

## Supplementary appendix

**Table S1:** Overall characteristics of the 4 organs studied (complication: yes; no). For each of these, the presence or absence of complication is indicated (yes; no). The clinical and immunophenotypic characteristics (SSc form and immunological profile) and the instrumental parameters used (mean value + DS) are evaluated within each organ. SSc: systemic sclerosis; LES: lower esophageal sphincter; FVC: forced vital capacity; FEV1: Forced expiratory volume in the 1st second; TLC: total lung capacity; DLCO: the carbon monoxide diffusing capacity; PASP: pulmonary arterial systolic pressure; TAPSE: tricuspid annular plane systolic excursion; ACEi: Angiotensin-converting enzyme (ACE) inhibitors; R.R.I.: renal resistance index.

\*:  $p < 0.05$ . \*\*:  $p < 0.001$ . ‘:  $p < 0.20$  for comparisons between patients with or without each organ involvement.

|                                                    | Overall,<br>N = 52        | Esophageal<br>involvement |                             | Cardiac<br>involvement    |                           | Pulmonary<br>involvement |                             | Renal<br>involvement      |                           |
|----------------------------------------------------|---------------------------|---------------------------|-----------------------------|---------------------------|---------------------------|--------------------------|-----------------------------|---------------------------|---------------------------|
|                                                    |                           | No,<br>N = 20             | Yes,<br>N = 32              | No,<br>N = 45             | Yes,<br>N = 7             | No,<br>N = 18            | Yes,<br>N = 34              | No,<br>N = 39             | Yes,<br>N = 13            |
| Age (Years),<br>Mean (SD)                          | 62.02<br>(13.29)          | 62.75<br>(13.86)          | 61.56<br>(13.13)            | 61.71<br>(12.78)          | 64.00<br>(17.30)          | 60.61<br>(13.53)         | 62.76<br>(13.31)            | 58.74<br>(12.44)          | 71.85<br>(11.01)<br>*     |
| Sex (M;F), N                                       | 13;39                     | 7;13                      | 6;26                        | 10;35                     | 3;4                       | 5;13                     | 8;26                        | 8;31                      | 5;8                       |
| SSc Type, N<br>(%)                                 |                           |                           |                             |                           |                           |                          |                             |                           |                           |
| Diffused                                           | 18 (34.6)                 | 5 (25.0)                  | 13 (40.6)                   | 16 (35.6)                 | 2 (28.6)                  | 5 (27.8)                 | 13 (38.2)                   | 14 (35.9)                 | 4 (30.8)                  |
| Limited                                            | 34 (65.4)                 | 15 (75.0)                 | 19 (59.4)                   | 29 (64.4)                 | 5 (71.4)                  | 13<br>(72.2)             | 21 (61.8)                   | 25 (64.1)                 | 9 (69.2)                  |
| Disease<br>duration<br>(years),<br>Median<br>[IQR] | 11.5<br>[7, 18] I         | 12<br>[10.5,<br>17.25]    | 9.5<br>[5, 18]              | 12<br>[7, 18]             | 10<br>[6, 11.5]           | 8.5<br>[5.25,<br>14.25]  | 12<br>[8.25,<br>18.75]’     | 11<br>[6.5,<br>17.5]      | 12<br>[10, 18]            |
| Infusion<br>delay (years),<br>Median<br>[IQR]      | 3<br>[1, 8]               | 4.00<br>[0.75,<br>9.25]   | 2.00<br>[1.00,<br>6.25]     | 3.00<br>[1.00,<br>8.00]   | 0.00<br>[0.00,<br>3.50]   | 5.50<br>[1.00,<br>8.00]  | 3.00<br>[0.00,<br>7.00]     | 2.00<br>[0.00,<br>7.00]   | 5.00<br>[3.00,<br>8.00]’  |
| Rodnan<br>Score,<br>Median<br>[IQR]                | 12.50<br>[5.00,<br>20.50] | 11.00<br>[4.75,<br>15.00] | 13.50<br>[5.75,<br>24.00] ‘ | 12.00<br>[5.00,<br>20.00] | 14.00<br>[4.50,<br>21.00] | 7.50<br>[4.00,<br>11.50] | 15.00<br>[8.25,<br>23.00] * | 14.00<br>[7.50,<br>20.00] | 7.00<br>[4.00,<br>22.00]’ |
| ENA<br>Antibodies, N<br>(%)                        |                           |                           |                             |                           |                           |                          |                             |                           |                           |
| Anti-<br>Centromere                                | 22 (42.3)                 | 8 (40.0)                  | 14 (43.8)                   | 20 (44.4)                 | 2 (28.6)                  | 9 (50.0)                 | 13 (38.2)                   | 16 (41.0)                 | 6 (46.2)                  |
| Anti-Scl70                                         | 17 (32.7)                 | 5 (25.0)                  | 12 (37.5)                   | 16 (35.6)                 | 1 (14.3)                  | 5 (27.8)                 | 12 (35.3)                   | 13 (33.3)                 | 4 (30.8)                  |
| Anti-RNA<br>polymerase<br>III                      | 6 (11.5)                  | 2 (10.0)                  | 4 (12.5)                    | 5 (11.1)                  | 1 (14.3)                  | 2 (11.1)                 | 4 (11.8)                    | 6 (15.4)                  | 0 (0.0)                   |
| Anti-RNP                                           | 3 (5.8)                   | 1 (5.0)                   | 2 (6.2)                     | 2 (4.4)                   | 1 (14.3)                  | 0 (0.0)                  | 3 (8.8)                     | 3 (7.7)                   | 0 (0.0)                   |

|                                         |                |                |                  |               |                |                |                  |               |                |
|-----------------------------------------|----------------|----------------|------------------|---------------|----------------|----------------|------------------|---------------|----------------|
| <b>Anti PM-Scl 100/75</b>               | 6 (11.5)       | 3 (15.0)       | 3 (9.4)          | 3 (6.7)       | 3 (42.9) *     | 1 (5.6)        | 5 (14.7)         | 6 (15.4)      | 0 (0.0)        |
| <b>Anti-SSA/Ro</b>                      | 18 (34.6)      | 7 (35.0)       | 11 (34.4)        | 16 (35.6)     | 2 (28.6)       | 6 (33.3)       | 12 (35.3)        | 13 (33.3)     | 5 (38.5)       |
|                                         |                |                |                  |               |                |                |                  |               |                |
| <b>Hypotonic LES, N (%)</b>             | 22 (42.3)      | 1 (5.0)        | 21 (65.6) *      | 18 (40.0)     | 4 (57.1)       | 7 (38.9)       | 15 (44.1)        | 16 (41.0)     | 6 (46.2)       |
| <b>LES pressure mmHg Mean (SD)</b>      | 15.69 (11.27)  | 18.91 (9.96)   | 13.68' (11.72)   | 16.05 (11.85) | 13.40 (6.61)   | 20.77 (13.49)  | 13.01 (9.01) *   | 16.40 (11.34) | 13.58 (11.23)  |
| <b>Ineffective peristalsis, N (%)</b>   | 24 (46.2)      | 0 (0.0)        | 24 (75.0) **     | 22 (48.9)     | 2 (28.6)       | 9 (50.0)       | 15 (44.1)        | 17 (43.6)     | 7 (53.8)       |
| <b>Distal Amplitude Waves Mean (SD)</b> | 41.55 (29.02)  | 63.25 (24.25)  | 27.98 (23.06) ** | 39.61 (28.41) | 54.00 (32.15)  | 40.72 (31.50)  | 41.99 (28.11)    | 45.14 (31.15) | 30.77 (18.44)' |
|                                         |                |                |                  |               |                |                |                  |               |                |
| <b>Warrick Score, Mean (SD)</b>         | 8.04 (7.52)    | 9.20 (8.24)    | 7.96 (6.88)      | 7.10 (6.72)   | 14.50 (10.05)  | 4.70 (4.01)    | 10.41 (8.02) **  | 7.47 (7.18)   | 9.91 (8.63)    |
| <b>FVC Mean (SD)</b>                    | 100.46 (25.59) | 101.25 (24.63) | 99.97 (26.55)    | 99.56 (26.29) | 106.29 (21.23) | 110.50 (17.72) | 95.15 (27.68) *  | 99.28 (26.50) | 104.00 (23.28) |
| <b>FEV1 Mean (SD)</b>                   | 93.58 (22.98)  | 96.40 (22.89)  | 91.81 (23.22)    | 92.29 (22.42) | 101.86 (26.64) | 100.72 (9.40)  | 89.79 (26.98)'   | 92.56 (24.19) | 96.62 (19.44)  |
| <b>TLC Mean (SD)</b>                    | 90.31 (22.57)  | 93.95 (24.84)  | 88.03 (21.11)    | 88.84 (23.18) | 99.71 (16.44)  | 100.11 (15.15) | 85.12 (24.26) *  | 89.72 (22.15) | 92.08 (24.63)  |
| <b>DLCO Mean (SD)</b>                   | 69.33 (19.35)  | 71.55 (20.91)  | 67.94 (18.52)    | 70.87 (19.50) | 59.43 (16.14)' | 88.67 (13.16)  | 59.09 (13.32) ** | 69.33 (20.77) | 69.31 (15.00)  |
|                                         |                |                |                  |               |                |                |                  |               |                |
| <b>TAPSE/PAS P Mean (SD)</b>            | 0.81 (0.19)    | 0.83 (0.20)    | 0.80 (0.18)      | 0.85 (0.17)   | 0.56 (0.07) ** | 0.83 (0.17)    | 0.80 (0.19)      | 0.84 (0.20)   | 0.70 (0.10) *  |
|                                         |                |                |                  |               |                |                |                  |               |                |
| <b>ACEi, N (%)</b>                      | 15 (28.8)      | 6 (30.0)       | 9 (28.1)         | 13 (28.9)     | 2 (28.6)       | 4 (22.2)       | 11 (32.4)        | 9 (23.1)      | 6 (46.2)       |
| <b>R.R.I., Mean (SD)</b>                | 0.67 (0.06)    | 0.67 (0.06)    | 0.67 (0.05)      | 0.67 (0.06)   | 0.67 (0.04)    | 0.66 (0.06)    | 0.67 (0.05)      | 0.64 (0.03)   | 0.74 (0.04) ** |

**Table S2:** Associations between overall characteristics, immunological profile, skin and organs involvement (instrumental values: mean +DS ) and type of cutaneous systemic sclerosis patients (limited or diffuse). SSc: systemic sclerosis; LES: lower esophageal sphincter; FVC: forced vital capacity; FEV1: Forced expiratory volume in the 1st second; TLC: total lung capacity; DLCO: the carbon monoxide diffusing capacity; PASP: pulmonary arterial systolic pressure; TAPSE: tricuspid annular plane systolic excursion; ACEi: Angiotensin-converting enzyme (ACE) inhibitors; R.R.I.: renal resistance index.

|                                               | <b>Diffused</b>     | <b>Limited</b>      | <b>p</b> |
|-----------------------------------------------|---------------------|---------------------|----------|
| <b>n</b>                                      | <b>18</b>           | <b>34</b>           |          |
| <b>Age (years), Mean (SD)</b>                 | 58.50 (12.90)       | 63.88 (13.30)       | 0.167    |
| <b>Sex (M;F), N</b>                           | 3;5                 | 10;24               | 0.312    |
| <b>Disease Duration (years), Median [IQR]</b> | 8.00 [5.00, 12.75]  | 12.00 [9.00, 18.00] | 0.108    |
| <b>Infusion delay (years), Median [IQR]</b>   | 2.50 [0.25, 6.50]   | 3.00 [1.00, 8.00]   | 0.56     |
| <b>Rodnan Score, Median [IQR]</b>             | 21.00 [9.75, 26.50] | 9.50 [4.25, 15.00]  | 0.012    |
| <b>Antibodies, N (%)</b>                      |                     |                     |          |
| <b>Anti-Centromere</b>                        | 0 (0.0)             | 22 (64.7)           | <0.001   |
| <b>Anti-Scl70</b>                             | 15 (83.3)           | 2 (5.9)             | <0.001   |
| <b>Anti-RNA polymerase III</b>                | 3 (16.7)            | 3 (8.8)             | 0.699    |
| <b>Anti-RNP</b>                               | 1 (5.6)             | 2 (5.9)             | 0.999    |
| <b>Anti PM-Scl 100/75</b>                     | 3 (16.7)            | 3 (8.8)             | 0.699    |
| <b>Anti-SSA/Ro</b>                            | 6 (33.3)            | 12 (35.3)           | 0.999    |
| <b>Ipotonic LES, N (%)</b>                    | 11 (61.1)           | 11 (32.4)           | 0.089    |
| <b>LES pressure mmHg Mean (SD)</b>            | 13.66 (12.10)       | 16.77 (10.84)       | 0.348    |
| <b>BODY (%)</b>                               |                     |                     |          |
| <b>Minimal hypokinetic alterations</b>        | 2 (11.1)            | 9 (26.5)            | 0.021    |
| <b>Dermatomyositis</b>                        | 1 (5.6)             | 0 (0.0)             |          |
| <b>Hyperkinetic</b>                           | 3 (16.7)            | 0 (0.0)             |          |
| <b>Normal pattern</b>                         | 2 (11.1)            | 11 (32.4)           |          |
| <b>Ineffective peristalsis</b>                | 10 (55.6)           | 14 (41.2)           |          |
| <b>Distal Amplitude Waves Mean (SD)</b>       | 34.64 (33.12)       | 45.21 (26.40)       | 0.215    |
| <b>Warrick Score, Mean (SD)</b>               | 11.39 (8.36)        | 6.58 (6.40)         | 0.03     |
| <b>FVC Mean (SD)</b>                          | 86.78 (18.37)       | 107.71 (26.12)      | 0.004    |
| <b>FEV1 Mean (SD)</b>                         | 83.17 (17.32)       | 99.09 (23.89)       | 0.016    |
| <b>TLC Mean (SD)</b>                          | 78.44 (18.00)       | 96.59 (22.42)       | 0.005    |
| <b>DLCO Mean (SD)</b>                         | 70.50 (23.32)       | 68.71 (17.24)       | 0.754    |

|                                               |              |              |       |
|-----------------------------------------------|--------------|--------------|-------|
| <b>PASP<br/>Mean (SD)</b>                     | 29.89 (6.47) | 30.12 (5.87) | 0.898 |
| <b>TAPSE<br/>Mean (SD)</b>                    | 24.28 (4.11) | 23.09 (3.80) | 0.302 |
| <b>TAPSE/PASP<br/>Mean (SD)</b>               | 0.84 (0.18)  | 0.79 (0.19)  | 0.388 |
| <b>ACEi,<br/>N (%)</b>                        | 4 (22.2)     | 11 (32.4)    |       |
| <b>R.R.I.,<br/>Mean (SD)</b>                  | 0.67 (0.06)  | 0.67 (0.06)  | 0.957 |
|                                               |              |              |       |
| <b>Esophagus<br/>Complications,<br/>N (%)</b> | 13 (72.2)    | 19 (55.9)    | 0.394 |
| <b>Lungs<br/>complications,<br/>N (%)</b>     | 13 (72.2)    | 21 (61.8)    | 0.654 |
| <b>Kidney<br/>complications,<br/>N (%)</b>    | 4 (22.2)     | 9 (26.5)     | 0.999 |
| <b>Heart<br/>complications,<br/>N (%)</b>     | 2 (11.1)     | 5 (14.7)     | 0.999 |
| <b>N. of complications,<br/>Mean (SD)</b>     | 1.78 (0.88)  | 1.59 (0.86)  | 0.455 |
| <b>No complications,<br/>N (%)</b>            | 1 (5.6)      | 3 (8.8)      | 0.999 |

**Table S3:** Associations between the various immunological profiles (Antibody type: yes; no) and the general, skin and organ characteristics examined (mean value +DS). SSc: systemic sclerosis; LES: lower esophageal sphincter; FVC: forced vital capacity; FEV1: Forced expiratory volume in the 1st second; TLC: total lung capacity; DLCO: the carbon monoxide diffusing capacity; PASP: pulmonary arterial systolic pressure; TAPSE: tricuspid annular plane systolic excursion; ACEi: Angiotensin-converting enzyme (ACE) inhibitors; R.R.I.: renal resistance index.

\*:  $p < 0.05$ . \*\*:  $p < 0.001$ . ‘:  $p < 0.20$  for comparisons between patients with or without each antibody positivity.

| Antibody<br>(Negative/Positive)                        | anti-Scl70                |                           | anti-Centromere           |                           | anti-RNA<br>polymerase III |                            | anti-RNP                  |                            | PM-Scl 100/75             |                           | anti-SSA/Ro               |                           |
|--------------------------------------------------------|---------------------------|---------------------------|---------------------------|---------------------------|----------------------------|----------------------------|---------------------------|----------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
|                                                        | -                         | +                         | -                         | +                         | -                          | +                          | -                         | +                          | -                         | +                         | -                         | +                         |
| <b>n</b>                                               | 35                        | 17                        | 30                        | 22                        | 46                         | 6                          | 49                        | 3                          | 46                        | 6                         | 34                        | 18                        |
| <b>Age (years),<br/>Mean (SD)</b>                      | 64.23<br>(13.38)          | 57.47<br>(12.25)          | 58.30<br>(14.53)          | 67.09<br>(9.54)*          | 63.17<br>(13.38)*          | 53.17<br>(9.20)            | 62.27<br>(13.58)          | 58.00<br>(7.21)            | 63.52<br>(13.07)*         | 50.50<br>(9.25)           | 61.26<br>(12.01)          | 63.44<br>(15.71)          |
| <b>Sex (M;F), N</b>                                    | 10;25                     | 3;14                      | 8;22                      | 5;17                      | 12;34                      | 1;5                        | 13;36                     | 0;3                        | 11;35                     | 2;4                       | 10;24                     | 3;15                      |
| <b>SSc type,<br/>N (%)</b>                             |                           |                           |                           |                           |                            |                            |                           |                            |                           |                           |                           |                           |
| <b>Diffused</b>                                        | 3 (8.6)                   | 15<br>(88.2)*             | 18<br>(60.0)              | 0 (0.0)                   | 15<br>(32.6)               | 3 (50.0)                   | 17<br>(34.7)              | 1 (33.3)                   | 15<br>(32.6)              | 3 (50.0)                  | 12<br>(35.3)              | 6 (33.3)                  |
| <b>Limited</b>                                         | 32<br>(91.4)              | 2 (11.8)                  | 12<br>(40.0)              | 22<br>(100.0)*            | 31<br>(67.4)               | 3 (50.0)                   | 32<br>(65.3)              | 2 (66.7)                   | 31<br>(67.4)              | 3 (50.0)                  | 22<br>(64.7)              | 12<br>(66.7)              |
| <b>Disease Duration<br/>(years),<br/>Median [IQR]</b>  | 12.00<br>[8.00,<br>18.00] | 10.00<br>[5.00,<br>14.00] | 9.50<br>[5.00,<br>17.00]  | 12.00<br>[9.50,<br>17.75] | 12.00<br>[7.25,<br>18.00]  | 8.00<br>[5.50,<br>11.25]   | 11.00<br>[7.00,<br>17.00] | 22.00<br>[15.00,<br>22.50] | 12.00<br>[8.00,<br>18.00] | 5.50<br>[2.50,<br>7.75]   | 11.50<br>[5.00,<br>17.00] | 11.50<br>[9.25,<br>18.00] |
| <b>Infusion delay<br/>(years),<br/>Median [IQR]</b>    | 3.00<br>[1.00,<br>8.00]   | 4.00<br>[0.00,<br>7.00]   | 2.50<br>[0.00,<br>7.75]   | 3.00<br>[1.00,<br>8.00]   | 3.00<br>[1.00,<br>8.00]    | 2.00<br>[0.25,<br>7.50]    | 3.00<br>[1.00,<br>8.00]   | 5.00<br>[4.00,<br>8.50]    | 3.50<br>[1.00,<br>8.00]   | 1.00<br>[0.00,<br>2.75]   | 2.50<br>[0.25,<br>8.00]   | 4.50<br>[1.00,<br>7.75]   |
| <b>Rodnan Score,<br/>Median [IQR]</b>                  | 10.00<br>[5.00,<br>18.00] | 15.00<br>[9.00,<br>24.00] | 14.50<br>[5.00,<br>23.75] | 11.00<br>[5.25,<br>17.25] | 12.00<br>[4.25,<br>20.00]  | 16.00<br>[10.25,<br>23.25] | 12.00<br>[5.00,<br>20.00] | 15.00<br>[15.00,<br>21.00] | 12.50<br>[5.25,<br>21.50] | 10.00<br>[4.25,<br>18.00] | 15.00<br>[5.00,<br>22.00] | 9.50<br>[5.50,<br>14.75]  |
| <b>Hypotonic LES, N<br/>(%)</b>                        | 14<br>(40.0)              | 8 (47.1)                  | 14<br>(46.7)              | 8 (36.4)                  | 19<br>(41.3)               | 3 (50.0)                   | 20<br>(40.8)              | 2 (66.7)                   | 20<br>(43.5)              | 2 (33.3)                  | 12<br>(35.3)              | 10<br>(55.6)              |
| <b>LES pressure<br/>mmHg<br/>Mean (SD)</b>             | 14.94<br>(8.72)           | 17.25<br>(15.48)          | 15.74<br>(12.88)          | 15.63<br>(8.93)           | 15.94<br>(11.73)           | 13.80<br>(7.26)            | 15.96<br>(11.53)          | 11.40<br>(4.35)            | 15.97<br>(11.80)          | 13.58<br>(6.11)           | 17.15<br>(12.82)          | 12.94<br>(7.08)           |
| <b>BODY, N (%)</b>                                     |                           |                           |                           |                           |                            |                            |                           |                            |                           |                           |                           |                           |
| <b>Minimal<br/>hypokinetic<br/>alterations</b>         | 9 (25.7)                  | 2 (11.8)                  | 4 (13.3)                  | 7 (31.8)                  | 11<br>(23.9)               | 0 (0.0)                    | 11<br>(22.4)              | 0 (0.0)                    | 11<br>(23.9)              | 0 (0.0)                   | 7 (20.6)                  | 4 (22.2)                  |
| <b>Dermatomyositis</b>                                 | 1 (2.9)                   | 0 (0.0)                   | 1 (3.3)                   | 0 (0.0)                   | 1 (2.2)                    | 0 (0.0)                    | 1 (2.0)                   | 0 (0.0)                    | 1 (2.2)                   | 0 (0.0)                   | 1 (2.9)                   | 0 (0.0)                   |
| <b>Hyperkinetic</b>                                    | 0 (0.0)                   | 3 (17.6)                  | 3 (10.0)                  | 0 (0.0)                   | 3 (6.5)                    | 0 (0.0)                    | 3 (6.1)                   | 0 (0.0)                    | 2 (4.3)                   | 1 (16.7)                  | 2 (5.9)                   | 1 (5.6)                   |
| <b>Normal pattern</b>                                  | 11<br>(31.4)              | 2 (11.8)                  | 9 (30.0)                  | 4 (18.2)                  | 10<br>(21.7)               | 3 (50.0)                   | 12<br>(24.5)              | 1 (33.3)                   | 10<br>(21.7)              | 3 (50.0)                  | 9 (26.5)                  | 4 (22.2)                  |
| <b>Ineffective<br/>peristalsis</b>                     | 14<br>(40.0)              | 10<br>(58.8)              | 13<br>(43.3)              | 11<br>(50.0)              | 21<br>(45.7)               | 3 (50.0)                   | 22<br>(44.9)              | 2 (66.7)                   | 22<br>(47.8)              | 2 (33.3)                  | 15<br>(44.1)              | 9 (50.0)                  |
| <b>Distal Amplitude<br/>Waves (mmHg)<br/>Mean (SD)</b> | 44.40<br>(26.45)          | 35.68<br>(33.82)          | 43.52<br>(32.67)          | 38.86<br>(23.64)          | 40.38<br>(28.50)           | 50.50<br>(34.24)           | 42.19<br>(28.85)          | 31.00<br>(36.37)           | 40.18<br>(27.66)          | 52.00<br>(39.48)          | 40.40<br>(29.57)          | 43.72<br>(28.66)          |
| <b>Warrick Score,<br/>Mean (SD)</b>                    | 6.88<br>(6.78)            | 10.79<br>(8.68)*          | 11.04<br>(8.24)*          | 4.00<br>(3.74)            | 7.83<br>(7.71)             | 9.50<br>(6.47)             | 8.23<br>(7.48)            | 5.33<br>(9.24)             | 7.12<br>(6.99)            | 14.33<br>(8.64)*          | 7.20<br>(6.24)            | 9.53<br>(9.39)            |
| <b>FVC<br/>Mean (SD)</b>                               | 105.71<br>(25.30)*        | 89.65<br>(23.29)          | 91.00<br>(23.17)          | 113.36<br>(23.39)*        | 100.11<br>(26.03)          | 103.17<br>(23.92)          | 101.49<br>(25.35)         | 83.67<br>(28.73)           | 102.17<br>(25.30)         | 87.33<br>(26.14)          | 101.85<br>(24.03)         | 97.83<br>(28.85)          |
| <b>FEV1<br/>Mean (SD)</b>                              | 97.91<br>(23.09)<br>*     | 84.65<br>(20.59)          | 87.23<br>(22.17)          | 102.23<br>(21.62)*        | 92.46<br>(23.20)           | 102.17<br>(21.03)          | 94.88<br>(22.45)          | 72.33<br>(25.48)           | 95.50<br>(22.92)          | 78.83<br>(19.00)          | 94.76<br>(21.14)          | 91.33<br>(26.61)          |
| <b>TLC<br/>Mean (SD)</b>                               | 95.97<br>(22.27)*         | 78.65<br>(18.84)          | 82.43<br>(20.64)          | 101.05<br>(20.95)*        | 89.87<br>(22.43)           | 93.67<br>(25.48)           | 90.53<br>(22.20)          | 86.67<br>(33.72)           | 91.48<br>(22.58)          | 81.33<br>(22.23)          | 91.59<br>(20.28)          | 87.89<br>(26.83)          |
| <b>DLCO<br/>Mean (SD)</b>                              | 68.54<br>(17.08)          | 70.94<br>(23.86)          | 67.77<br>(21.22)          | 71.45<br>(16.71)          | 70.11<br>(18.75)           | 63.33<br>(24.62)           | 70.02<br>(19.37)          | 58.00<br>(18.36)           | 69.57<br>(20.39)          | 67.50<br>(8.48)           | 72.74<br>(18.37)          | 62.89<br>(20.02)          |
| <b>PASP<br/>Mean (SD)</b>                              | 30.11<br>(5.97)           | 29.88<br>(6.30)           | 30.50<br>(6.10)           | 29.41<br>(6.00)           | 30.35<br>(5.96)            | 27.67<br>(6.53)            | 29.96<br>(5.95)           | 31.33<br>(8.50)            | 29.74<br>(5.93)           | 32.33<br>(6.77)           | 30.53<br>(5.52)           | 29.11<br>(6.95)           |
| <b>TAPSE<br/>Mean (SD)</b>                             | 23.23<br>(3.90)           | 24.06<br>(4.01)           | 23.67<br>(3.85)           | 23.27<br>(4.07)           | 23.48<br>(3.96)            | 23.67<br>(3.88)            | 23.69<br>(3.90)           | 20.33<br>(3.06)            | 23.52<br>(4.10)           | 23.33<br>(2.25)           | 23.26<br>(3.64)           | 23.94<br>(4.47)           |
| <b>TAPSE/PASP<br/>Mean (SD)</b>                        | 0.80<br>(0.19)            | 0.83<br>(0.17)            | 0.80<br>(0.17)            | 0.82<br>(0.21)            | 0.80<br>(0.18)             | 0.90<br>(0.23)             | 0.82<br>(0.19)            | 0.66<br>(0.08)             | 0.81<br>(0.18)            | 0.75<br>(0.21)            | 0.78<br>(0.18)            | 0.85<br>(0.19)            |
| <b>ACEi,<br/>N (%)</b>                                 | 11<br>(31.4)              | 4 (23.5)                  | 10<br>(33.3)              | 5 (22.7)                  | 15<br>(32.6)               | 0 (0.0)                    | 13<br>(26.5)              | 2 (66.7)                   | 13<br>(28.3)              | 2 (33.3)                  | 11<br>(32.4)              | 4 (22.2)                  |
| <b>R.R.I.,<br/>Mean (SD)</b>                           | 0.67<br>(0.06)            | 0.67<br>(0.06)            | 0.67<br>(0.05)            | 0.68<br>(0.06)            | 0.67<br>(0.06)             | 0.63<br>(0.04)             | 0.67<br>(0.06)            | 0.65<br>(0.05)             | 0.67<br>(0.06)            | 0.65<br>(0.03)            | 0.67<br>(0.05)            | 0.67<br>(0.07)            |

Figure S1. Complication risk modeling procedure.

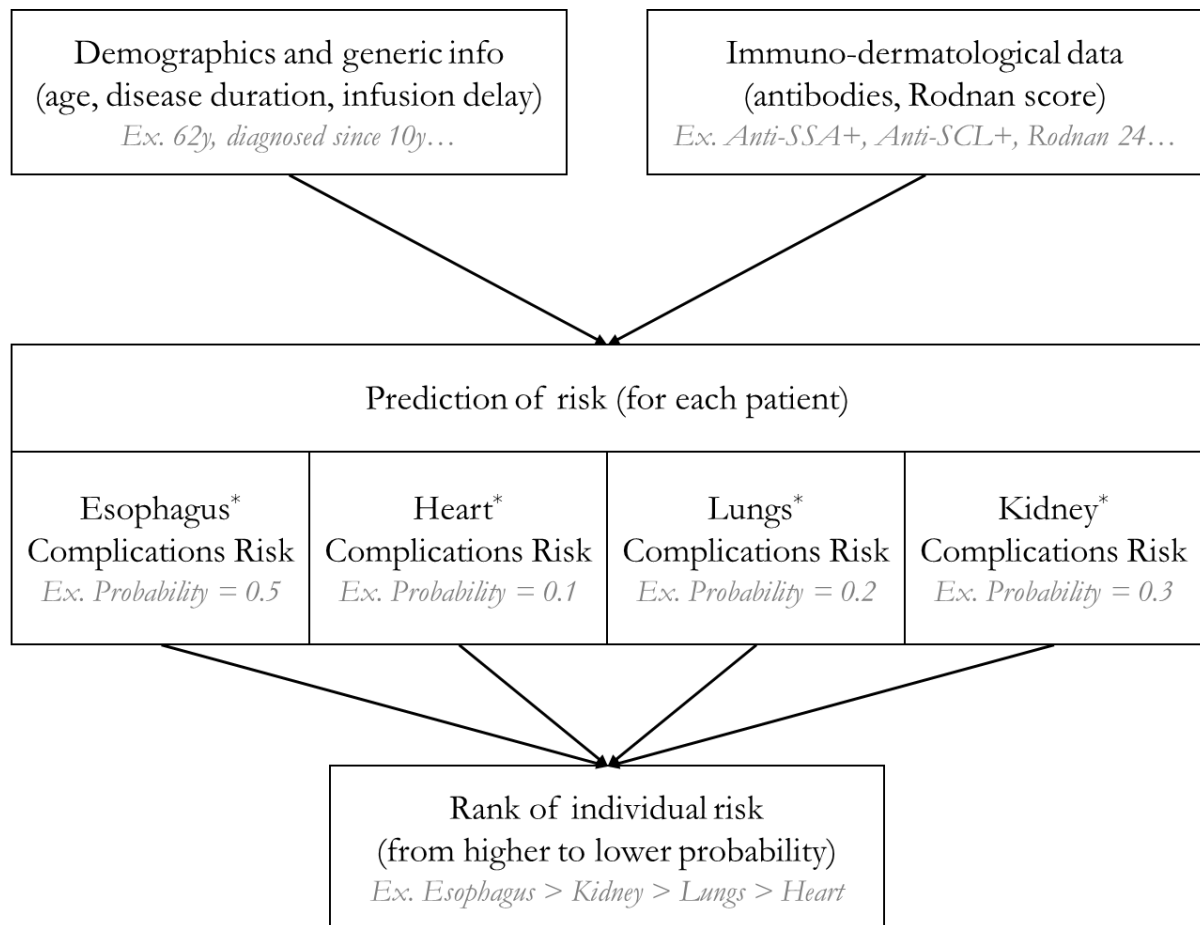


Figure S2. Exemplification of the goodness of fit estimation procedure.

