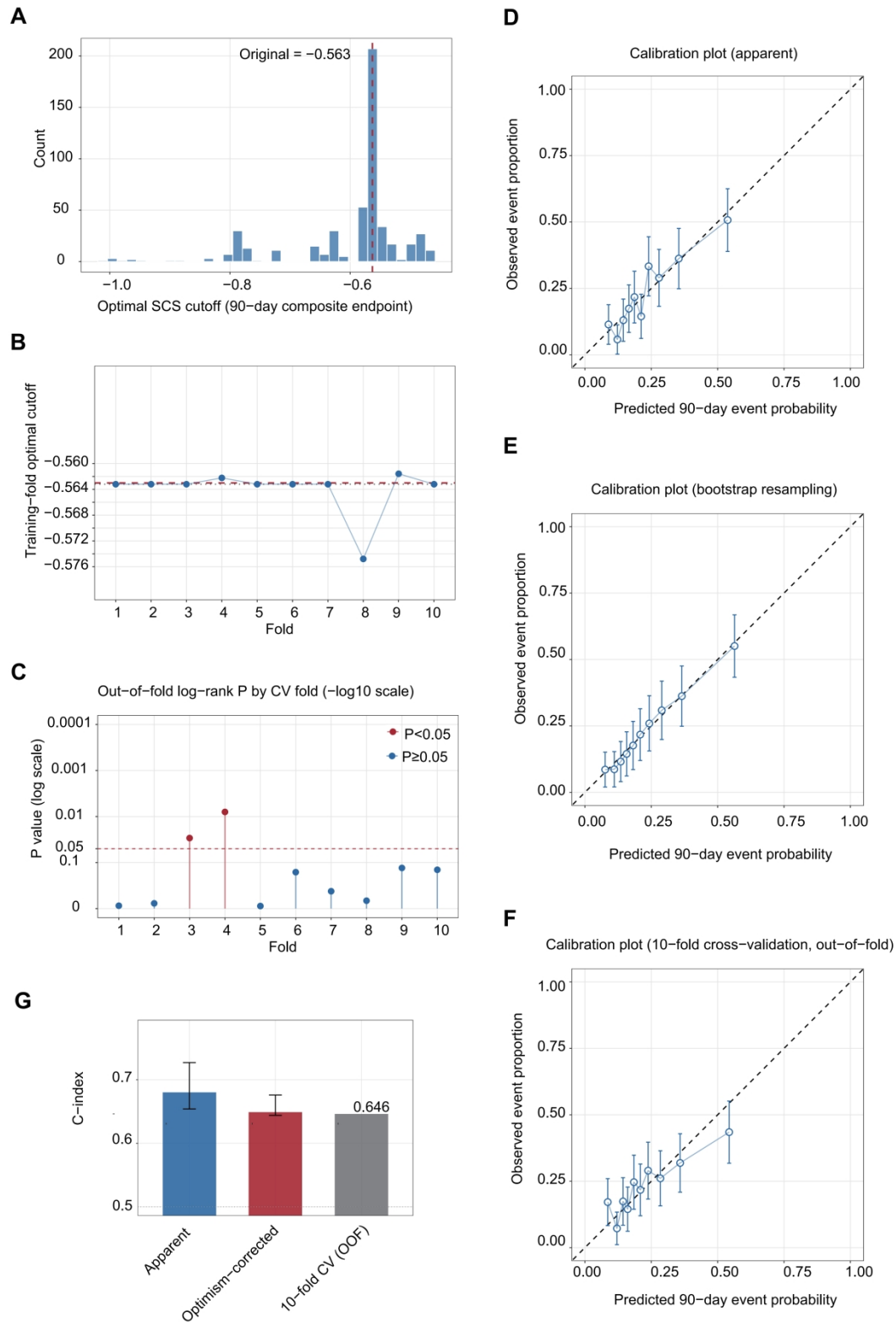
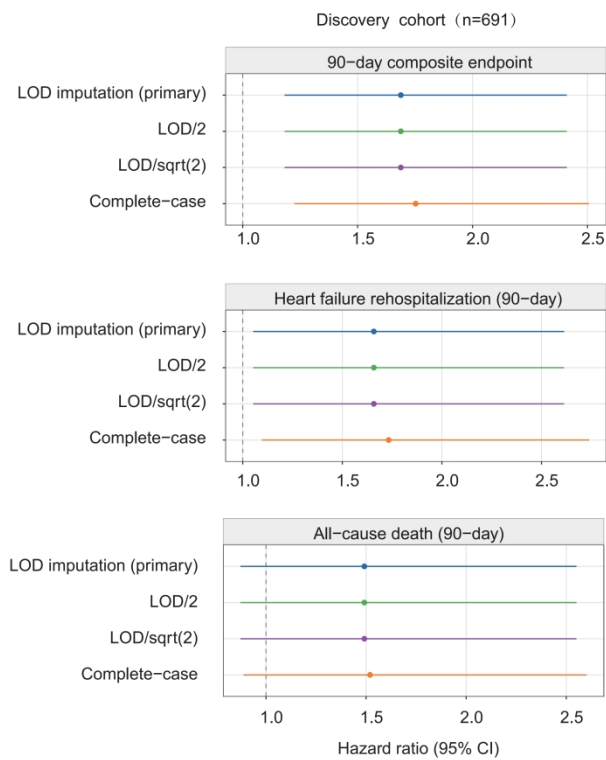


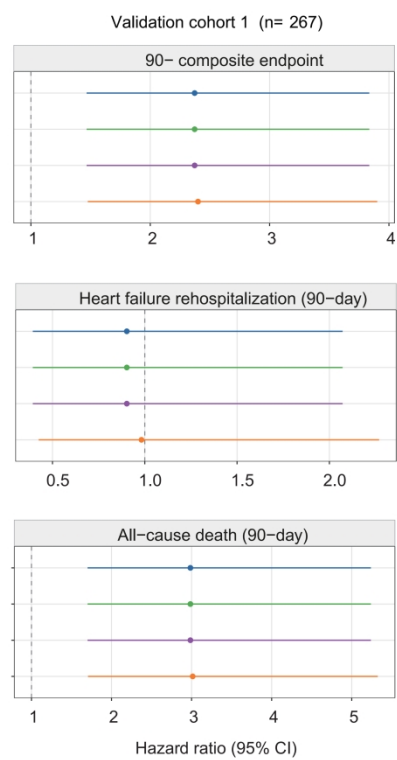


**Supplementary Figure S1. Internal validation of the SCS model.** Bootstrap and 10-fold cross-validation were performed in the discovery cohort (n=691). Panels (A) and (B) show cut-off stability. Panel (C) shows out-of-fold log-rank P values across folds. Panels (D–F) show calibration (apparent, bootstrap-corrected, and cross-validated). Panel (G) shows Harrell’s C-index (apparent, optimism-corrected, and cross-validated).

A



B



**Supplementary Figure S2. Comparison of four LOD imputation strategies for SCS prognostic value.** HRs (95% CI) are shown for the discovery cohort (n=691) and validation cohort 1 (n=267). The four strategies (LOD, LOD/2, LOD/ $\sqrt{2}$ , and complete-case) produced highly consistent effect estimates, indicating robustness of the primary imputation method.

**Table S1. LOD and imputation proportions of 18 steroids in the discovery, validation 1, and validation 2 cohorts.**

| Steroid hormone        | LOD<br>(ng/mL) | Discovery<br>(N=691) |       | Validation cohort 1<br>(N=267) |       | Validation cohort 2<br>(N=92) |       |
|------------------------|----------------|----------------------|-------|--------------------------------|-------|-------------------------------|-------|
|                        |                | N imputed            | %     | N imputed                      | %     | N imputed                     | %     |
| Pregnenolone           | 0.01           | 2                    | 0.29  | 0                              | 0     | 0                             | 0     |
| Progesterone           | 0.05           | 238                  | 34.44 | 87                             | 32.58 | 32                            | 34.78 |
| 11-Deoxycorticosterone | 0.02           | 143                  | 20.69 | 75                             | 28.09 | 20                            | 21.74 |
| 17-OH progesterone     | 0.02           | 3                    | 0.43  | 5                              | 1.87  | 0                             | 0     |
| Corticosterone         | 0.02           | 12                   | 1.74  | 15                             | 5.62  | 4                             | 4.35  |
| 11-Deoxycortisol       | 0.02           | 11                   | 1.59  | 3                              | 1.12  | 1                             | 1.09  |
| Cortisone              | 0.1            | 0                    | 0     | 0                              | 0     | 0                             | 0     |
| Cortisol               | 0.5            | 5                    | 0.72  | 5                              | 1.87  | 0                             | 0     |
| Aldosterone            | 0.002          | 2                    | 0.29  | 1                              | 0.37  | 1                             | 1.09  |
| Estrone                | 0.01           | 482                  | 69.75 | 168                            | 62.92 | 70                            | 76.09 |
| Estradiol              | 0.01           | 225                  | 32.56 | 99                             | 37.08 | 39                            | 42.39 |
| Estriol                | 0.01           | 531                  | 76.85 | 206                            | 77.15 | 77                            | 83.7  |
| 17-OH pregnenolone     | 0.02           | 47                   | 6.8   | 15                             | 5.62  | 3                             | 3.26  |
| DHEAS                  | 5              | 3                    | 0.43  | 0                              | 0     | 0                             | 0     |
| DHEA                   | 0.05           | 80                   | 11.58 | 32                             | 11.99 | 10                            | 10.87 |
| Androstenedione        | 0.02           | 3                    | 0.43  | 6                              | 2.25  | 0                             | 0     |
| Testosterone           | 0.02           | 15                   | 2.17  | 4                              | 1.5   | 1                             | 1.09  |
| DHT                    | 0.01           | 38                   | 5.5   | 16                             | 5.99  | 0                             | 0     |

Abbreviations: LOD, limit of detection.

**Table S2. Spearman Correlations between Steroid Hormones and Clinical Parameters in the Discovery Cohort.**

|                    | BMI   |         | BNP   |         | CCS   |         | Cr    |         | DBP   |         | Heart rate |         | Hb    |         | Na    |         | SBP   |         |
|--------------------|-------|---------|-------|---------|-------|---------|-------|---------|-------|---------|------------|---------|-------|---------|-------|---------|-------|---------|
|                    | r     | P-value | r     | P-value | r     | P-value | r     | P-value | r     | P-value | r          | P-value | r     | P-value | r     | P-value | r     | P-value |
| DHEAS              | 0.08  | 0.032   | -0.06 | 0.090   | -0.13 | <0.001  | -0.04 | 0.292   | 0.01  | 0.694   | 0.05       | 0.170   | 0.05  | 0.223   | -0.06 | 0.134   | -0.00 | 0.922   |
| Pregnenolone       | 0.01  | 0.709   | -0.05 | 0.233   | 0.12  | 0.001   | 0.04  | 0.240   | 0.08  | 0.026   | 0.11       | 0.003   | 0.12  | 0.002   | 0.02  | 0.636   | 0.01  | 0.696   |
| Cortisol           | -0.10 | 0.007   | 0.09  | 0.024   | 0.11  | 0.004   | 0.16  | <0.001  | 0.02  | 0.608   | 0.18       | <0.001  | -0.02 | 0.665   | -0.11 | 0.003   | -0.03 | 0.431   |
| DHEA               | -0.05 | 0.157   | 0.00  | 0.975   | -0.07 | 0.062   | -0.11 | 0.003   | 0.05  | 0.225   | 0.07       | 0.054   | 0.13  | <0.001  | 0.02  | 0.601   | -0.02 | 0.535   |
| Estriol            | 0.10  | 0.012   | 0.01  | 0.737   | 0.06  | 0.105   | 0.04  | 0.329   | 0.05  | 0.166   | 0.08       | 0.035   | 0.10  | 0.006   | -0.04 | 0.353   | 0.00  | 0.980   |
| Testosterone       | 0.10  | 0.007   | 0.05  | 0.219   | 0.06  | 0.147   | 0.10  | 0.006   | 0.10  | 0.009   | -0.04      | 0.329   | 0.36  | <0.001  | -0.01 | 0.811   | 0.03  | 0.398   |
| Estradiol          | 0.04  | 0.260   | -0.01 | 0.831   | -0.05 | 0.223   | -0.02 | 0.551   | 0.00  | 0.963   | 0.03       | 0.405   | 0.15  | <0.001  | -0.02 | 0.534   | -0.06 | 0.139   |
| 17-OH pregnenolone | -0.03 | 0.370   | -0.06 | 0.122   | -0.04 | 0.263   | -0.06 | 0.121   | 0.11  | 0.005   | 0.11       | 0.003   | 0.05  | 0.154   | 0.00  | 0.967   | 0.04  | 0.312   |
| Androstenedione    | -0.03 | 0.371   | 0.04  | 0.343   | 0.04  | 0.284   | 0.07  | 0.054   | 0.10  | 0.006   | 0.18       | <0.001  | 0.02  | 0.634   | -0.02 | 0.556   | -0.02 | 0.675   |
| Aldosterone        | -0.04 | 0.266   | 0.08  | 0.037   | -0.04 | 0.310   | 0.03  | 0.497   | -0.05 | 0.184   | 0.08       | 0.034   | 0.09  | 0.025   | -0.15 | <0.001  | -0.08 | 0.030   |
| Estrone            | -0.08 | 0.031   | 0.04  | 0.267   | 0.04  | 0.347   | 0.06  | 0.111   | 0.00  | 0.938   | 0.14       | <0.001  | -0.02 | 0.565   | -0.09 | 0.024   | -0.08 | 0.028   |
| Progesterone       | -0.07 | 0.057   | 0.03  | 0.444   | 0.04  | 0.353   | 0.07  | 0.058   | 0.05  | 0.219   | 0.17       | <0.001  | 0.01  | 0.784   | -0.12 | 0.002   | -0.05 | 0.223   |
| Cortisone          | -0.01 | 0.696   | -0.04 | 0.300   | -0.03 | 0.489   | -0.22 | <0.001  | 0.12  | 0.002   | 0.05       | 0.156   | 0.30  | <0.001  | 0.09  | 0.025   | -0.10 | 0.009   |
| Corticosterone     | -0.13 | <0.001  | 0.10  | 0.006   | 0.02  | 0.578   | 0.02  | 0.597   | -0.01 | 0.863   | 0.16       | <0.001  | 0.03  | 0.360   | -0.07 | 0.087   | -0.08 | 0.027   |
| 17-OH progesterone | 0.04  | 0.253   | -0.04 | 0.357   | -0.02 | 0.587   | 0.02  | 0.620   | 0.10  | 0.012   | 0.08       | 0.044   | 0.14  | <0.001  | -0.01 | 0.856   | 0.06  | 0.119   |
| DHT                | 0.06  | 0.106   | -0.01 | 0.778   | -0.02 | 0.627   | -0.02 | 0.560   | 0.05  | 0.163   | -0.06      | 0.115   | 0.33  | <0.001  | 0.04  | 0.325   | 0.00  | 0.953   |
| DOC                | -0.11 | 0.004   | 0.05  | 0.195   | -0.01 | 0.779   | 0.02  | 0.566   | 0.03  | 0.507   | 0.22       | <0.001  | -0.01 | 0.733   | -0.10 | 0.009   | -0.05 | 0.166   |
| 11-Deoxycortisol   | -0.08 | 0.035   | 0.06  | 0.142   | -0.00 | 0.913   | 0.06  | 0.095   | 0.02  | 0.636   | 0.16       | <0.001  | -0.04 | 0.308   | 0.00  | 0.987   | -0.03 | 0.485   |

**Table S3. Cox Regression Analysis for the Association of SCS with 90-Day Outcomes in the Discovery Cohort.**

| Endpoint                           | HR<br>(95% CI)      | P<br>Value | Adjusted HR<br>(95% CI) | P Value | Adjusted HR<br>(95% CI) | P<br>Value | Adjusted<br>HR (95%<br>CI) | P<br>Value |
|------------------------------------|---------------------|------------|-------------------------|---------|-------------------------|------------|----------------------------|------------|
|                                    | model 1             |            | model 2                 |         | model 3                 |            | model 4                    |            |
| Composite<br>Endpoint              |                     |            |                         |         |                         |            |                            |            |
| SCS (per 1 SD)                     | 1.22<br>(1.05-1.42) | 0.009      | 1.23<br>(1.05-1.44)     | 0.010   | 1.12<br>(0.95-1.32)     | 0.187      | 1.12<br>(0.95-1.33)        | 0.179      |
| SCS < -0.563                       | Ref.                |            | Ref.                    |         |                         |            |                            |            |
| SCS ≥ -0.563                       | 1.95<br>(1.39-2.73) | <0.001     | 2.02<br>(1.42-2.88)     | <0.001  | 1.69<br>(1.18-2.41)     | 0.004      | 1.68<br>(1.17-2.41)        | 0.005      |
| All-cause<br>Mortality             |                     |            |                         |         |                         |            |                            |            |
| SCS (per 1 SD)                     | 1.15<br>(0.91-1.44) | 0.242      | 1.15<br>(0.92-1.45)     | 0.220   | 1.01<br>(0.78-1.31)     | 0.932      | 1.02<br>(0.79-1.32)        | 0.862      |
| SCS < -0.563                       | Ref.                |            | Ref.                    |         |                         |            |                            |            |
| SCS ≥ -0.563                       | 1.89<br>(1.15-3.12) | 0.013      | 1.96<br>(1.16-3.31)     | 0.011   | 1.49<br>(0.87-2.55)     | 0.144      | 1.60<br>(0.93-2.75)        | 0.091      |
| Heart Failure<br>Rehospitalization |                     |            |                         |         |                         |            |                            |            |
| SCS (per 1 SD)                     | 1.28<br>(1.06-1.54) | 0.01       | 1.27<br>(1.04-1.54)     | 0.017   | 1.18<br>(0.96-1.45)     | 0.114      | 1.18<br>(0.96-1.46)        | 0.11       |
| SCS < -0.563                       | Ref.                |            | Ref.                    |         |                         |            |                            |            |
| SCS ≥ -0.563                       | 1.96<br>(1.27-3.01) | 0.002      | 1.95<br>(1.24-3.07)     | 0.004   | 1.66<br>(1.05-2.61)     | 0.029      | 1.62<br>(1.02-2.56)        | 0.041      |

**Table S4. Subgroup Analysis for the Association of SCS with 90-Day Outcomes in Validation Cohort 1**

|              | Composite Endpoint |               | Mortality        |               |
|--------------|--------------------|---------------|------------------|---------------|
|              | HR (95% CI)        | P interaction | HR (95% CI)      | P interaction |
| All Patients | 1.39 (1.14-1.70)   |               | 1.64 (1.32-2.04) |               |
| Age          |                    | 0.235         |                  | 0.623         |
| <60 y        | 1.63 (1.06-2.51)   |               | 2.40 (1.53-3.77) |               |
| ≥60 y        | 1.50 (1.19-1.90)   |               | 1.63 (1.25-2.12) |               |
| Sex          |                    | 0.549         |                  | 0.466         |
| Female       | 1.41 (1.02-1.96)   |               | 1.68 (1.17-2.42) |               |
| Male         | 1.43 (1.11-1.84)   |               | 1.64 (1.23-2.18) |               |
| Hypertension |                    | 0.082         |                  | 0.142         |
| No           | 1.93 (1.29-2.91)   |               | 2.52 (1.55-4.09) |               |
| Yes          | 1.27 (0.98-1.66)   |               | 1.48 (1.11-1.98) |               |
| Diabetes     |                    | 0.341         |                  | 0.228         |
| No           | 1.60 (1.18-2.16)   |               | 1.95 (1.39-2.75) |               |
| Yes          | 1.29 (0.97-1.71)   |               | 1.57 (1.15-2.14) |               |
| LVEF         |                    | 0.220         |                  | 0.459         |
| <50%         | 1.53 (1.21-1.93)   |               | 1.80 (1.39-2.32) |               |
| ≥50%         | 1.19 (0.68-2.06)   |               | 1.47 (0.76-2.81) |               |
| Diuretics    |                    | 0.094         |                  | 0.071         |
| No           | 1.40 (0.99-1.99)   |               | 1.98 (1.27-3.09) |               |
| Yes          | 1.74 (1.29-2.33)   |               | 2.14 (1.54-2.96) |               |

**Supplementary Table S5. Comparison of four LOD imputation strategies for SCS prognostic value.**

| <b>Discovery cohort (n=691)</b>                 | <b>HR (95% CI)</b> | <b>P value</b> |
|-------------------------------------------------|--------------------|----------------|
| <b>90-day composite endpoint</b>                |                    |                |
| LOD imputation (primary)                        | 1.69 (1.18-2.41)   | 0.004          |
| LOD/2                                           | 1.69 (1.18-2.41)   | 0.004          |
| LOD/sqrt(2)                                     | 1.69 (1.18-2.41)   | 0.004          |
| Complete-case                                   | 1.75 (1.22-2.51)   | 0.002          |
| <b>All-cause death (90-day)</b>                 |                    |                |
| LOD imputation (primary)                        | 1.49 (0.87-2.55)   | 0.144          |
| LOD/2                                           | 1.49 (0.87-2.55)   | 0.144          |
| LOD/sqrt(2)                                     | 1.49 (0.87-2.55)   | 0.144          |
| Complete-case                                   | 1.52 (0.89-2.60)   | 0.127          |
| <b>Heart failure rehospitalization (90-day)</b> |                    |                |
| LOD imputation (primary)                        | 1.66 (1.05-2.61)   | 0.029          |
| LOD/2                                           | 1.66 (1.05-2.61)   | 0.029          |
| LOD/sqrt(2)                                     | 1.66 (1.05-2.61)   | 0.029          |
| Complete-case                                   | 1.73 (1.10-2.74)   | 0.019          |
| <b>Validation cohort 1 (n=267)</b>              |                    |                |
| <b>90-day composite endpoint</b>                |                    |                |
| LOD imputation (primary)                        | 2.37 (1.47-3.84)   | <0.001         |
| LOD/2                                           | 2.37 (1.47-3.84)   | <0.001         |
| LOD/sqrt(2)                                     | 2.37 (1.47-3.84)   | <0.001         |
| Complete-case                                   | 2.40 (1.48-3.90)   | <0.001         |
| <b>All-cause death (90-day)</b>                 |                    |                |
| LOD imputation (primary)                        | 2.99 (1.70-5.24)   | <0.001         |
| LOD/2                                           | 2.99 (1.70-5.24)   | <0.001         |
| LOD/sqrt(2)                                     | 2.99 (1.70-5.24)   | <0.001         |
| Complete-case                                   | 3.01 (1.71-5.33)   | <0.001         |
| <b>Heart failure rehospitalization (90-day)</b> |                    |                |
| LOD imputation (primary)                        | 0.90 (0.39-2.07)   | 0.809          |
| LOD/2                                           | 0.90 (0.39-2.07)   | 0.809          |
| LOD/sqrt(2)                                     | 0.90 (0.39-2.07)   | 0.809          |
| Complete-case                                   | 0.98 (0.43-2.27)   | 0.966          |

HR, hazard ratio; CI, confidence interval; LOD, limit of detection; LOD/2, imputation with half the LOD value; LOD/√2, imputation with LOD divided by the square root of 2; complete-case, analysis excluding all samples with values below the LOD.

**Table S6. Subgroup Analysis for the Association of SCS with Long-Term Outcomes (1200 Days) in Validation Cohort 1.**

|              | Composite Endpoint |               | Mortality         |               |
|--------------|--------------------|---------------|-------------------|---------------|
|              | HR (95% CI)        | P interaction | HR (95% CI)       | P interaction |
| All Patients | 1.96 (1.33-2.90)   |               | 2.02 (1.28-3.18)  |               |
| Age          | 2.10 (1.43-3.07)   | 0.181         | 2.33 (1.49-3.63)  | 0.212         |
| <60 y        | 6.05 (1.99-18.42)  |               | 9.33 (2.65-32.80) |               |
| ≥60 y        | 1.81 (1.18-2.78)   |               | 1.91 (1.15-3.16)  |               |
| Sex          | 1.96 (1.32-2.89)   | 0.598         | 2.03 (1.29-3.19)  | 0.881         |
| Female       | 1.54 (0.85-2.80)   |               | 1.86 (0.94-3.70)  |               |
| Male         | 2.14 (1.22-3.75)   |               | 2.79 (1.40-5.55)  |               |
| Hypertension | 1.97 (1.34-2.90)   | 0.404         | 2.04 (1.29-3.21)  | 0.929         |
| No           | 3.14 (1.54-6.43)   |               | 2.78 (1.24-6.21)  |               |
| Yes          | 1.72 (1.05-2.81)   |               | 2.05 (1.16-3.63)  |               |
| Diabetes     | 1.87 (1.27-2.73)   | 0.951         | 2.01 (1.28-3.16)  | 0.419         |
| No           | 1.91 (1.13-3.23)   |               | 2.65 (1.45-4.83)  |               |
| Yes          | 2.24 (1.17-4.28)   |               | 2.12 (0.99-4.55)  |               |
| LVEF         | 1.96 (1.33-2.90)   | 0.036         | 2.02 (1.28-3.18)  | 0.054         |
| <50%         | 2.76 (1.72-4.42)   |               | 2.93 (1.68-5.11)  |               |
| ≥50%         | 0.66 (0.24-1.80)   |               | 0.63 (0.19-2.06)  |               |
| Diuretics    | 1.98 (1.35-2.91)   | 0.135         | 2.04 (1.30-3.20)  | 0.117         |
| No           | 1.26 (0.57-2.76)   |               | 1.68 (0.68-4.15)  |               |
| Yes          | 2.44 (1.51-3.94)   |               | 2.47 (1.39-4.36)  |               |



**Table S7. Association of baseline SCS with 90-day congestion change in Validation Cohort 2 ( n=46 paired patients)**

| <b>Outcome (Recongestion)</b> | <b>Odds Ratio (95% CI)</b> |
|-------------------------------|----------------------------|
| SCS- High vs SCS- Low         | 1.57 (0.07-35.03)          |
| SCS- High vs SCS- Mid         | 2.02 (0.30-13.83)          |