

Table S1. Initial vital signs and laboratory findings at time zero in the derivation dataset.

| Variables | Total (N=7,436) | Survivor (N=4,688) | Non-survivor (N=2,748) |
|-----------------------------|--------------------|-----------------------|---------------------------|
| Initial vital signs | | | |
| Systolic blood pressure | 96±29 | 97±29 | 95±29 |
| Diastolic blood pressure | 58±18 | 58±17 | 57±18 |
| Heart rate | 107±26 | 107±25 | 109±26 |
| Respiratory rate | 24±5 | 24±5 | 25±5 |
| Body temperature | 37.3±1.3 | 37.5±1.3 | 37.0±1.2 |
| Initial laboratory findings | | | |
| WBC | 12.9±12 | 12.6±10.3 | 13.3±14.4 |
| Hb | 10.5±2.5 | 10.7±2.5 | 10.2±2.6 |
| Platelet | 176±123 | 182±120 | 165±127 |
| BUN | 40±29 | 36±27 | 46±31 |
| Creatinine | 1.9±1.8 | 1.8±1.7 | 2.1±1.8 |
| AST | 129±559 | 92±274 | 192±843 |
| ALT | 68±217 | 59±190 | 82±256 |
| Bilirubin | 2.0±3.8 | 1.7±3.0 | 2.6±4.8 |
| Albumin | 2.9±0.7 | 3.0±0.7 | 2.7±0.7 |
| INR | 1.5±1.0 | 1.4±0.8 | 1.6±1.2 |
| CRP | 12.9±10.7 | 12.2±10.5 | 14.3±10.9 |
| Lactate (mmol/L) | 4.1±3.5 | 3.3±2.8 | 5.3±4.2 |

Abbreviations: WBC, white blood cell; Hb, hemoglobin; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; CRP, C-reactive protein.

Data are presented as means ± standard deviations.

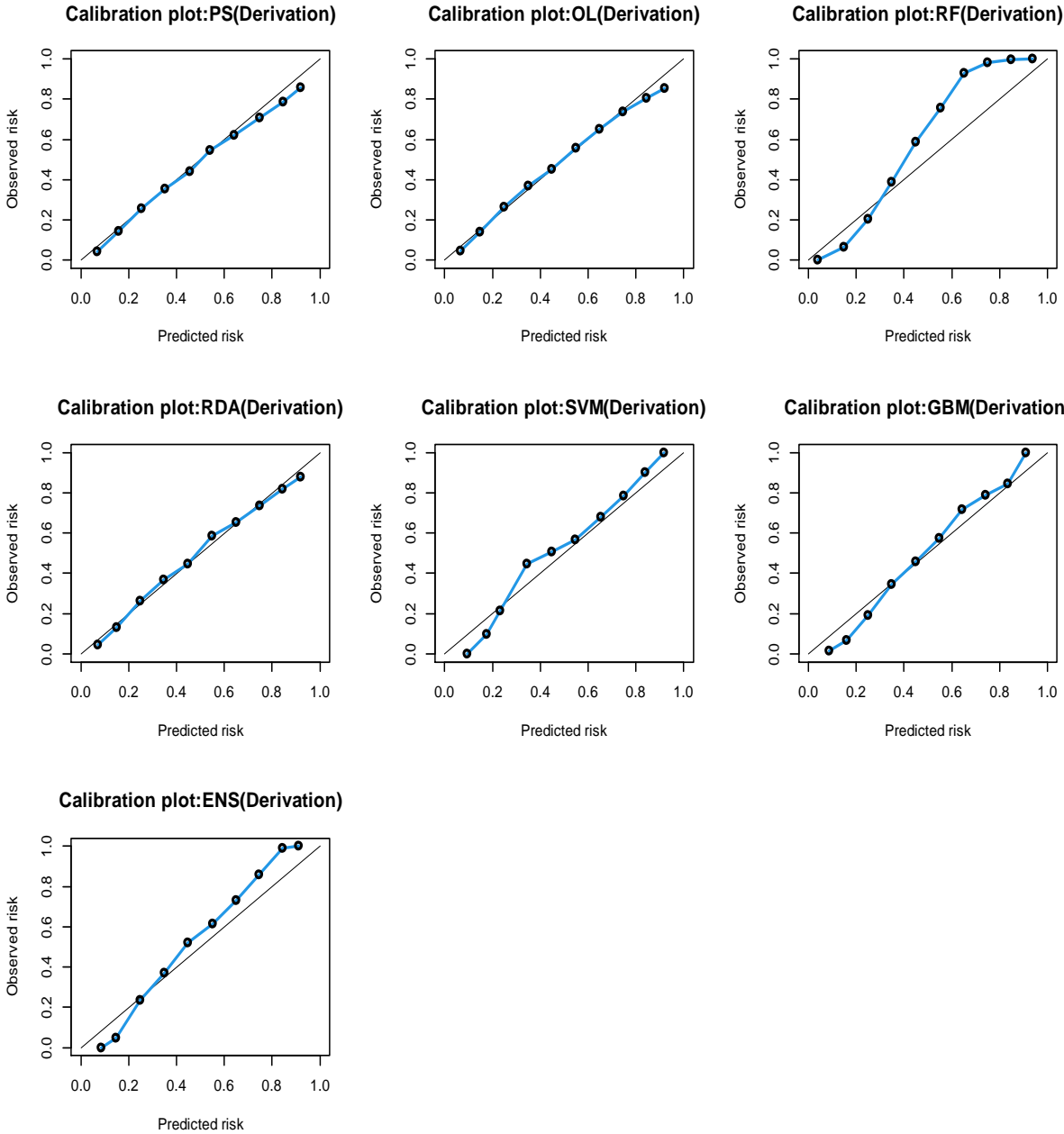
Table S2. Predictors of 28-day mortality after sepsis diagnosis using logistic regression analysis with the derivation dataset

| Risk factors | Estimated Coefficient | Standard Error | Odds ratio | 95% CI | P value |
|--|-----------------------|----------------|------------|-------------|---------|
| Age | 0.016 | 0.002 | 1.02 | 1.011–1.021 | ,<0.001 |
| Clinical frailty scale (1–3 points) | | | Reference | | |
| 4–5 points | 0.540 | 0.089 | 1.72 | 1.442–2.041 | <0.001 |
| 6–9 points | 0.877 | 0.079 | 2.40 | 2.057–2.807 | <0.001 |
| Presence of malignancy | 0.834 | 0.063 | 2.30 | 2.036–2.602 | <0.001 |
| SOFA score | 0.105 | 0.010 | 1.11 | 1.088–1.133 | <0.001 |
| Sepsis caused by respiratory infection | 0.688 | 0.061 | 1.99 | 1.765–2.242 | <0.001 |
| CRRT use | 0.811 | 0.082 | 2.25 | 1.914–2.642 | <0.001 |
| Body temperature (>38°C, BT) | | | Reference | | <0.001 |
| 36°C ≤ BT ≤ 38°C | 0.462 | 0.070 | 1.59 | 1.383–1.820 | <0.001 |
| <36°C | 0.892 | 0.107 | 2.44 | 1.978–3.009 | <0.001 |
| Albumin (≥3.5 g/dL) | | | Reference | | |
| 2.5 g/dL ≤ albumin <3.5 g/dL | 0.423 | 0.085 | 1.53 | 1.291–1.804 | <0.001 |
| <2.5 g/dL | 0.864 | 0.097 | 2.37 | 1.963–2.867 | <0.001 |

| | | | | | |
|--------------------------------|-------|-------|------|-------------|--------|
| INR (>1.3) | 0.326 | 0.062 | 1.39 | 1.227–1.563 | <0.001 |
| CRP (mg/dL) | 0.010 | 0.003 | 1.01 | 1.005–1.016 | <0.001 |
| Lactic acid (≥ 4 mmol/L) | 0.787 | 0.062 | 2.20 | 1.946–2.478 | <0.001 |

Abbreviations: SOFA, Sequential Organ Failure Assessment; CRRT, continuous renal replacement therapy; BT, body temperature; INR, International normalized ratio; CRP, C-reactive protein.

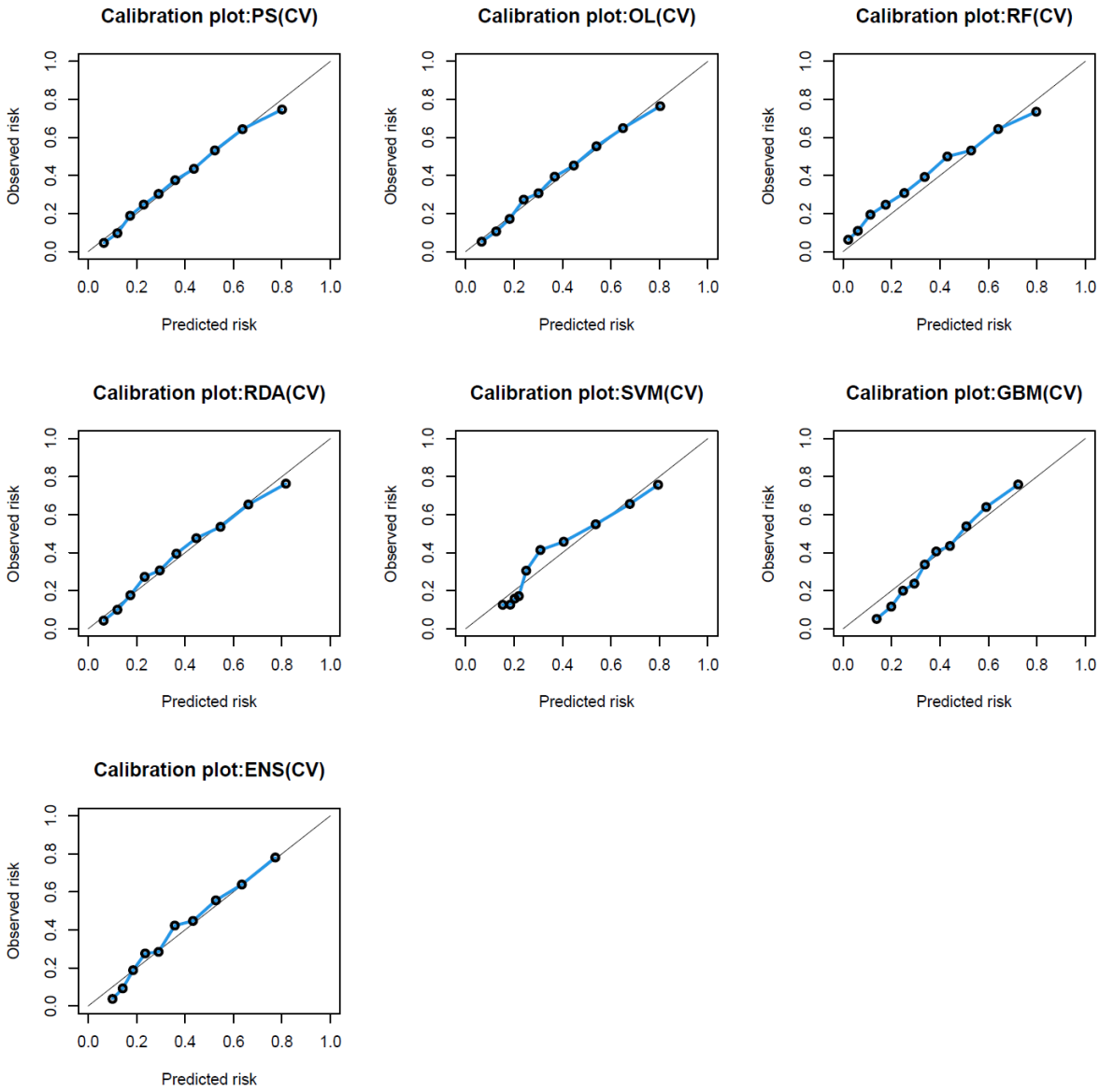
Table S3. Evaluating Model Performance via Area Under the ROC Curve, Calibration Plots, Hosmer-Lemeshow Test, and Brier Score in the Derivation Dataset



| Method | AUC | 95% confidence interval | Hosmer-Lemeshow test | Brier Score |
|--------|--------|-------------------------|----------------------|-------------|
| PS | 0.7743 | 0.763–0.785 | 28.8 | 0.184 |
| OL | 0.7787 | 0.768–0.790 | 15.2 | 0.182 |
| RF | 0.9632 | 0.959–0.967 | 613.7 | 0.090 |
| RDA | 0.7780 | 0.767–0.789 | 19.0 | 0.181 |
| SVM | 0.8196 | 0.809–0.830 | 122.5 | 0.168 |
| GBM | 0.7718 | 0.760–0.783 | 109.3 | 0.187 |
| ENS | 0.8545 | 0.846–0.863 | 268.8 | 0.155 |

Abbreviations: PS, point system; OL, ordinary logistic regression; RF, random forest; RDA, regularized discriminant analysis; SVM, support vector machine; GBM, gradient-boosting machine; ENS, ensemble method; AUC, area under the ROC curve.

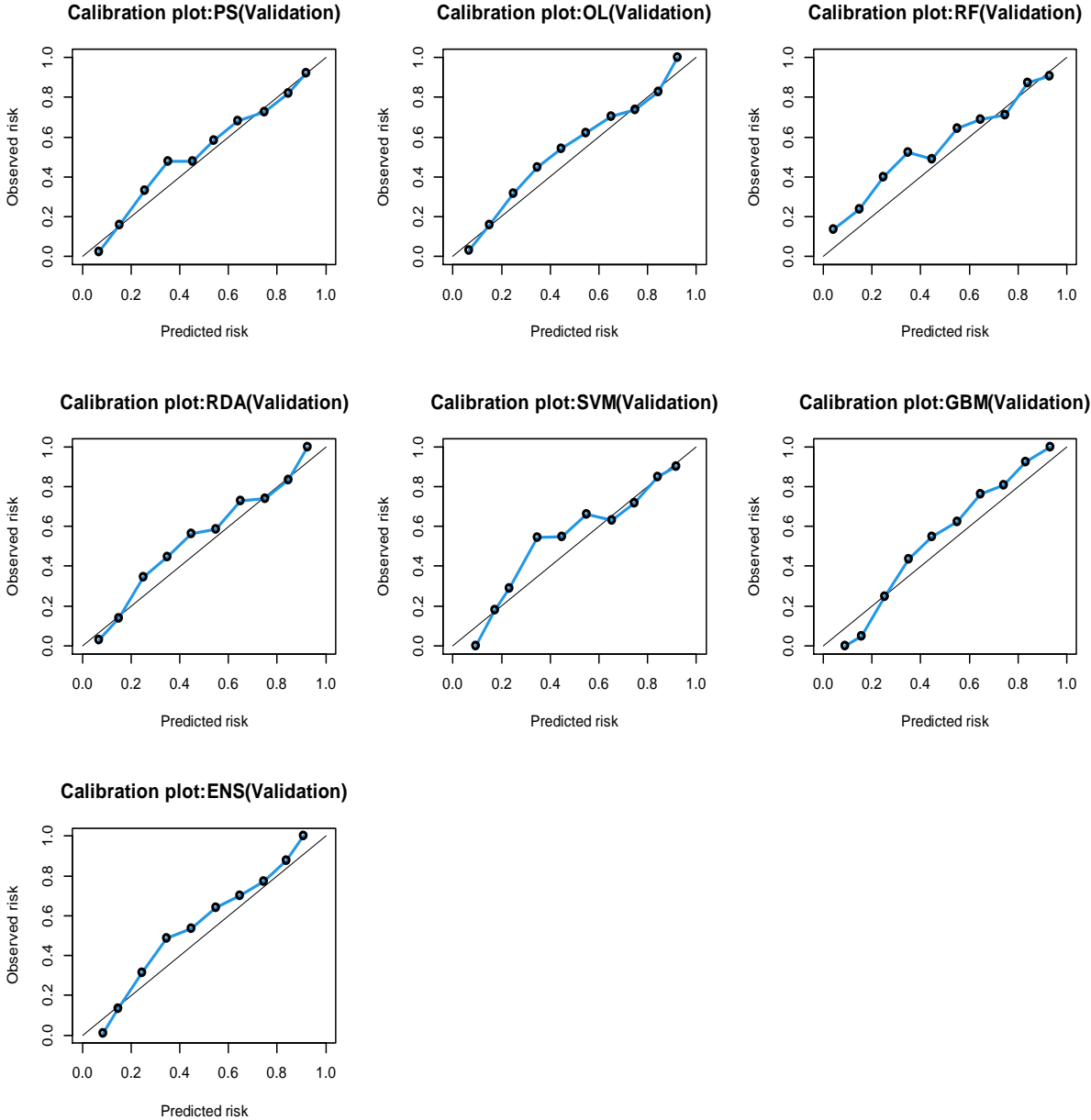
Table S4. Evaluating Model Performance via Area Under the ROC Curve, Calibration Plots, Hosmer-Lemeshow Test, and Brier Score in the Cross Validation.



| Method | AUC | 95% confidence interval | Hosmer-Lemeshow test | Brier Score |
|--------|--------|-------------------------|----------------------|-------------|
| PS | 0.7722 | 0.747–0.797 | 11.74 | 0.185 |
| OL | 0.7765 | 0.752–0.802 | 12.89 | 0.184 |
| RF | 0.7693 | 0.744–0.795 | 50.24 | 0.189 |
| RDA | 0.7764 | 0.751–0.801 | 14.88 | 0.183 |
| SVM | 0.7650 | 0.739–0.791 | 1711.55 | 0.189 |
| GBM | 0.7695 | 0.744–0.795 | 31.13 | 0.188 |
| ENS | 0.7754 | 0.750–0.800 | 63.91 | 0.182 |

Abbreviations: PS, point system; OL, ordinary logistic regression; RF, random forest; RDA, regularized discriminant analysis; SVM, support vector machine; GBM, gradient-boosting machine; ENS, ensemble method; AUC, area under the ROC curve.

Table S5. Evaluating Model Performance via Area Under the ROC Curve, Calibration Plots, Hosmer-Lemeshow Test, and Brier Score in the Validation dataset.



| Method | AUC | 95% confidence interval | Hosmer-Lemeshow test | Brier Score |
|--------|--------|-------------------------|----------------------|-------------|
| PS | 0.7717 | 0.752–0.792 | 41.7 | 0.195 |
| OL | 0.7790 | 0.759–0.799 | 42.8 | 0.193 |
| RF | 0.7652 | 0.745–0.786 | 192.9 | 0.204 |
| RDA | 0.7779 | 0.758–0.798 | 56.6 | 0.195 |
| SVM | 0.7536 | 0.732–0.775 | 67.8 | 0.206 |
| GBM | 0.7753 | 0.756–0.795 | 74.0 | 0.197 |
| ENS | 0.7807 | 0.761–0.800 | 63.3 | 0.195 |

Abbreviations: PS, point system; OL, ordinary logistic regression; RF, random forest; RDA, regularized discriminant analysis; SVM, support vector machine; GBM, gradient-boosting machine; ENS, ensemble method; AUC, area under the ROC curve.

Table S6. Mortality risk according to total point of new sepsis mortality model.

| Point | Risk | Point | Risk | Point | Risk | Point | Risk |
|-------|-------|-------|-------|-------|-------|-------|-------|
| 0 | 1.38 | 19 | 12.03 | 38 | 57.21 | 57 | 92.89 |
| 1 | 1.55 | 20 | 13.36 | 39 | 60.12 | 58 | 93.65 |
| 2 | 1.75 | 21 | 14.81 | 40 | 62.96 | 59 | 94.32 |
| 3 | 1.97 | 22 | 16.39 | 41 | 65.71 | 60 | 94.93 |
| 4 | 2.21 | 23 | 18.10 | 42 | 68.36 | 61 | 95.48 |
| 5 | 2.49 | 24 | 19.95 | 43 | 70.90 | 62 | 95.97 |
| 6 | 2.79 | 25 | 21.93 | 44 | 73.31 | 63 | 96.41 |
| 7 | 3.14 | 26 | 24.06 | 45 | 75.59 | 64 | 96.80 |
| 8 | 3.52 | 27 | 26.32 | 46 | 77.74 | 65 | 97.15 |
| 9 | 3.96 | 28 | 28.71 | 47 | 79.75 | 66 | 97.47 |
| 10 | 4.44 | 29 | 31.23 | 48 | 81.62 | 67 | 97.75 |
| 11 | 4.98 | 30 | 33.86 | 49 | 83.35 | 68 | 98.00 |
| 12 | 5.57 | 31 | 36.60 | 50 | 84.95 | 69 | 98.22 |
| 13 | 6.24 | 32 | 39.42 | 51 | 86.42 | 70 | 98.42 |
| 14 | 6.98 | 33 | 42.32 | 52 | 87.77 | 71 | 98.59 |
| 15 | 7.80 | 34 | 45.28 | 53 | 89.00 | 72 | 98.75 |
| 16 | 8.71 | 35 | 48.26 | 54 | 90.12 | 73 | 98.89 |
| 17 | 9.71 | 36 | 51.26 | 55 | 91.14 | | |
| 18 | 10.82 | 37 | 54.25 | 56 | 92.06 | | |

Table S7. IRB numbers in the derivation dataset (KSA 3)

| Number | Institution | IRB number |
|--------|--|-----------------|
| 1 | Asan Medical Center | 2018-0675 |
| 2 | Chonnam National University Hospital | CNUH2029075 |
| 3 | Chungnam National University Hospital | 2019-11-048-001 |
| 4 | Chungnam National University Sejong Hospital | 2020-08-017 |
| 5 | Daegu Catholic University Medical Center | CR-18-163-L |
| 6 | Hallym University Sacred Heart Hospital | 2018-09-004 |
| 7 | Hanyang University Guri Hospital | 2020-08-015 |
| 8 | Inje University Sanggye Paik Hospital | 2018-08-014 |
| 9 | Jeju National University Hospital | 2018-06-012 |
| 10 | Jeonbuk National University Hospital | CUH-2018-10-027 |
| 11 | Kangwon National University Hospital | 2018-08-004-001 |
| 12 | Korea University Anam Hospital | 2019AN0027 |
| 13 | Pusan National University Yangsan Hospital | 05-2019-092 |
| 14 | Samsung Medical Center | 2018-05-108 |
| 15 | Seoul National University Bundang Hospital | B-1810-500-402 |
| 16 | Seoul National University Hospital | H-1808-135-967 |
| 17 | Severance Hospital | 4-2020-0706 |
| 18 | Ulsan University Hospital | UUH2018-08-003 |
| 19 | Yeungnam University Medical Center | 2020-08-051 |
| 20 | Inje University Ilsan Paik Hospital | 2021-08-003 |

Abbreviations: IRB, institutional review board; KSA, Korean Sepsis Alliance.

Table S8. IRB numbers in the validation dataset (KSA 4)

| Number | Institution | IRB number |
|--------|--|-----------------|
| 1 | Seoul National University Bundang Hospital | B-1810-500-402 |
| 2 | Samsung Medical Center | 2018-05-108 |
| 3 | Asan Medical Center | 2018-0675 |
| 4 | Inje University Sanggye Paik Hospital | 2018-08-014 |
| 5 | Seoul National University Hospital | H-1808-135-967 |
| 6 | Hallym University Sacred Heart Hospital | 2018-09-004 |
| 7 | Hanyang University Guri Hospital | 2020-08-015 |
| 8 | Inje University Ilsan Paik Hospital | 2021-08-003 |
| 9 | Kangwon National University Hospital | 2018-08-004-001 |
| 10 | Chungnam National University Hospital | 2019-11-048-001 |
| 11 | Chungnam National University Sejong Hospital | 2020-08-017 |
| 12 | Jeonbuk National University Hospital | CUH-2018-10-027 |
| 13 | Chonnam National University Hospital | CNUH2029075 |
| 14 | Pusan National University Yangsan Hospital | 05-2019-092 |
| 15 | Jeju National University Hospital | 2018-06-012 |

Abbreviations: IRB, institutional review board; KSA, Korean Sepsis Alliance.