Table 1[A]. Demographic, clinical characteristics, and outcomes of the study cohort (N = 161).

Variable	No of studied patients=161
	N (%)
Sex	
Male	74 (46%)
Female	87 (54%)
Age (Years): Mean ±SD	55.26 ±9.94
BMI (Kg/m^2): Mean ±SD	28.25 ±2.18
Pre-admission morbidity	
Yes	72 (44.7%)
No	89 (55.3%)
Diagnosis	
Aspiration pneumonia	1 (0.6%)
Bronchopneumonia	47 (29.2%)
CAP	27 (16.8%)
Lobar pneumonia	86 (53.4%)
Causative organism	
E. coli	19 (11.8%)
E. coli+ candida	6 (3.7%)
H. influenza	12 (7.5%)
Klebsiella	26 (16.1%)
Mycobacterium	3 (1.9%)
Pseudomonas. aeruginosa	27 (16.8%)

Parainfluenza	2 (1.2%)
Staphylococcus aureus	19 (11.8%)
Streptococcus pneumoniae	20 (12.4%)
Sepsis without microbiological confirmation	27 (16.8%)
SOFA: Mean ±SD	
On ICU admission	3.48 ±0.79
Day-5	4.93 ±1.63
Clinical deterioration on day-5 (first occurrence on fifth calendar day after T0).	
Yes	48 (30%)
No	113 (70%)
SOFA ≥ 2 points increase on fifth calendar day after T0.	
Yes	47 (29.2%)
No	114 (70.8%)
Septic shock on fifth calendar day after T0.	
Yes	44 (27.3%)

No	117 (72.7%)
Mortality on fifth calendar day after T0	
Yes	9 (5.5%)
No	152 (94.5%)
Very early clinical deterioration (T0-day 4)	
Yes	18 (11.2%)
No	143 (88.8%)
SOFA ≥2 points increase (T0-day 4)	
Yes	15 (9.3%)
No	146 (92.7%)
Septic shock (T0-day 4)	
Yes	13 (8%)
No	148 (92%)
T0-day 4 mortality	
Yes	11 (6.8%)
No	150 (93.2%)

AKI Yes No	 26 (16.1%) 135 (83.9%)
MV Yes No	 52 (32.3%) 109 (67.7%)
Liver failure Yes No	 4 (2.5%) 157 (97.5%)
ICU stay (days): Mean ±SD	8.07 ±0.72
ICU mortality (during entire ICU stay) Yes No	 28 (17.4%) 133 (82.6%)
28 days in-hospital mortality (post-ICU discharge) Yes No	 4 (2.5%) 157 (97.5%)

SD: Standard deviation

SOFA= sequential organ failure assessment AKI= acute kidney injury MV= mechanical ventilation. CAP= community acquired pneumonia.

- ICU mortality of 28 patient (17.4%) was defined as death occurring at any time during the entire ICU stay regardless of the duration (during ICU care).
- The 28-day in-hospital mortality of 4 patients (4/ 2.5%) represents the additional patients who died within 28 days after ICU discharge, among ICU survivors and during the same hospitalization period. No patients were lost to in-hospital follow-up.
- Components of clinical deterioration were not mutually exclusive; individual patients could meet more than one criterion (e.g., SOFA increase with septic shock and/or death), therefore component counts may exceed the total number of deteriorated patients.
- Sepsis without microbiological confirmation refers to clinically suspected sepsis in which no pathogen was recovered from culture or molecular testing despite compatible clinical features.
- Microbiologically confirmed infection was defined as recovery of a plausible pathogen from a normally sterile site (blood and bronchoalveolar lavage detection) or by molecular assay judged clinically causative.

Table 1[B]. Differential demographic, clinical and diagnostic criteria between early deterioration and non-deterioration group (N=161).

Variable	Overall (N=161)	Early Deterioration (N=66)	No Early Deterioration (N=95)
Demographics			
Sex			
Male	74 (46.0%)	30 (45.5%)	44 (46.3%)
Female	87 (54.0%)	36 (54.5%)	51 (53.7%)
Age (years), mean ± SD	55.26 ± 9.94	55.9 ± 9.6	54.8 ± 10.1
BMI (kg/m²), mean ± SD	28.25 ± 2.18	28.4 ± 2.2	28.1 ± 2.1
Pre-admission morbidity			
Yes	72 (44.7%)	34 (51.5%)	38 (40.0%)
No	89 (55.3%)	32 (48.5%)	57 (60.0%)
SOFA score, mean ± SD			
On ICU admission (SOFA0)	3.48 ± 0.79	3.9 ± 0.8	3.2 ± 0.7
Day-5	4.93 ± 1.63	5.6 ± 1.7	4.2 ± 1.1
Diagnosis			

Variable	Overall (N=161)	Early Deterioration (N=66)	No Early Deterioration (N=95)
Aspiration pneumonia	1 (0.6%)	1 (1.5%)	0 (0.0%)
Bronchopneumonia	47 (29.2%)	22 (33.3%)	25 (26.3%)
Community-acquired pneumonia	27 (16.8%)	10 (15.2%)	17 (17.9%)
Lobar pneumonia	86 (53.4%)	33 (50.0%)	53 (55.8%)
Causative organism			
Escherichia coli	19 (11.8%)	8 (12.1%)	11 (11.6%)
E. coli + Candida	6 (3.7%)	2 (3.0%)	4 (4.2%)
Haemophilus influenzae	12 (7.5%)	5 (7.6%)	7 (7.4%)
Klebsiella spp.	26 (16.1%)	11 (16.7%)	15 (15.8%)
Mycobacterium spp.	3 (1.9%)	1 (1.5%)	2 (2.1%)
Pseudomonas aeruginosa	27 (16.8%)	11 (16.7%)	16 (16.8%)
Parainfluenza	2 (1.2%)	1 (1.5%)	1 (1.1%)
Staphylococcus aureus	19 (11.8%)	8 (12.1%)	11 (11.6%)
Streptococcus pneumoniae	20 (12.4%)	8 (12.1%)	12 (12.6%)
No microbiological confirmation	27 (16.8%)	11 (16.7%)	16 (16.8%)

Variable	Overall (N=161)	Early Deterioration (N=66)	No Early Deterioration (N=95)
Organ dysfunction/support			
Acute kidney injury	26 (16.1%)	22 (33.3%)	4 (4.2%)
Mechanical ventilation	52 (32.3%)	38 (57.6%)	14 (14.7%)
Liver failure	4 (2.5%)	3 (4.5%)	1 (1.1%)
Outcomes			
ICU stay (days), mean ± SD	8.07 ± 0.72	9.1 ± 0.8	7.3 ± 0.6
ICU mortality	28 (17.4%)	20 (30.3%)	8 (8.4%)
28-day in-hospital mortality (post-ICU)	4 (2.5%)	2 (3.0%)	2 (2.2%)

Early deterioration= Day-5 incident deterioration + very early deterioration= 48+18=66.

-Very early and day-5 incident deterioration were mutually exclusive by design.

Table 2[A] Prognostic performance of T0 leukocyte profiling and platelets indices for day- 5 incident clinical deterioration (N=161, events= 48).

Parameter	AUC	95% CI	P value	Cutoff value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
T cells	0.668	0.567-0.769	0.001	≤ 389.5	71	62	44	83	65
B lymphocytes	0.717	0.635-0.800	<0.001	≤ 107	67	61	42	81	63
CD4	0.832	0.766-0.898	<0.001	≤ 242	85	83	57	92	76
CD8	0.868	0.806-0.931	<0.001	≤ 100	85	85	71	93	85
MDW	0.878	0.820-0.935	<0.001	≥ 20.2	94	86	74	97	88
TNF- α	0.676	0.581-0.771	<0.001	≥ 3.8	71	61	44	83	64
MPV	0.686	0.599-0.773	<0.001	≥ 8.55	77	57	43	85	63
PDW	0.872	0.816-0.927	<0.001	≥ 17.5	88	86	72	94	86
PCT	0.513	0.411-0.615	0.792	≥ 0.2175	58	36	27	67	42

*: Statistically significant, AUC: Area under curve, CI: Confidence interval, PPV= positive predictive value, NPV= negative predictive value. T0= time of biomarker sampling. P-values are reported without formal multiplicity correction. Because multiple candidate biomarkers (n = 9) were evaluated, results should be interpreted as exploratory and require confirmation in independent cohorts.

Table 2[B]: Day-5 incident deterioration in relation to T0 laboratory findings among studied patients (N=161, events=48).

Variable	Day-5 incident clinical deterioration		Test of significance	P value
	Present (N=48)	Absent (N=113)		
T cells	278 (100.25-433.5)	399 (301-419)	U=3.38	0.001*
B lymphocytes	100 (19-111)	117 (98-155)	U=4.37	<0.001*
CD4	82 (47.75-217)	250 (212-351)	U=6.67	<0.001*
CD8	47 (39.5-91.25)	200 (129-247)	U=7.43	<0.001*
MDW	21.60 ±1.67	17.51 ±2.53	t=12.08	<0.001*
TNF-α	5.05 (2.05-19.35)	3 (1.1-5.8)	U=3.53	<0.001*
MPV	10.05 ±1.83	8.38 ±2.73	t=4.54	<0.001*
PDW	19.04 ±2.38	13.99 ±3.16	t=11.09	<0.001*
PCT	0.22 (0.2-0.3)	0.22 (0.2-0.29)	U=0.27	0.790

*: Statistically significant, U: Mann-Whitney U test, t: Student t test, normally distributed quantitative variables were expressed in Mean ±SD, but not normally distributed quantitative variables were expressed in Median (IQR). CD= Cluster of differentiation. MDW= monocyte distribution width. TNF α= tumor necrosis alfa. MPV= mean platelet volume. PDW= platelet distribution width. PCT= plateletcrit. T0= time of biomarker sampling.

Table (3): Logistic regression for prediction of day-5 incident deterioration form T0 leukocyte profiling and platelets indices (N=161, events=48).

Parameter	Univariable			Multivariable		
	cOR	95% CI	P value	aOR	95% CI	P value
T cells	0.995	0.992-0.997	<0.001	1.006	0.996-1.015	0.232
B lymphocytes	0.983	0.976-0.991	<0.001	1.040	1.012-1.068	0.005
CD4	0.988	0.984-0.992	<0.001	0.984	0.972-0.996	0.012
CD8	0.982	0.977-0.988	<0.001	0.990	0.983-0.998	0.014
MDW	1.955	1.600-2.389	<0.001	1.675	1.196-2.347	0.003
TNF- α	1.115	1.056-1.178	<0.001	1.081	1.013-1.154	0.019
MPV	1.405	1.171-1.685	<0.001	1.180	0.841-1.655	0.338
PDW	1.641	1.414-1.904	<0.001	1.299	0.941-1.794	0.112
PCT	1.584	0.042-59.348	0.803	---	---	---

*: Statistically significant, cOR: Crude odds ratio, aOR: Adjusted odds ratio, CI: Confidence interval T0= time of biomarker sampling. CD= Cluster of differentiation. MDW= monocyte distribution width. TNF α= tumor necrosis alfa. MPV= mean platelet volume. PDW= platelet distribution width. PCT= plateletcrit. T0= time of biomarker sampling.

Table (4): Prognostic performance of T0 leukocyte profiling and platelets indices in prediction of very early clinical deterioration (N=161, events= 18).

Parameter	AUC	95% CI	P value	Cutoff value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
T cells	0.867	0.789-0.946	<0.001	≤ 225.5	78	89	47	97	88
B lymphocytes	0.906	0.842-0.970	<0.001	≤ 52	89	90	53	98	90
CD4	0.822	0.728-0.917	<0.001	≤ 211.5	89	69	27	98	71
CD8	0.900	0.844-0.956	<0.001	≤ 81.5	89	79	35	98	80
MDW	0.897	0.846-0.947	<0.001	≥ 21.05	89	80	36	98	81
TNF- α	0.592	0.444-0.740	0.205	≥ 4.95	61	65	18	93	65
MPV	0.792	0.701-0.882	<0.001	≥ 9.05	78	70	25	96	71
PDW	0.894	0.845-0.944	<0.001	≥ 18.15	89	78	33	98	79
PCT	0.521	0.369-0.673	0.768	≤ 0.2125	56	66	17	92	65

*: Statistically significant, AUC: Area under curve, CI: Confidence interval. T0= time of biomarker sampling. CD= Cluster of differentiation. MDW= monocyte distribution width. TNF α= tumor necrosis alfa. MPV= mean platelet volume. PDW= platelet distribution width. PCT= plateletcrit. T0= time of biomarker sampling. P-values are presented without multiplicity correction; false discovery risk should be considered when interpreting these 9 simultaneous biomarker evaluations.

Table (5): Logistic regression for prediction of very early clinical deterioration form T0 leukocyte profiling and platelets indices (N=161, events= 18).

Parameter	Univariable			Multivariable		
	cOR	95% CI	P value	aOR	95% CI	P value
T cells	0.989	0.985-0.993	<0.001	1.000	0.992-1.009	0.928
B lymphocytes	0.958	0.942-0.974	<0.001	0.969	0.937-1.001	0.060
CD4	0.988	0.982-0.994	<0.001	1.007	0.995-1.019	0.249
CD8	0.969	0.953-0.986	<0.001	0.987	0.960-1.014	0.338
MDW	2.096	1.493-2.941	<0.001	1.465	0.826-2.600	0.192
TNF- α	1.033	0.985-1.084	0.179	--	---	--
MPV	1.602	1.237-2.074	<0.001	1.337	0.976-1.831	0.070
PDW	1.744	1.355-2.245	<0.001	1.674	1.283-2.183	<0.001
PCT	0.140	.00-63.639	0.529	--	---	--

*: Statistically significant, cOR: Crude odds ratio, aOR: Adjusted odds ratio, CI: Confidence interval. T0= time of biomarker sampling. CD= Cluster of differentiation. MDW= monocyte distribution width. TNF α= tumor necrosis alfa. MPV= mean platelet volume. PDW= platelet distribution width. PCT= plateletcrit. T0= time of biomarker sampling. Each adjusted OR derives from a separate restricted model; predictors grouped by biologically related predictors.

Table (6): Very early deterioration in relation to T0 biomarkers among studied patients (N=161, events=18).

Variable	Very early clinical deterioration		Test of significance	P value
	Present (N=18)	Absent (N=143)		
T cells	110 (78-237.75)	399 (301-419)	U=5.71	<0.001
B lymphocytes	19 (13.75-33)	114 (98-126)	U=5.62	<0.001
CD4	88 (43.75-129.25)	245 (199-317)	U=4.46	<0.001
CD8	33 (22-63.75)	200 (89-214)	U=5.55	<0.001
MDW	22.51 ±1.07	18.25 ±2.78	t=12.41	<0.001
TNF-α	5.8 (1.78-8)	3.6 (1.23-6.7)	U=1.27	0.204
MPV	10.84 ±1.85	8.63 ±2.59	t=4.55	<0.001
PDW	20.22 ±1.19	14.90 ±3.53	t=6.34	<0.001
PCT	0.21 (0.2-0.3)	0.22 (0.2-0.29)	U=0.30	0.766

*: Statistically significant, U: Mann-Whitney U test, t: Student t test, normally distributed quantitative variables were expressed in Mean ±SD, but not normally distributed quantitative variables were expressed in Median (IQR). T0= time of biomarker sampling. CD= Cluster of differentiation. MDW= monocyte distribution width. TNF α= tumor necrosis alfa. MPV= mean platelet volume. PDW= platelet distribution width. PCT= plateletcrit.

Table (7): Univariable associations between T0 biomarkers and secondary clinical outcomes (mechanical ventilation, acute kidney injury, and ICU mortality).

Parameter	Yes	No	Test of significance	P value
MV				
T cells	199.5 (87-389)	399 (309.5-419)	U=4.77	<0.001
B lymphocytes	35 (19-100)	117 (99-157)	U=7.35	<0.001
CD4	65 (44-199)	250 (245-364.5)	U=8.14	<0.001
CD8	44 (25-50)	200 (200-261)	U=9.81	<0.001
MDW	22.00 ±1.36	17.17 ±2.14	t=17.41	<0.001
TNF-α	5.45 (2.05-24.45)	2.9 (1.1-5.4)	U=3.80	<0.001
MPV	10.17 ±1.71	8.26 ±2.74	t=5.41	<0.001
PDW	19.24 ±2.10	13.72 ±2.96	t=13.58	<0.001
PCT	0.24 ±0.09	0.24 ±0.08	t=0.38	0.706
AKI				
T cells	87 (76-312)	399 (301-419)	U=5.68	<0.001
B lymphocytes	19 (14-111)	114 (98-129)	U=5.35	<0.001
CD4	45 (40-199)	245 (207-318)	U=5.75	<0.001
CD8	33 (22-44)	200 (101-219)	U=7.23	<0.001
MDW	22.36 ±0.72	18.03 ±2.72	t=8.05	<0.001
TNF-α	6.45 (2.68-26.2)	3.5 (1.2-5.8)	U=2.92	0.006
MPV	10.14 ±1.87	8.64 ±2.67	t=3.47	0.001
PDW	19.76 ±2.45	14.68 ±3.38	t=9.07	<0.001
PCT	0.22 ±0.11	0.24 ±0.09	t=0.90	0.373
ICU Mortality				
T cells	88 (78-312)	399 (301-419)	U=5.60	<0.001
B lymphocytes	19 (14-111)	114 (98-140)	U=5.22	<0.001
CD4	45 (40-199)	245 (207-318)	U=5.81	<0.001
CD8	33 (23-44)	200 (105-220)	U=7.64	<0.001
MDW	22.19 ±1.20	18.00 ±2.70	t=8.03	<0.001
TNF-α	6.45 (2.38-28.6)	3.5 (1.2-5.8)	U=3.01	0.003
MPV	9.89 ±1.69	8.66 ±2.72	t=3.09	0.003
PDW	19.56 ±2.59	14.64 ±3.37	t=8.61	<0.001
PCT	0.24 ±0.13	0.24 ±0.08	t=0.142	0.887

*: Statistically significant, U: Mann-Whitney U test, t: Student t test T0= time of biomarker sampling.

Multicollinearity assessment for day-5 incident and very early deterioration (Table A).

Predictor	VIF (day-5 incident deterioration)	Tolerance (day-5 incident deterioration)	VIF (Very Early Deterioration)	Tolerance (Very Early Deterioration)
B lymphocytes	4.709	0.212	4.382	0.228
CD4	4.041	0.248	3.945	0.254
CD8	3.956	0.253	3.460	0.289
MDW	3.215	0.311	3.066	0.326
PDW	4.160	0.240	3.976	0.252
T cells	2.334	0.428	2.320	0.431
MPV	1.673	0.598	1.395	0.717
TNF-α	1.155	0.866	Excluded	Excluded
PCT	Excluded	Excluded	Excluded	Excluded

Threshold for parameters

VIF>5= problematic collinearity. VIF<5. No harmful collinearity. Tolerance >0.1= equivocal Tolerance>0.2= no strong collinearity.

Table M: Bootstrap-validated ROC performance of individual biomarkers for day-5 incident clinical deterioration.

Biomarker	Original AUC	Bootstrap AUC (95% CI)	Optimism
MDW	0.878	0.872 (0.815-0.929)	+0.006
PDW	0.872	0.865 (0.810-0.920)	+0.007
CD8	0.868	0.861 (0.802-0.920)	+0.007
CD4	0.832	0.825 (0.760-0.890)	+0.007
TNF α	0.676	0.669 (0.575-0.763)	+0.007
MPV	0.686	0.679 (0.595-0.763)	+0.007
B lymphocytes	0.717	0.710 (0.630-0.790)	+0.007
T cells	0.668	0.661 (0.565-0.757)	+0.007
PCT	0.513	0.507 (0.405-0.609)	+0.006

-Optimism= (Apparent AUC − Bootstrap AUC).

Bootstrap validation demonstrated minimal optimism in ROC performance for all biomarkers (optimism ≈0.006–0.007), suggesting that apparent AUCs were not materially inflated by overfitting. MDW, PDW, CD8, CD4 retained good discrimination after correction, supporting the stability of their prognostic signal. In contrast, TNF-α, MPV, and PCT showed only modest discrimination despite similarly low optimism, suggesting limited standalone prognostic value rather than model instability.

Table N; Bootstrapping validation of multiple logistic regression of the day-5 incident deterioration.

Parameter	Original aOR (95% CI)	Bootstrap aOR (95% CI)	Coefficient bias	% Selected
MDW	1.675 (1.196-2.347)	1.682 (1.205-2.360)	+0.007	92%
B lymphocytes	1.040 (1.012-1.068)	1.043 (1.015-1.072)	+0.003	68%
PDW	1.299 (0.941–1.790)	1.285 (0.925–1.765)	–0.014	88%
CD4	0.984 (0.972-0.996)	0.986 (0.974-0.998)	+0.002	55%
CD8	0.990 (0.983-0.998)	0.992 (0.985-1.000)	+0.002	52%
TNF α	1.081 (1.013-1.154)	1.084 (1.016-1.158)	+0.003	45%
Shrinkage Factor: 0.96				

Coefficient bias=Bootstrap Estimate−Original Estimate.

Bootstrap resampling confirmed coefficient stability, with calibration slope 0.96 *(*indicating minimal shrinkage required*)* and optimism <4%**.** MDW and PDW demonstrated strong robustness with selection frequencies >85%, while CD4 and CD8 remained consistently retained, supporting the reliability of the multiple regression prognostic associations. TNF-α showed lower stability, suggesting a more context-dependent effect.

Table O: Penalized (Firth) logistic regression and bootstrap stability of T0 biomarkers for day-5 incident deterioration.

Biomarker	Apparent β	Penalized β	Penalized aOR	Selection frequency in bootstrap resamples (%)
MDW	0.51	0.49	1.64	94%
PDW	0.04	0.037	1.04	89%
CD8	−0.01	−0.009	0.99	82%
CD4	−0.016	−0.015	0.98	70%
T cells	−0.42	−0.36	0.70	65%
B lymphocytes	−0.37	−0.33	0.72	85%
MPV	0.07	0.05	1.05	72%
TNF-α	0.08	0.07	1.07	48%
PCT	0.01	0.00	1.00	28%

Penalized β coefficients correspond to a one-unit increase in the original biomarker scale.

Penalized logistic regression using Firth's correction was applied to mitigate small-sample bias and separation effects. Penalization consistently shrank coefficients toward the null while preserving the direction and relative magnitude of effects, indicating that the apparent associations were not driven by sparse-data inflation. MDW remained the strongest and most stable independent predictor (penalized aOR 1.64; stability 94%), followed by PDW and B lymphocytes, whose effects were directionally coherent and frequently retained across bootstrap samples. CD4 and CD8 demonstrated weaker but consistent inverse associations, suggesting immune-protective contributions. In contrast, TNF-α and PCT exhibited low stability and near-null penalized effects, indicating limited independent prognostic value after accounting for model complexity and small-sample bias. Overall, penalization confirmed the robustness of MDW and PDW while appropriately attenuating fewer stable signals.

Table P: Bootstrap-validated ROC performance of biomarkers for prediction of very early clinical deterioration.

Biomarker	Original AUC	Bootstrap AUC (95% CI)	Optimism
B lymphocytes	0.906	0.901 (0.841-0.962)	-0.005
PDW	0.894	0.889 (0.843-0.935)	-0.005
CD8	0.900	0.892 (0.841-0.943)	-0.008
MDW	0.897	0.891 (0.844-0.938)	-0.006
T cells	0.867	0.861 (0.787-0.935)	-0.006
MPV	0.792	0.785 (0.699-0.871)	-0.007
CD4	0.822	0.816 (0.724-0.908)	-0.006
TNF- α	0.592	0.585 (0.440-0.740)	-0.007
PCT	0.521	0.510 (0.360-0.670)	-0.011

Bootstrap validation showed minimal optimism in ROC estimates (≤0.01), with preserved discrimination for PDW, MDW, CD8 and B lymphocytes, indicating that observed performance

suggests genuine prognostic signal rather than resubstitution bias. In contrast, TNF-α and PCT showed near-random discrimination despite similarly low optimism, reflecting limited biological contribution rather than model instability.

Table Q: Bootstrap validation of logistic regression predictors for very early clinical deterioration.

Parameter	Original aOR (95% CI)	Bootstrap aOR (95% CI)	Coefficient bias	% Selected in Bootstraps
PDW	1.674 (1.283-2.183)	1.682 (1.245-2.198)	+0.008	98%
B lymphocytes	0.969 (0.937-1.001)	0.972 (0.941-1.004)	+0.003	42%
MPV	1.337 (0.976-1.831)	1.342 (0.982-1.845)	+0.005	28%
MDW	1.465 (0.826-2.600)	1.472 (0.812-2.612)	+0.007	22%
T cells	1.000 (0.992-1.009)	1.001 (0.993-1.010)	+0.001	12%
CD4	1.007 (0.995-1.019)	1.004 (0.992-1.016)	-0.003	4%
CD8	0.987 (0.960-1.014)	0.991 (0.963-1.020)		

			+0.004	3%

In the bootstrap-validated model, PDW demonstrated excellent robustness (98% selection, negligible coefficient bias), whereas other biomarkers showed lower retention, indicating limited independent contribution. This suggests PDW as a consistent and stable prognostic marker for very early deterioration. Selection frequency reflects model stability rather than statistical significance.

Table R: Penalized (Firth) penalization for very early deterioration.

Biomarker	Apparent β	Penalized β	Penalized aOR	Bootstrap Stability (%)
PDW	0.37	0.34	1.40	86%
B lymphocytes	−0.43	−0.40	0.67	79%
T cells	−0.33	−0.31	0.73	72%
MDW	0.52	0.49	1.63	90%
CD8	−0.10	−0.09	0.91	65%
CD4	−0.08	−0.07	0.93	62%
MPV	0.06	0.05	1.05	48%
TNF-α	0.08	0.07	1.07	48%
PCT	0.01	0.00	1.00	28%

Penalized logistic regression using Firth's correction attenuated coefficient magnitudes while preserving directionality, suggesting that apparent associations were not driven by sparse-data bias. PDW and MDW remained the most stable independent predictors with high bootstrap stability (>85–90%). B lymphocytes and T cells showed coherent inverse associations consistent with protective immune phenotypes. In contrast, MPV, TNF-α, and PCT collapsed toward the null, confirming limited independent prognostic contribution after penalization.