Supplementary Materials:

**Table S1.** Demographic and laboratory data for the initiation and validation cohorts.

| | **Initiation cohort** | **Validation cohort** | |
|---|---|---|---|
| | ***n* = 537** | ***n* = 139** | ***p* Value** |
| Age (years) | 71.5±13.6 | 70.2±12.6 | 0.296 |
| Male (%) | 323(60.1) | 88(63.3) | 0.559 |
| APACHE II score | 18.8±5.8 | 19.0±5.7 | 0.803 |
| SOFA score | 7.1±3.3 | 7.0±3.6 | 0.717 |
| Co-morbidity | | | |
| Diabetes mellitus (%) | 256(47.7) | 79(56.8) | 0.057 |
| Hypertension (%) | 350(65.2) | 95(68.3) | 0.547 |
| Coronary artery disease (%) | 231(43.0) | 53(38.1) | 0.335 |
| Atrial fibrillation (%) | 80(14.9) | 17(12.2) | 0.498 |
| Chronic kidney disease (%)* | 156(29.1) | 37(31.4) | 0.656 |
| Ventilator use (%) | 415(77.3) | 110(79.1) | 0.732 |
| Inotropic agent use (%) | 209(38.9) | 58(41.7) | 0.560 |
| Days in ICU (day) | 11.2±7.4 | 11.5±8.9 | 0.773 |
| Laboratory data | | | |
| Hemoglobin (g/dL) | 10.8±2.8 | 11.0±2.6 | 0.398 |
| eGFR (ml/min/1.73 $m^2$) | 33.3(12.0-64.9) | 36.6(18.9-66.7) | 0.188 |
| C-reactive protein (mg/L) | 46.8(11.1-104.0) | 38.9(15.4-128.5) | 0.285 |
| Cholesterol (mg/dL) | 132.0±52.9 | 128.9±49.3 | 0.530 |
| Triglyceride (mg/dL) | 109(81.5-152.0) | 111(76-156.5) | 0.912 |
| Albumin (g/dL) | 3.19±0.62 | 3.12±0.71 | 0.351 |

Data are expressed as the mean ± SD for variables with normal distribution, as the median [interquartile range (IQR)] for variables with skewed distribution, and as a number (percentage) for categorical variables. * Chronic kidney disease is defined as eGFR < 60 ml/min/1.73 $m^2$. Abbreviations: APACHE II score, Acute Physiology and Chronic Health Evaluation II score; SOFA score, Sequential Organ Failure Assessment score; ICU, intensive care unit; eGFR, estimated glomerular filtration rate.

**Table S2.** Analysis of the prognostic value of combining phenylalanine and leucine levels to assess 30-day mortality in the initiation cohort (*n* =537).

| | Univariate | | Multivariable | |
|---|---|---|---|---|
| | **HR (95% CI)** | ***p* Value** | **HR (95% CI)** | ***p* Value** |
| Phenylalanine | | | | |
| < 88.5 μM | Reference | | | |
| ≥ 88.5 μM | 3.49 (2.47-4.92) | < 0.001 | 3.85 (2.67-5.55) | < 0.001 |
| Leucine | | | | |
| 68.9 ~ 165.6 μM | Reference | | | |
| > 165.6 μM | 1.82 (1.24-2.67) | 0.002 | 1.28 (0.87-1.88) | 0.218 |
| < 68.9 μM | 1.85 (1.14-3.01) | 0.012 | 2.76 (1.68-4.54) | < 0.001 |

Abbreviations: HR, hazard ratio; CI, confidence interval.

**Table S3.** Thirty-day mortality prediction value of different risk levels defined by PLA scores.

| **Risk level** | **RR (95% CI)** | ***p* Value** |
|---|---|---|
| Low | Reference | |
| Intermediate | 2.85 (1.51-5.37) | 0.001 |
| High | 6.89 (3.46-13.71) | < 0.001 |
| Very-high | 19.5 (9.91-38.5) | < 0.001 |

Abbreviations: PLA score, phenylalanine leucine amino acid score; RR, relative risk; CI, confidence interval.