

Table S1. Cox models of 90-day mortality by number of LEB days within ICU days 1–7

Follow-up started on ICU Day 7 (landmark) and continued until day 90 after ICU admission (censored on day

90). Complete case analysis: N=553; events=112.

Unadjusted models include each covariate separately. The adjusted model includes all covariates listed in

this table. The groups were defined as described in Fig. 1. The LEB occurrence count represents the number

of days with LEB within the first seven days after ICU admission.

Variable	Unadjusted HR (95% CI)	<i>p</i> value	Adjusted HR (95% CI)	<i>p</i> value
LEB occurrence count within 7 days (per 1 additional day)	1.575 (1.351 – 1.836)	<0.001	1.243 (1.035 – 1.493)	0.02
Age (per 10 years)	1.251 (1.080 – 1.448)	0.003	1.142 (0.976 – 1.336)	0.097
Male sex	1.228 (0.830 – 1.816)	0.304	0.980 (0.653 – 1.469)	0.921
BMI (per 1 kg/m ²)	0.943 (0.902 – 0.986)	0.01	0.945 (0.901 – 0.992)	0.022
Charlson comorbidity index (per 1-point)	1.111 (1.019 – 1.210)	0.017	1.055 (0.957 – 1.164)	0.281
SOFA score at ICU admission (excluding CNS; per 1-point)	1.177 (1.115 – 1.242)	<0.001	1.103 (1.035 – 1.177)	0.003
Lactate at ICU admission (per 1mmol/L)	1.082 (1.037 – 1.130)	<0.001	1.018 (0.959 – 1.079)	0.562
Septic shock	1.908 (1.315 – 2.767)	<0.001	1.042 (0.661 – 1.643)	0.858
CRRT	2.775 (1.713 – 4.496)	<0.001	1.825 (1.080 – 3.083)	0.025

HR, hazard ratio; CI, confidence interval; BMI, body mass index; SOFA, Sequential Organ Failure

Assessment; CNS, central nervous system; ICU, intensive care unit; LEB, leukoerythroblastosis; CRRT,

continuous renal replacement therapy.

Table S2. Time-dependent Cox proportional hazards models for 90-day mortality (ICU day 1–7 exposure updating)

The outcome was 90-day all-cause mortality. Follow-up started on ICU admission (day 0) and continued until day 90 (censored on day 90). Daily smear status was treated as a time-varying exposure and updated using smear findings during ICU days 1–7; for days without smear review, exposure status was imputed using two prespecified assumptions: (A) last observation carried forward (LOCF; current-status model) and (B) persistence after first positivity (first onward model). After ICU day 7, the last available exposure status was assessed at the end of the follow-up. Robust (sandwich) standard errors were used to account for within-patient correlations arising from multiple start–stop intervals per patient. The complete case analysis included 580 patients, contributing to 41,322 intervals with 137 deaths. The analytical sample differs from the day-7 landmark cohort because this model does not condition on survival to day 7 and excludes intervals with missing covariates. The groups (LEB, single-positive, and double-negative) were defined as described in Fig. 1.

S2A. Current-status model (exposure can change daily)

Variable	Unadjusted HR (95% CI)	p value	Adjusted HR (95% CI)	p value (adj.)
Single-positive vs Double-negative	1.75 (1.08–2.82)	0.022	1.42 (0.85–2.37)	0.186
LEB vs Double-negative	4.79 (3.03–7.58)	<0.001	2.90 (1.76–4.78)	<0.001
Age (per 10 years)	1.20 (1.06–1.35)	0.003	1.10 (0.96–1.27)	0.171
Sex, male	1.09 (0.77–1.54)	0.63	0.84 (0.58–1.22)	0.366
BMI (per 1 kg/m ²)	0.95 (0.90–1.00)	0.056	0.95 (0.89–1.01)	0.097
Charlson comorbidity index (per 1-point)	1.13 (1.05–1.22)	0.001	1.12 (1.02–1.23)	0.014
SOFA score at ICU admission (excluding CNS; per 1-point)	1.22 (1.16–1.29)	<0.001	1.14 (1.06–1.23)	<0.001
Lactate at ICU admission (per 1 mmol/L)	1.11 (1.06–1.16)	<0.001	1.04 (0.99–1.09)	0.162
Septic shock	2.34 (1.66–3.28)	<0.001	1.08 (0.70–1.67)	0.713
CRRT	2.84 (1.84–4.39)	<0.001	1.56 (0.92–2.64)	0.097

S2B. First-onward model (hierarchical: once Single-positive/LEB occurs, status is carried forward)

Variable	Unadjusted HR (95% CI)	p value	Adjusted HR (95% CI)	p value (adj.)
Single-positive vs Double-negative	1.63 (1.07–2.48)	0.024	1.14 (0.73–1.79)	0.566
LEB vs Double-negative	3.88 (2.59–5.81)	<0.001	2.13 (1.35–3.36)	0.001
Age (per 10 years)	1.20 (1.06–1.35)	0.003	1.11 (0.96–1.28)	0.144
Sex, male	1.09 (0.77–1.54)	0.63	0.91 (0.62–1.32)	0.609
BMI (per 1 kg/m ²)	0.95 (0.90–1.00)	0.056	0.95 (0.89–1.01)	0.091
Charlson comorbidity index (per 1-point)	1.13 (1.05–1.22)	0.001	1.11 (1.00–1.22)	0.043
SOFA score at ICU admission (excluding CNS; per 1-point)	1.22 (1.16–1.29)	<0.001	1.14 (1.05–1.22)	<0.001
Lactate at ICU admission (per 1 mmol/L)	1.11 (1.06–1.16)	<0.001	1.04 (0.98–1.09)	0.195
Septic shock	2.34 (1.66–3.28)	<0.001	1.06 (0.68–1.65)	0.795
CRRT	2.84 (1.84–4.39)	<0.001	1.51 (0.90–2.53)	0.123

CNS, central nervous system; CRRT, continuous renal replacement therapy; ICU, intensive care unit; IG,

immature granulocytes; NRBC, nucleated red blood cells; SOFA, Sequential Organ Failure Assessment.

Table S3. Key baseline characteristics of the day-7 landmark cohort by smear-classified five-group classification

Patients who survived until day 7 in the ICU were included in the study. The groups were defined as described in Fig. 1. Data are presented as median (interquartile range) or number (percentage). P-values were calculated using the Kruskal–Wallis test for continuous variables and the chi-square test for categorical variables. SOFA score (excluding the central nervous system component) and lactate were measured at ICU admission.

Variable	LEB group (n=110)	Non-concurrent both-positive group (n=22)	IG-only group (n=122)	NRBC-only group (n=19)	Double- negative group (n=296)	<i>p</i> value
Age, years	73 (61–77)	72 (67–79)	71 (56–77)	73 (70–77)	72 (63–80)	0.21
Sex, male, n (%)	64 (58.2)	14 (63.6)	82 (67.2)	8 (42.1)	190 (64.2)	0.218
APACHE II score	24 (18–29)	26 (21–30)	20 (16–25)	24 (16–28)	18 (14–24)	<0.001
SOFA score (excluding CNS) at ICU admission	9 (7–12)	10 (8–13)	8 (6–10)	8 (7–11)	7 (5–8)	<0.001
Lactate at ICU admission, mmol/L	2.8 (1.6–5.7)	2.8 (1.9–6.2)	2.3 (1.2–3.7)	1.9 (1.1–3.2)	1.6 (1.1–2.7)	<0.001
Septic shock, n (%)	70 (63.6)	16 (72.7)	68 (55.7)	6 (31.6)	94 (31.8)	<0.001
CRRT, n (%)	92 (83.6)	17 (77.3)	90 (73.8)	16 (84.2)	156 (52.7)	<0.001
Chronic steroid use, n (%)	23 (20.9)	3 (13.6)	12 (9.8)	4 (21.1)	29 (9.8)	0.024

CNS, central nervous system; CRRT, continuous renal replacement therapy; ICU, intensive care unit; IQR, interquartile range; LEB, leukoerythroblastosis; NRBC, nucleated red blood cells; SOFA, Sequential Organ Failure Assessment.

Table S4. Cox proportional hazards models for 90-day mortality in the day-7 landmark cohort (five-group classification)

Follow-up started on ICU day 7 (landmark) and continued until day 90 after ICU admission (censored on day 90). The groups were defined as described in Fig. 1 (double-negative reference). Complete case analysis: N=552; events=111. The multivariable model was adjusted for age, sex, body mass index, Charlson comorbidity index, and SOFA score, excluding the CNS component at ICU admission, lactate level at ICU admission, septic shock, and continuous renal replacement therapy.

Variable	Unadjusted HR (95% CI)	<i>p</i> value	Adjusted HR (95% CI)	<i>p</i> value
Five-group classification (reference: Double-negative group)				
LEB group	2.64 (1.80–3.86)	<0.001	1.94 (1.19–3.16)	0.008
Non-concurrent both-positive group	1.52 (0.67–3.46)	0.318	1.41 (0.59–3.39)	0.442
NRBC-only group	0.50 (0.12–2.03)	0.327	0.24 (0.03–1.74)	0.157
IG-only group	0.94 (0.60–1.47)	0.773	1.25 (0.74–2.11)	0.413
Covariates				
Age (per 10 years)	1.25 (1.08–1.45)	0.003	1.17 (1.00–1.37)	0.054
Male sex	1.23 (0.83–1.82)	0.304	0.95 (0.63–1.44)	0.823
Body mass index (per 1 kg/m ²)	0.94 (0.90–0.99)	0.01	0.95 (0.90–0.99)	0.019
Charlson comorbidity index (per 1-point)	1.11 (1.02–1.21)	0.017	1.06 (0.96–1.17)	0.26
SOFA score (excluding CNS) at ICU admission (per 1-point)	1.17 (1.10–1.24)	<0.001	1.11 (1.04–1.18)	0.001
Lactate at ICU admission (per 1mmol/L)	1.08 (1.04–1.13)	<0.001	1.02 (0.97–1.09)	0.438
Septic shock	1.91 (1.32–2.77)	<0.001	0.94 (0.59–1.50)	0.784
Continuous renal replacement therapy	2.78 (1.71–4.50)	<0.001	1.81 (1.07–3.08)	0.027

BMI, body mass index; CI, confidence interval; CNS, central nervous system; CRRT, continuous renal replacement therapy; HR, hazard ratio; ICU, intensive care unit; IG, immature granulocytes; NRBC, nucleated red blood cells; LEB, leukoerythroblastosis; SOFA, Sequential Organ Failure Assessment.