW demonstrated that SSc was negatively correlated with the risk of hypertension after removing abnormal single nucleotide polymorphisms(SNPs) (IVW: OR = 0.996, 95%CI: 0.993–1.000, p = 0.036). The heterogeneity test showed no significant heterogeneity among selected instrumental variables(IVs) (Q_p value >0.05) except for miocardial infarction(MI)(MR Egger: Q_p value = 0.0974) and AF(MR Egger: Q_p value = 0.0001; IVW: Q_p value = 0.0001). Moreover, no significant evidence of horizontal pleiotropy was observed for IVs. There was no causal genetic relationship between SSc and other CVDs, such as coronary heart disease, heart failure, and pulmonary embolism.

**Conclusion:** We verified that SSc could cause pathological hypertension processes. Furthermore, SSc may be causally impacted by AF. The main mechanism of this causal relationship may be conduction system ischemia and left ventricular systolic failure.

**REFERENCES:**
