Additional file 1: Interaction analysis

Table S1. Additive and multiplicative interactions between GV and LogSII

Endpoint	RERI (95% CI)	AP (95% CI)	SI (95% CI)	Multiplicative interaction *P*
28-day all-cause mortality	-0.297 (-0.708–0.114)	-0.152 (-0.372–0.068)	0.762 (0.530–1.098)	0.016
ICU mortality	-0.449 (-0.939–0.041)	-0.260 (-0.560–0.040)	0.618 (0.375–1.018)	0.016

High GV and high LogSII denote the highest tertile of each marker, with the lower two tertiles defined as low. Group 1 (low GV/low LogSII) was the reference. Both models included 5564 patients; there were 1055 deaths within 28 days and 681 ICU deaths.

Model III adjusted for age, sex, mean blood pressure, heart rate, respiratory rate, peripheral oxygen saturation, temperature, diabetes mellitus, hypertension, heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, hemoglobin, creatinine, blood urea nitrogen, lactate, SOFA, and insulin use.

The 28-day endpoint was all-cause death after ICU admission, with survivors censored at day 28 regardless of ICU discharge. For the ICU endpoint, documented in-ICU death was the event, and other patients were censored at ICU discharge.

Interaction estimates were derived from the fully adjusted joint-category Cox models using the exact coefficient covariance matrix. RERI and AP used the multivariate delta method; SI used a log-scale delta interval. Multiplicative interaction was assessed by a Wald test of $\log(HR_{11}) - \log(HR_{10}) - \log(HR_{01}) = 0$. Cox models used Efron handling of tied event times.

For RERI and AP, the no-interaction value is 0; for SI it is 1. All additive-interaction intervals included their corresponding no-interaction values. These hazard-ratio-based indices describe statistical interaction and should not be interpreted as proof of biological synergy or causal risk interaction.

Abbreviations: AP, attributable proportion due to interaction; CI, confidence interval; GV, glycemic variability; HR, hazard ratio; ICU, intensive care unit; LogSII, natural logarithm of the systemic immune-inflammation index; RERI, relative excess risk due to interaction; SI, synergy index; SOFA, Sequential Organ Failure Assessment.