

| <b>Supplementary Table 1. Baseline demographics in ultra-early vs 24-72h group</b>  |  |                                  |                |
|---|--|----------------------------------|----------------|
|   | Ultra-early anticoagulation<br>(n=111) | 24-72h anticoagulation<br>(n=30) | <i>P</i> value |
| Common patient characteristics  |  |                                  |                |
| Age, y  | 72 (63-78)                             | 67 (60-77)                       | 0.33           |
| Male  | 44 (39.6%)                             | 8 (26.7%)                        | 0.19           |
| Admission NIHSS   | 17 (12-22)                             | 14 (12-19)                       | 0.22           |
| Ischemia in left hemisphere   | 58 (52.3%)                             | 16 (53.3%)                       | 0.92           |
| Treatment with intravenous thrombolysis   | 52 (46.8%)                             | 14 (46.7%)                       | 0.99           |
| Premorbid oral anti-thrombotic use  | 44 (39.6%)                             | 6 (20.0%)                        | 0.05*          |
| Smoke   | 24 (21.6%)                             | 4 (13.3%)                        | 0.31           |
| Hypertension  | 51 (45.9%)                             | 13 (43.3%)                       | 0.80           |
| Diabetes mellitus   | 24 (21.6%)                             | 8 (26.7%)                        | 0.56           |
| Previous stroke   | 12 (10.8%)                             | 4 (13.3%)                        | 0.70           |
| Systolic blood pressure   | 143.72±23.84                           | 138.27±22.09                     | 0.26           |
| Diastolic blood pressure  | 83.39±16.80                            | 84.50±14.31                      | 0.74           |
| INR   | 1.04 (0.99-1.12)                       | 1.06 (0.99-1.16)                 | 0.41           |
| Trombocyte count  | 165 (128-220)                          | 196 (167-222)                    | 0.06           |
| Glucose level   | 7.35 (6.12-9.17)                       | 8.50 (6.64-9.47)                 | 0.10           |
| CHA2DS2-VASc score  | 5 (3-5)                                | 4 (3-5)                          | 0.39           |
| HASBLED score   | 3 (3-4)                                | 4 (3-4)                          | 0.36           |
| Heparin during procedure  | 51 (45.9%)                             | 13 (43.3%)                       | 0.80           |
| Tirofiban during procedure  | 31 (27.9%)                             | 5 (16.7%)                        | 0.21           |
| Imaging   |  |                                  |                |
| ASPECTS   | 9 (8-10)                               | 9 (8-9)                          | 0.17           |
| Occlusion site  |  |                                  | 0.55           |
| ICA   | 32 (28.8%)                             | 7 (23.3%)                        |                |
| M1  | 58 (52.3%)                             | 19 (63.3%)                       |                |
| M2  | 21 (18.9%)                             | 4 (13.4%)                        |                |
| Reperfusion before intervention (mTICI)   |  |                                  | 0.09           |
| 0   | 97 (87.4%)                             | 22 (73.3%)                       |                |
| 1   | 3 (2.7%)                               | 5 (16.7%)                        |                |
| 2a  | 4 (3.6%)                               | 1 (3.3%)                         |                |
| 2b  | 7 (6.3%)                               | 2 (6.7%)                         |                |
| Workflow (in minutes)   |  |                                  |                |
| Symptom onset to admission ER   | 201 (111-330)                          | 225 (72-368)                     | 0.79           |
| Admission ER to groin puncture  | 118 (95-157)                           | 130 (105-177)                    | 0.21           |
| Duration procedure  | 60 (40-96)                             | 66 (40-129)                      | 0.62           |
| Symptom onset to reperfusion  | 410 (290-615)                          | 449 (353-572)                    | 0.30           |
| <b>Baseline variables with ultra-early and 24-72h anticoagulation group. *<i>P</i>&lt;0.05. ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; ER, emergency room; ICA, internal carotid artery; INR, international normalized ratio; MCA-M1/M2, the first/second segment of middle cerebral artery; mTICI, modified thrombolysis in cerebral infarction; NIHSS, National Institutes of Health Stroke Scale.</b> |  |                                  |                |

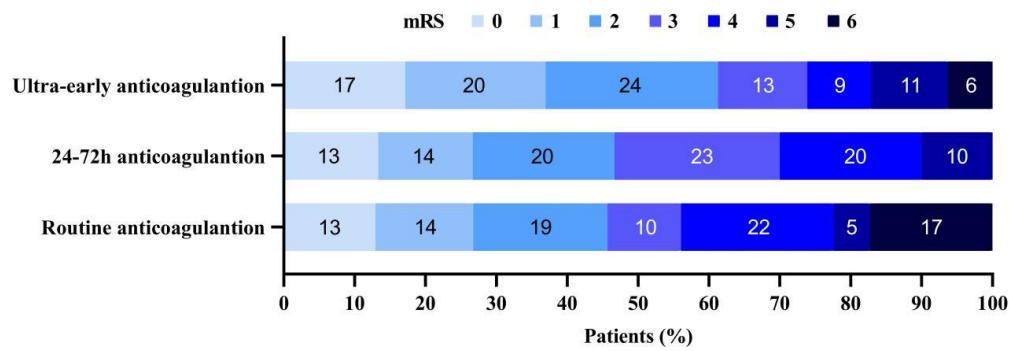
| <b>Supplementary Table 2. Baseline demographics in UFH vs LMWH group</b>  |                  |                   |         |
|---|------------------|-------------------|---------|
|   | UFH group (n=69) | LMWH group (n=72) | P Value |
| <b>Common patient characteristics</b>   |                  |                   |         |
| Age, y  | 71 (61-78)       | 71 (62-78)        | 0.33    |
| Male  | 27 (39.1%)       | 25 (34.7%)        | 0.59    |
| Admission NIHSS   | 17 (13-22)       | 15 (12-20)        | 0.22    |
| Ischemia in left hemisphere   | 37 (53.6%)       | 37 (51.4%)        | 0.79    |
| Treatment with intravenous thrombolysis   | 33 (47.8%)       | 33 (45.8%)        | 0.81    |
| Premorbid oral anti-thrombotic use  | 28 (40.6%)       | 22 (30.6%)        | 0.21    |
| Smoke   | 10 (14.5%)       | 18 (25.0%)        | 0.12    |
| Hypertension  | 35 (50.7%)       | 29 (40.3%)        | 0.21    |
| Diabetes mellitus   | 15 (21.7%)       | 17 (23.6%)        | 0.79    |
| Previous stroke   | 4 (5.8%)         | 12 (16.7%)        | 0.04*   |
| Systolic blood pressure   | 144.99±24.88     | 140.24±22.03      | 0.23    |
| Diastolic blood pressure  | 82.94±17.79      | 84.28±14.74       | 0.63    |
| INR   | 1.04 (0.98-1.11) | 1.05 (1.00-1.13)  | 0.41    |
| Trombocyte count  | 171 (132-225)    | 182 (143-220)     | 0.06    |
| Glucose level   | 7.30 (6.17-9.50) | 8.00 (6.10-9.20)  | 0.10    |
| CHA2DS2-VASc score  | 4 (3-5)          | 5 (3-5)           | 0.39    |
| HASBLED score   | 3 (3-4)          | 3 (3-4)           | 0.36    |
| Heparin during procedure  | 35 (50.7%)       | 29 (40.3%)        | 0.21    |
| Tirofiban during procedure  | 21 (30.4%)       | 15 (20.8%)        | 0.19    |
| <b>Imaging</b>  |                  |                   |         |
| ASPECTS   | 9 (8-10)         | 9 (8-10)          | 0.17    |
| Occlusion site  |                  |                   | 0.07    |
| ICA   | 24 (34.8%)       | 15 (20.8%)        |         |
| MCA-M1  | 31 (44.9%)       | 46 (63.9%)        |         |
| MCA-M2  | 14 (20.3%)       | 11 (15.3%)        |         |
| Reperfusion before intervention (mTICI)   |                  |                   | 0.68    |
| 0   | 59 (85.5%)       | 60 (83.3%)        |         |
| 1   | 4 (5.8%)         | 4 (5.6%)          |         |
| 2a  | 3 (4.3%)         | 2 (2.8%)          |         |
| 2b  | 3 (4.3%)         | 6 (8.3%)          |         |
| <b>Workflow (in minutes)</b>  |                  |                   |         |
| Symptom onset to admission ER   | 204 (127-323)    | 207 (84-384)      | 0.84    |
| Admission ER to groin puncture  | 120 (96-156)     | 126 (100-165)     | 0.84    |
| Duration procedure  | 57 (40-93)       | 70 (40-100)       | 0.26    |
| Symptom onset to reperfusion  | 390 (314-604)    | 439 (315-581)     | 0.69    |
| <b>Baseline variables with UFH and LMWH group. *P&lt;0.05. ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; ER, emergency room; ICA, internal carotid artery; INR, international normalized ratio; LMWH, low-molecular-weight heparin; MCA-M1/M2, the first/second segment of middle cerebral artery; mTICI, modified thrombolysis in cerebral infarction; NIHSS, National Institutes of Health Stroke Scale; UFH, unfractionated heparin.</b> |                  |                   |         |

| <b>Supplementary Table 3. Baseline demographics in minimal-dose vs low-dose group</b>  |                           |                       |         |
|--|---------------------------|-----------------------|---------|
|  | Minimal-dose group (n=76) | Low-dose group (n=65) | P Value |
| <b>Common patient characteristics</b>  |                           |                       |         |
| Age, y   | 71 (63-78)                | 70 (60-78)            | 0.56    |
| Male   | 27 (35.5%)                | 25 (38.5%)            | 0.72    |
| Admission NIHSS  | 17 (13-22)                | 16 (12-21)            | 0.14    |
| Ischemia in left hemisphere  | 44 (57.9%)                | 30 (46.2%)            | 0.16    |
| Treatment with intravenous thrombolysis  | 34 (44.7%)                | 32 (49.2%)            | 0.59    |
| Premorbid oral anti-thrombotic use   | 24 (31.6%)                | 26 (40.0%)            | 0.30    |
| Smoke  | 9 (11.8%)                 | 19 (29.2%)            | 0.01*   |
| Hypertension   | 36 (47.4%)                | 28 (43.1%)            | 0.61    |
| Diabetes mellitus  | 16 (21.1%)                | 16 (24.6%)            | 0.62    |
| Previous stroke  | 6 (6.6%)                  | 11 (16.9%)            | 0.05    |
| Systolic blood pressure  | 142.55±23.04              | 142.57±24.23          | 0.99    |
| Diastolic blood pressure   | 83.68±17.04               | 83.55±15.43           | 0.96    |
| INR  | 1.03(0.98-1.12)           | 1.07 (0.99-1.14)      | 0.09    |
| Trombocyte count   | 183 (144-220)             | 165 (125-221)         | 0.25    |
| Glucose level  | 7.30 (6.03-9.20)          | 7.70 (6.75-9.28)      | 0.36    |
| CHA2DS2-VASc   | 5 (3-5)                   | 4 (3-5)               | 0.83    |
| HASBLED  | 3 (2-4)                   | 3 (3-4)               | 0.74    |
| Heparin during procedure   | 35 (46.1%)                | 29 (44.6%)            | 0.86    |
| Tirofiban during procedure   | 23 (30.3%)                | 13 (20.0%)            | 0.16    |
| <b>Imaging</b>   |                           |                       |         |
| ASPECTS  | 9 (8-10)                  | 9 (8-10)              | 0.12    |
| Occlusion site   |                           |                       | 0.98    |
| ICA  | 21 (27.6%)                | 18 (27.7%)            |         |
| MCA-M1   | 42 (55.3%)                | 35 (53.8%)            |         |
| MCA-M2   | 13 (17.1%)                | 12 (18.5%)            |         |
| Reperfusion before intervention (mTICI)  |                           |                       | 0.01*   |
| 0  | 58 (76.3%)                | 61 (93.8%)            |         |
| 1  | 6 (7.9%)                  | 2 (3.1%)              |         |
| 2a   | 5 (6.6%)                  | 0 (0.0%)              |         |
| 2b   | 7 (9.2%)                  | 2 (3.1%)              |         |
| <b>Workflow (in minutes)</b>   |                           |                       |         |
| Symptom onset to admission ER  | 220 (93-417)              | 198 (115-303)         | 0.36    |
| Admission ER to groin puncture   | 113(96-151)               | 127 (99-185)          | 0.24    |
| Duration procedure   | 61 (37-95)                | 60 (41-99)            | 0.48    |
| Symptom onset to reperfusion   | 441 (295-624)             | 429 (324-558)         | 0.86    |
| <b>Baseline variables with low-dose and moderate-dose group. *P&lt;0.05. ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; ER, emergency room; ICA, internal carotid artery; INR, international normalized ratio; MCA-M1/M2, the first/second segment of middle cerebral artery; mTICI, modified thrombolysis in cerebral infarction; NIHSS, National Institutes of Health Stroke Scale.</b> |                           |                       |         |

| <b>Supplementary Table 4. Univariate analyses for the outcomes between ultra-early and 24-72h groups</b>   |                                     |                               |                |                  |
|--|-------------------------------------|-------------------------------|----------------|------------------|
| Variable   | Ultra-early anticoagulation (n=111) | 24-72h anticoagulation (n=30) | <i>P</i> value | OR (95% CI)      |
| <b>Primary outcomes</b>  |                                     |                               |                |                  |
| mRS  | 2 (1-4)                             | 3 (1-4)                       | 0.43           | 1.33 (0.65-2.70) |
| sICH   | 1 (0.9%)                            | 1 (3.3%)                      | 0.38           | 0.26 (0.02-4.34) |
| <b>Secondary outcomes</b>  |                                     |                               |                |                  |
| mRS <sub>≤2</sub>  | 68 (61.3%)                          | 14 (46.7%)                    | 0.15           | 1.81 (0.80-4.07) |
| Mortality  | 7 (6.3%)                            | 0 (0.0%)                      | 0.35           | NA               |
| aICH   | 15 (13.5%)                          | 9 (30.0%)                     | 0.03           | 0.37 (0.14-0.94) |
| New ischemic stroke  | 7 (6.3%)                            | 2 (6.7%)                      | 1.00           | 0.94 (0.19-4.79) |
| aICH indicates asymptomatic intracranial hemorrhage; mRS, modified Rankin Scale; NA, not available; OR, odds ratio; sICH, symptomatic intracranial hemorrhage. |                                     |                               |                |                  |

| <b>Supplementary Table 5. Univariate analyses for the outcomes between UFH and LMWH groups</b>   |                     |                      |                |                   |
|--|---------------------|----------------------|----------------|-------------------|
| Variable   | UFH group<br>(n=69) | LMWH group<br>(n=72) | <i>P</i> value | OR (95% CI)       |
| <b>Primary outcomes</b>  |                     |                      |                |                   |
| mRS  | 2 (1-4)             | 2 (1-4)              | 0.84           | 0.94 (0.53-1.68)  |
| sICH   | 1 (1.4%)            | 1 (1.4%)             | 1.00           | 1.04 (0.06-17.03) |
| <b>Secondary outcomes</b>  |                     |                      |                |                   |
| mRS $\leq$ 2   | 41 (59.4%)          | 41 (56.9%)           | 0.77           | 1.11 (0.57-2.16)  |
| Mortality  | 2 (2.9%)            | 5 (6.9%)             | 0.47           | 0.40 (0.08-2.13)  |
| aICH   | 9 (13.0%)           | 15 (20.8%)           | 0.22           | 0.57 (0.23-1.41)  |
| New ischemic stroke  | 4 (5.8%)            | 5 (6.9%)             | 1.00           | 0.83 (0.21-3.21)  |
| aICH indicates asymptomatic intracranial hemorrhage; LMWH, low-molecular-weight heparin; mRS, modified Rankin Scale; OR, odds ratio; sICH, symptomatic intracranial hemorrhage; UFH, unfractionated heparin. |                     |                      |                |                   |

| <b>Supplementary Table 6. Univariate analyses for the outcomes between minimal-dose and low-dose groups</b>                                 |                              |                          |                |                   |
|---|------------------------------|--------------------------|----------------|-------------------|
| Variable  | Minimal-dose group<br>(n=76) | Low-dose group<br>(n=65) | <i>P</i> value | OR (95% CI)       |
| Primary outcomes  |                              |                          |                |                   |
| mRS   | 2 (1-4)                      | 2 (1-4)                  | 0.41           | 0.78 (0.44-1.40)  |
| sICH  | 1 (1.3%)                     | 1 (1.5%)                 | 1.00           | 0.85 (0.05-13.92) |
| Secondary outcomes  |                              |                          |                |                   |
| mRS <sub>≤</sub> 2  | 44 (57.9%)                   | 38 (58.5%)               | 0.95           | 0.98 (0.50-1.91)  |
| Mortality   | 4 (5.3%)                     | 4 (4.6%)                 | 1.00           | 1.15 (0.25-5.33)  |
| aICH  | 13 (17.1%)                   | 11 (16.9%)               | 0.98           | 1.01 (0.42-2.45)  |
| New ischemic stroke   | 5 (6.6%)                     | 4 (6.2%)                 | 1.00           | 1.07 (0.28-4.18)  |
| aICH indicates asymptomatic intracranial hemorrhage; mRS, modified Rankin Scale; OR, odds ratio; sICH, symptomatic intracranial hemorrhage. |                              |                          |                |                   |



Supplementary Figure 1. Distribution of modified Rankin Scale (mRS) scores at 90 days for patients allocated to ultra-early, 24-72h and routine anticoagulation group. There was a significant shift towards better functional outcomes for ultra-early versus routine anticoagulation (adjusted common odds ratio [acOR] 2.03 [95% CI 1.20-3.44]), and a non-significant shift towards better functional outcome for 24-72h versus routine anticoagulation (acOR 1.95 [95% CI 0.89-4.30]).