SUPPLEMENTARY MATERIALS

Title: Latent trajectory modeling of pulmonary artery pressure in systemic sclerosis: A retrospective cohort study

Supplemental Table 1. Results of the selection indicators for each model generated by group-based trajectory modeling

Number and shape		Judgement	Minimum APPA	Minimum OCC	Relative entropy	Size of minimum group (%)	BIC
2 groups	Linear	Candidate	0.926	8.682	0.8	30.08	3786.18
2 groups	Quadratic	Candidate	0.925	9.019	0.801	30.51	3789.45
2 groups	Cubic	Candidate	0.924	8.937	0.8	30.51	3793.34
3 groups	Linear	Candidate	0.842	9.382	0.754	13.56	3727.98
3 groups	Quadratic	Violation	0.822	3.769	0.649	15.25	3772.38
3 groups	Cubic	Violation	0.807	4.093	0.689	16.53	3771.55
4 groups	Linear	Violation	0.739	4.167	0.635	13.56	3721.39
4 groups	Quadratic	Candidate	0.804	5.522	0.709	8.05	3723.22
4 groups	Cubic	Candidate	0.815	6.04	0.705	10.59	3722.35
5 groups	Linear	Violation	0.79	5.533	0.7	2.97	3714.03
5 groups	Quadratic	**Identified**	0.739	5.318	0.709	3.81	3723.34
5 groups	Cubic	Violation	0.664	5.16	0.649	4.24	3712.2
6 groups	Linear	Violation	0.811	5.95	0.743	1.27	3710.14
6 groups	Quadratic	Violation	0.77	7.041	0.732	2.97	3695.88
6 groups	Cubic	Violation	0.554	4.67	0.581	5.08	3715.48
7 groups	Linear	Violation	0.549	3.071	0.55	3.39	3719.41
7 groups	Quadratic	Violation	0.703	4.441	0.633	1.69	3682.04
7 groups	Cubic	Violation	0.575	5.516	0.655	2.97	3708.02

The appropriate model was determined on the basis of the following adequacy criteria: (a) the APPA for each trajectory should be > 0.7, (b) the OCC for each trajectory should be > 5, (c) the relative entropy should be > 0.5, and (d) the minimum number of individuals assigned to each trajectory should exceed 3% of the total population. Of the models that met all of the above criteria, one model was identified based on the BIC and clinical interpretability for the number and shape of the trajectories.

APPA, average posterior probability of assignments; OCC, odds of correct classification; BIC, Bayesian information criterion.

Supplemental Table 2. Clinical findings regarding PH in 36 patients diagnosed with PH

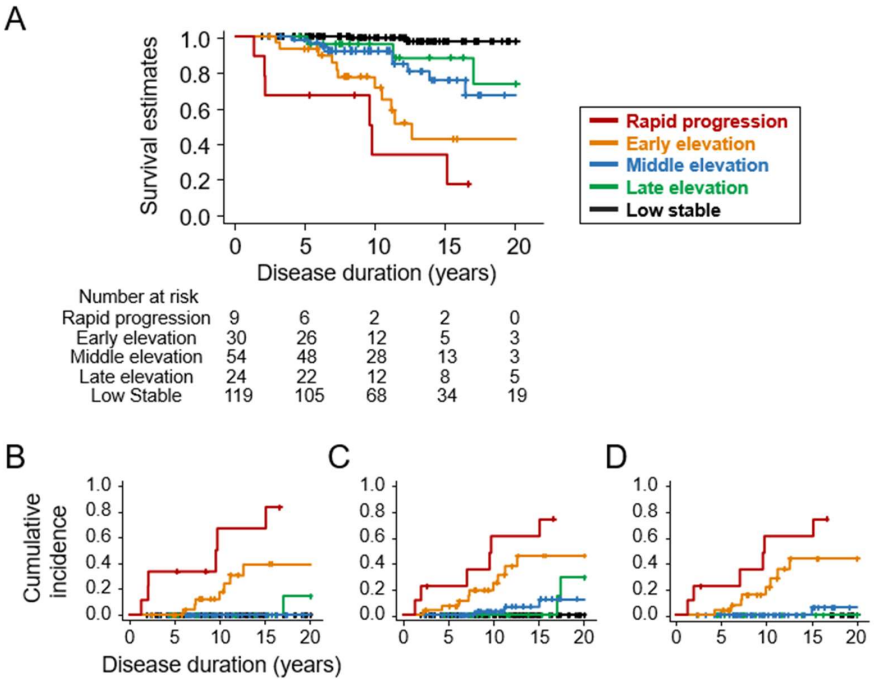
	PAP trajectories				
	Rapid progression (n=8)	Early elevation (n=12)	Middle elevation (n=9)	Late elevation (n=5)	Low stable (n=2)
Clinical classification*, n (%)					
-Group 1 (isolated)	3 (38)	7 (58.3)	5 (56)	3 (60)	1 (50)
-Group 2 (isolated)	2 (25)	1 (8.3)	1 (11)	0 (0)	1 (50)
-Group 3 (isolated)	0 (0)	1 (8.3)	1 (11)	0 (0)	0 (0)
-Group 1+2 (combined)	2 (25)	1 (8.3)	0 (0)	0 (0)	0 (0)
-Group 1+3 (combined)	1 (13)	1 (8.3)	2 (22)	2 (40)	0 (0)
-Group 1+4 (combined)	0 (0)	1 (8.3)	0 (0)	0 (0)	0 (0)
Hemodynamic parameters, median [IQR], (number of patients†)					
-mean RAP (mmHg)	7 [6–8] (n=7)	6 [4–7] (n=9)	7 [7–9] (n=5)	3 [2–4] (n=4)	10 [7–13] (n=2)
-systolic PAP (mmHg)	42 [36–53] (n=8)	39 [36–42] (n=10)	32 [30–38] (n=6)	38 [35–38] (n=5)	40 [39–40] (n=2)
-diastolic PAP (mmHg)	18 [14–28] (n=8)	17 [15–18] (n=10)	14 [13–16] (n=6)	16 [16–18] (n=5)	16 [15–18] (n=2)
-mean PAP (mmHg)	27 [24–39] (n=8)	24 [22–28] (n=12)	22 [21–23] (n=9)	25 [22–26] (n=5)	26 [24–27] (n=2)
-PAWP (mmHg)	10 [8–11] (n=8)	10 [6–13] (n=12)	11 [10–12] (n=9)	10 [9–10] (n=5)	15 [11–18] (n=2)
-CO (L/min)	2.8 [2.5–4.2] (n=8)	3.9 [3.6–4.2] (n=9)	3.8 [3.7–4.1] (n=6)	4.4 [3.6–5.7] (n=5)	4.2 [4.0–4.4] (n=2)
-PVR (WU)	4.4 [3.1–13.0] (n=8)	3.9 [3.8–4.7] (n=9)	2.6 [2.0–3.6] (n=6)	2.7 [2.5–4.5] (n=5)	2.9 [2.8–2.9] (n=2)

* With reference to the clinical classification of the 6th World Symposium on Pulmonary Hypertension. Group 1, pulmonary arterial hypertension; group 2, PH associated with left heart disease; group 3, PH associated with lung diseases and/or hypoxia. All patients classified in Group 1 (both isolated and combined) met the definition of pre-capillary PH in this study (mPAP >20 mmHg and PAWP ≤15 mmHg).

† Indicating the number of patients for whom data were available.

PH, pulmonary hypertension; PAP, pulmonary arterial pressure; IQR, interquartile range; RAP, right atrial pressure; PAWP, pulmonary arterial wedge pressure; CO, cardiac output; PVR, pulmonary vascular resistance; WU, Wood Units.

Supplemental Figure 1.



Supplemental Figure 1. Sensitivity analysis of pulmonary artery pressure trajectories and clinical outcomes in patients with systemic sclerosis. PH was redefined with mPAP ≥25 mmHg instead of mPAP >20 mmHg, and pre-capillary PH was redefined with PVR >2 or >3 WU in addition to mPAP >20 mmHg and PAWP ≤15 mmHg. **A,** Kaplan–Meier survival estimates for PH-free survival in each trajectory. **B–D,** Cumulative incidence functions of PH **(B)**, pre-capillary PH with PVR >2 WU **(C)**, and pre-capillary PH with PVR >3 WU **(D)** in each trajectory. PH, pulmonary hypertension; mPAP, mean systolic pulmonary arterial pressure; PVR, pulmonary vascular resistance; WU, Wood Units; PAWP, pulmonary arterial wedge pressure.

Supplemental Table 3. Clinical factors associated with a shift in membership towards trajectories with earlier sPAP elevation*

Clinical factors	OR	95% CI
Age of onset (years)	**1.05**	**1.02–1.07**
Female	1.60	0.70–3.77
Ever smoking	1.59	0.83–3.02
Hypertension	1.52	0.89–2.60
Type of autoantibody		
-Anti-centromere	1.08	0.50–2.42
-Anti-topoisomerase I	0.77	0.30–1.94
-Anti-RNA polymerase III	1.66	0.45–5.95
Diffuse cutaneous SSc	**2.47**	**1.19–5.16**
Lung fibrosis	1.77	0.96–3.28
Cardiac involvement	**4.02**	**1.51–11.0**
Digital ulcers	1.58	0.89–2.82

The proportional odds ratios and 95% confidence intervals adjusted for all 11 variables in the ordinal logistic regression model are shown. Results are highlighted in bold when the 95% confidence interval did not exceed 1.0 (the null value).

* Rapid progression, early elevation, middle elevation, late elevation, and low stable, in that order.

sPAP, systolic pulmonary arterial pressure; OR, odds ratio; 95% CI, 95% confidence interval; SSc, systemic sclerosis.

Supplemental Table 4. Clinical characteristics of patients excluded due to the lack of testing

	Eligible (n=236)	Lack of testing (n=89)
Baseline clinical factors		
Age of onset (years)	61 [49–69]	61 [55–66]
Female	204 (86)	86 (97)
Ever smoking	65 (28)	24 (27)
Hypertension	81 (34)	21 (24)
Type of autoantibody		
-Anti-centromere	142 (60)	77 (87)
-Anti-topoisomerase I	47 (20)	7 (7.9)
-Anti-RNA polymerase III	13 (5.5)	0 (0)
Diffuse cutaneous SSc	58 (25)	6 (6.7)
Lung fibrosis	82 (35)	12 (14)
Cardiac involvement	18 (7.6)	1 (1.1)
Digital ulcers	70 (30)	5 (5.6)
Clinical outcomes		
Observation period (years)	10.7 [6.6–15.6]	7.6 [5.6–12.5]
PH	36 (15)	0 (0)
Hospitalization for heart failure from any cause	30 (13)	2 (2.2)
Death from any cause	23 (9.7)	1 (1.1)

Age of onset and observation period is described as median [interquartile range], and other categorical variables are described as number (%).