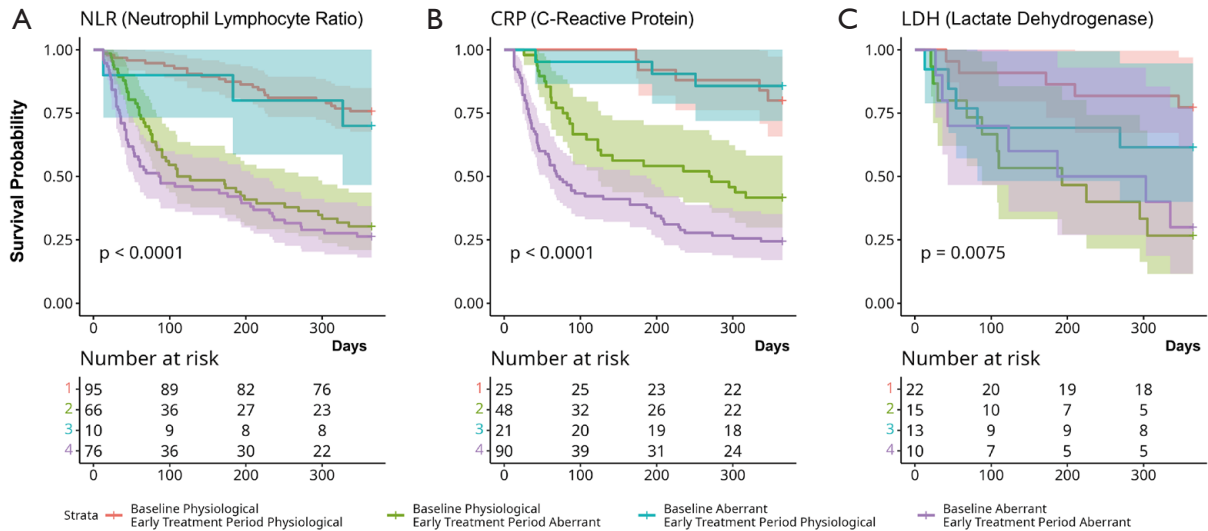
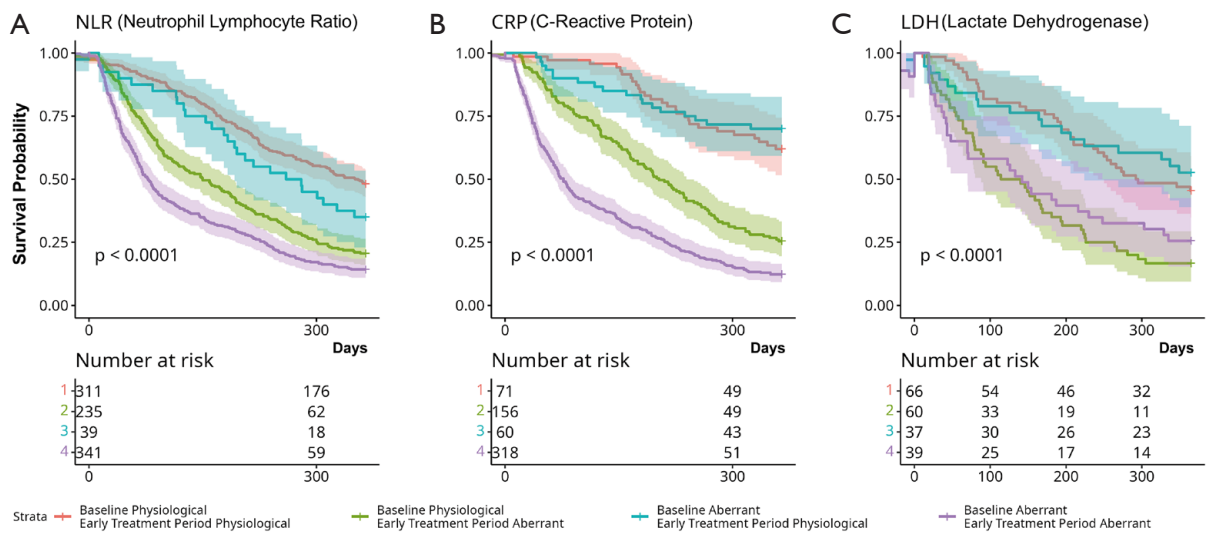


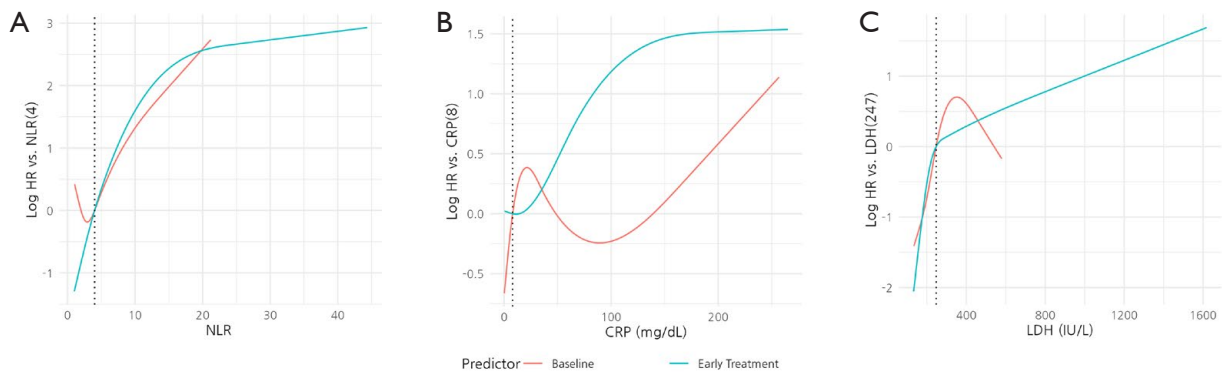
**Figure S1** Correlations in the NLR, CRP, LDH and PD-L1 before immunotherapy prescription. (A) Correlation plot for categorized variables. (B) Correlation plot for continuous variables. NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein, LDH, lactate dehydrogenase; PD-L1, programmed cell death ligand 1.



**Figure S2** Kaplan-Meier curves for OS stratified based on aberrant laboratory parameters at baseline and early treatment period in patients with non-small cell lung cancer undergoing immunotherapy only for patients with EGFR mutation. Strata 1, 2, 3, and 4 indicate baseline physiological and early treatment period physiological, baseline physiological and early treatment period aberrant, baseline aberrant laboratory physiological and early treatment period physiological, and baseline aberrant laboratory parameter and early treatment period aberrant laboratory parameter respectively. (A) Kaplan-Meier curves of OS stratified based on aberrant NLR at baseline and early treatment period. (B) Kaplan-Meier curves of OS stratified based on aberrant CRP at baseline and early treatment period. (C) Kaplan-Meier curves of OS stratified based on aberrant LDH at baseline and early treatment period. OS, overall survival; NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein, LDH, lactate dehydrogenase.



**Figure S3** Kaplan-Meier curves for OS stratified based on aberrant laboratory parameters at baseline and early treatment period in patients with non-small cell lung cancer undergoing immunotherapy only for patients including patients less than one-year survival. (A) Kaplan-Meier curves of OS stratified based on aberrant NLR at baseline and early treatment period. (B) Kaplan-Meier curves of OS stratified based on aberrant CRP at baseline and early treatment period. (C) Kaplan-Meier curves of OS stratified based on aberrant LDH at baseline and early treatment period. OS, overall survival; NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein, LDH, lactate dehydrogenase. We see that the survival curve is similar to original *Figure 2*. Moreover, the curve difference becomes drastic in LDH.



**Figure S4** Cox regression analysis of changes in the hazard ratio with changes in NLR, CRP, and LDH. NLR, neutrophil-lymphocyte ratio; CRP (mg/dL), C-reactive protein; LDH (IU/L), lactate dehydrogenase; HR, hazard ratio.

**Table S1** Comparative analysis of laboratory parameter values between the inflamed and non-inflamed groups at the baseline and early treatment periods

Parameters	Baseline			Early treatment period		
	Survival group	Non-survival group	P value	Survival group	Non-survival group	P value
NLR; median (IQR)	2.6 (1.8–3.9)	4.2 (2.7–7.1)	<0.001	3 (2–4)	7 (4–14)	<0.001
CRP (mg/dL); median (IQR)	7 (2–26)	29 (6–70)	<0.001	7 (2–38)	64 (29–112)	<0.001
LDH (IU/L); median (IQR)	224 (181–292)	216 (188–270)	0.9	205 (177–240)	320 (236–482)	<0.001

NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein; LDH, lactate dehydrogenase; IQR, interquartile range.

**Table S2** Post-hoc analysis of survival curves

lab	Stratum 1	Stratum 2	P value	Significance <sup>1</sup>
NLR	nlr_baseline_label=1, nlr_label=2	nlr_baseline_label=1, nlr_label=1	0.0000000	*
NLR	nlr_baseline_label=2, nlr_label=1	nlr_baseline_label=1, nlr_label=1	0.3608680	
NLR	nlr_baseline_label=2, nlr_label=1	nlr_baseline_label=1, nlr_label=2	0.0100008	*
NLR	nlr_baseline_label=2, nlr_label=2	nlr_baseline_label=1, nlr_label=1	0.0000000	*
NLR	nlr_baseline_label=2, nlr_label=2	nlr_baseline_label=1, nlr_label=2	0.0003801	*
NLR	nlr_baseline_label=2, nlr_label=2	nlr_baseline_label=2, nlr_label=1	0.0003799	*
CRP	crp_baseline_label=1, crp_label=2	crp_baseline_label=1, crp_label=1	0.0000021	*
CRP	crp_baseline_label=2, crp_label=1	crp_baseline_label=1, crp_label=1	0.3554171	
CRP	crp_baseline_label=2, crp_label=1	crp_baseline_label=1, crp_label=2	0.0000007	*
CRP	crp_baseline_label=2, crp_label=2	crp_baseline_label=1, crp_label=1	0.0000000	*
CRP	crp_baseline_label=2, crp_label=2	crp_baseline_label=1, crp_label=2	0.0000007	*
CRP	crp_baseline_label=2, crp_label=2	crp_baseline_label=2, crp_label=1	0.0000000	*
LDH	ldh_baseline_label=1, ldh_label=2	ldh_baseline_label=1, ldh_label=1	0.0000118	*
LDH	ldh_baseline_label=2, ldh_label=1	ldh_baseline_label=1, ldh_label=1	0.5075553	
LDH	ldh_baseline_label=2, ldh_label=1	ldh_baseline_label=1, ldh_label=2	0.0009933	*
LDH	ldh_baseline_label=2, ldh_label=2	ldh_baseline_label=1, ldh_label=1	0.0059943	*
LDH	ldh_baseline_label=2, ldh_label=2	ldh_baseline_label=1, ldh_label=2	0.1977183	
LDH	ldh_baseline_label=2, ldh_label=2	ldh_baseline_label=2, ldh_label=1	0.0595699	

<sup>1</sup>, \*, P<0.05. NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein; LDH, lactate dehydrogenase

**Table S3** Cox regression analysis with only baseline NLR, CRP, and LDH levels

Dependent: Surv (observation_days, death)	Subtypes	Count, n (%)	HR (univariable)	HR (multivariable)
Age	Mean (SD)	60.0 (10.7)	0.99 (0.97–1.00; P=0.071)	1.00 (0.98-1.01; P=0.787)
Sex	Female	160 (26.8)	1	1
	Male	437 (73.2)	0.85 (0.62–1.17; P=0.322)	1.04 (0.71-1.52; P=0.860)
BMI	Mean (SD)	22.9 (3.2)	0.94 (0.90-0.99; P=0.010)	0.97 (0.92-1.01; P=0.008)
ECOG	Mean (SD)	0.7 (0.8)	1.71 (1.44-2.02; P<0.001)	1.28 (1.07-1.54; P=0.008)
Stage	III	2 (0.3)	1	1
	IV	575 (96.3)	0.30 (0.04-2.14; P<0.001)	0.29 (0.19-0.44; P<0.001)
Line of chemotherapy	1	97 (16.2)	1	1
	2	255 (42.7)	1.95 (1.20-3.17; P=0.007)	1.81 (1.06-3.09; P=0.029)
	≥3	201 (33.7)	2.59 (1.58-4.25; P<0.001)	1.90 (1.08-3.35; P=0.027)
nlr_baseline_label	Physiological	355 (59.5)	1	1
	Aberrant	242 (40.5)	2.73 (2.20–3.40; P<0.001)	3.14 (2.07-4.76; P<0.001)
crp_baseline_label	Physiological	189 (39.1)	1	1
	Aberrant	294 (60.9)	2.16 (1.67–2.79; P<0.001)	1.42 (0.93-2.16; P=0.107)
ldh_baseline_label	Physiological	114 (60.6)	1	1
	Aberrant	74 (39.4)	0.80 (0.54–1.18; P =0.257)	0.92 (0.62-1.40; P=0.698)

NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein; LDH, lactate dehydrogenase; HR, hazard ratio; BMI, body mass index; ECOG, European Cooperative Oncology Group.

**Table S4** Multivariate analyses of predictors of 2-year and 3-year overall survival using the Cox proportional hazards regression model

Variables	Subtypes	HR (2-year OS)		HR (3-year OS)	
		HR (95% CI)	P value	HR (95% CI)	P value
Age		1.00 (0.97-1.03)	0.925	1.00 (0.97-1.02)	0.780
Sex	Female	1		1	
	Male	1.66 (0.78-3.53)	0.185	1.69 (0.81-3.52)	0.160
BMI	Mean (SD)	1.02 (0.93-1.11)	0.742	1.03 (0.94-1.13)	0.512
ECOG	Mean (SD)	1.32 (0.93-1.88)	0.117	1.37 (0.97-1.93)	0.074
Stage	III	-	-	-	-
	IV	NA		NA	
Line of Chemotherapy	1	1		1	
	2	1.18 (0.42-3.32)	0.753	1.44 (0.52-4.01)	0.488
	3	1.68 (0.62-4.55)	0.310	1.69 (0.62-4.61)	0.302
Baseline NLR levels	Physiological	1		1	
	Aberrant	1.62 (0.84-3.12)	0.151	1.55(0.85-2.84)	0.155
Early treatment period NLR levels	Physiological	1		1	
	Aberrant	1.43 (0.69-2.96)	0.339	1.49 (0.73-3.04)	0.269
Baseline CRP levels	Physiological	1		1	
	Aberrant	2.28 (1.24-4.18)	0.008	1.97 (1.11-3.52)	0.021
Early treatment period CRP levels	Physiological	1		1	
	Aberrant	2.43 (1.14-5.45)	0.039	2.27 (1.03-5.00)	0.043
Baseline LDH levels	Physiological	1		1	
	Aberrant	0.74 (0.39-1.39)	0.344	0.84 (0.45-1.54)	0.564
Early treatment period LDH levels	Physiological	1		1	
	Aberrant	5.33 (2.55-11.12)	<0.001	4.26 (2.07-8.80)	<0.001

HR, hazard ratio; OS, overall survival; BMI, body mass index; ECOG, European Cooperative Oncology Group; NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein; LDH, lactate dehydrogenase.

**Table S5** Time-varying Cox regression analysis with NLR, CRP, and LDH levels

Dependent: Survival (observation_days, death)	Subtypes	Count, n (%)	HR (univariable)	HR (multivariable)
Age	Mean (SD)	60.0 (10.7)	0.99 (0.97–1.00; P=0.064)	1.00 (0.98–1.01, P=0.787)
Sex	Female	160 (26.8)	1	1
	Male	437 (73.2)	0.85 (0.62–1.17; P=0.322)	1.04 (0.71–1.52, P=0.860)
BMI	Mean (SD)	22.9 (3.2)	0.94 (0.90–0.99, P=0.001)	0.97 (0.92–1.01, P=0.139)
ECOG	Mean (SD)	0.7 (0.8)	1.71 (1.44–2.02, P<0.001)	1.28 (1.07–1.55, P=0.008)
Stage	III	2 (0.3)	1	1
	IV	575 (96.3)	0.30 (0.04–2.14)	0.29 (0.19–0.44, P<0.001)
Line of Chemotherapy	1	97 (16.2)	1	1
	2	255 (42.7)	1.95 (1.20–3.17, P=0.007)	1.81 (1.06–3.09, P=0.029)
	≥3	201 (33.7)	2.59 (1.58–4.25, P<0.001)	1.90 (1.08–3.35, P=0.027)
NLR	Physiological	355 (59.5)	1	1
	Aberrant	242 (40.5)	4.81 (3.52–6.57; P<0.001)	2.45 (1.74–3.45, P<0.001)
CRP	Physiological	189 (39.1)	1	1
	Aberrant	294 (60.9)	5.59 (3.65–8.58; P<0.001)	3.37 (2.19–5.17, P<0.001)
LDH	Physiological	114 (60.6)	1	1
	Aberrant	1334 (60.6)	5.27 (3.85–7.22; P<0.001)	3.31 (2.32–4.72, P<0.001)

NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein; LDH, lactate dehydrogenase; HR, hazard ratio; BMI, body mass index; ECOG, European Cooperative Oncology Group.

**Table S6** Univariate and multivariate analyses of predictors of overall for patients with EGFR mutation survival using the Cox proportional hazards regression model

Variables	Subtypes	HR (univariate)		HR (multivariate)	
		HR (95% CI)	P value	HR (95% CI)	P value
Age	Mean (SD)	1.00 (0.98–1.02)	0.854	1.01 (0.96–1.06)	0.682
Sex	Female	1		1	0.944
	Male	0.78 (0.54–1.14)	0.089	1.05 (0.29–3.79)	
BMI	Mean (SD)	0.93 (0.88–0.99)	0.017	1.11 (0.94–1.30)	0.211
ECOG	Mean (SD)	1.71 (1.43–2.05)	<0.001	1.45 (0.89–2.37)	0.134
Stage	III	1		-	-
	IV	0.38 (0.05–2.76)	0.341	-	-
Line of Chemotherapy	1	1		1	
	2	1.75 (1.04–2.94)	0.035	8.12 (1.27–51.70)	0.027
	≥3	2.09 (1.20–3.65)	0.009	4.64 (0.81–26.50)	0.085
Baseline NLR levels	Physiological	1		1	
	Aberrant	2.22 (1.58–3.13)	<0.001	3.10 (1.08–8.90)	0.036
Early treatment period NLR levels	Physiological	1		1	
	Aberrant	4.72 (3.06–7.28)	<0.001	1.87 (0.52–6.75)	0.342
Baseline CRP levels	Physiological	1		1	
	Aberrant	1.85 (1.26–2.73)	0.002	2.22 (0.82–5.98)	0.116
Early treatment period CRP levels	Physiological	1		1	
	Aberrant	6.42 (3.35–12.31)	<0.001	1.27 (0.37–4.43)	0.705
Baseline LDH levels	Physiological	1		1	
	Aberrant	1.00 (0.54–1.85)	0.993	0.53 (0.18–1.55)	0.245
Early treatment period LDH levels	Physiological	1		1	
	Aberrant	4.96 (3.09–7.94)	<0.001	4.26 (1.41–12.81)	0.010

HR, hazard ratio; BMI, body mass index; ECOG, European Cooperative Oncology Group; NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein; LDH, lactate dehydrogenase.

**Table S7** Baseline characteristics of the identified patients including patients with less than one-year observation window

Characteristics	Total (N=970)	Survival group (N=265)	Non-survival (N=705)	P value
Age (years); mean (SD)	61.7 (10.3)	62.0 (10.0)	61.6 (10.4)	0.617
Sex; n (%)				0.091
Male	699 (72.1)	202 (76.2)	497 (70.5)	
Female	271 (27.9)	63 (23.8)	208 (29.5)	
BMI; mean (SD)	23.0 (3.8)	23.4 (3.2)	22.9 (4.0)	0.033
ECOG; mean (SD)	0.6 (0.8)	0.4 (0.6)	0.6 (0.8)	<0.001
Stage				
III	2 (0.3)	0 (0.0)	2 (0.6)	0.937
IV	937 (96.6)	258 (97.4)	679 (96.3)	
Line of chemotherapy				
1	143 (14.7)	66 (24.9)	77 (10.9)	<0.001
2	425 (43.8)	120 (45.3)	305 (43.3)	
≥3	336 (34.6)	71 (26.8)	265 (37.6)	
Immunotherapy type; n (%)				<0.001
Atezolizumab	372 (38.4)	63 (23.8)	309 (43.8)	
Pembrolizumab	292 (30.1)	118 (44.5)	174 (24.7)	
Nivolumab	306 (31.5)	84 (31.7)	222 (31.5)	
Histological type; n (%)				0.198
Adenocarcinoma	687 (70.8)	185 (69.8)	502 (71.2)	
Squamous cell carcinoma	255 (26.3)	76 (28.7)	179 (25.4)	
Others	28 (2.9)	4 (1.5)	24 (3.4)	
EGFR status; n (%)				
Wild-type	403 (41.5)	119 (44.9)	284 (40.3)	0.009
Mutant	127 (13.1)	22 (8.3)	105 (14.9)	
Unknown	440 (45.4)	124 (46.8)	316 (44.8)	
PD-L1 expression (%); mean (SD)	32.7 (38.3)	47.0 (40.8)	27.1 (35.9)	<0.001
Observation (days); mean (SD)	189.5 (141.3)	365 (0.0)	123.6 (107.4)	<0.001

SD, standard deviation; BMI, body mass index; ECOG, European Cooperative Oncology Group; EGFR, epidermal growth factor receptor; PD-L1, programmed cell death ligand 1.



**Table S8** Univariate and multivariate analyses of predictors of overall for patients including patients with less than one-year observation window using the Cox proportional hazards regression model

Variables	Subtypes	HR (univariate)		HR (multivariate)	
		HR (95% CI)	P value	HR (95% CI)	P value
Age	Mean (SD)	1.00 (0.99–1.01)	0.674	1.00 (0.98–1.03)	0.705
Sex	Female	-		-	
	Male	0.85 (0.72–1.00)	0.048	0.97 (0.56–1.70)	0.927
BMI	Mean (SD)	0.96 (0.92–0.98)	0.001	1.02 (0.98–1.06)	0.264
ECOG	Mean (SD)	1.41 (1.28–1.54)	<0.001	1.33 (1.06–1.68)	0.016
Stage	III	1		1	
	IV	0.51 (0.13–2.05)	0.343	NA	
Line of Chemotherapy	1	1		1	
	2	1.61 (1.25–2.07)	<0.001	2.03 (0.92–4.50)	0.080
	≥3	1.99 (1.55–2.57)	<0.001	2.23 (0.97–5.10)	0.059
Baseline NLR levels	Physiological	1		1	
	Aberrant	2.03 (1.75–2.36)	<0.001	1.64 (0.99–2.70)	0.053
Early treatment period NLR levels	Physiological	1		1	
	Aberrant	2.63 (2.22–3.11)	<0.001	1.46 (0.86–2.46)	0.159
Baseline CRP levels	Physiological	1		1	
	Aberrant	1.70 (1.43–2.02)	<0.001	1.57 (1.00–2.49)	0.052
Early treatment period CRP levels	Physiological	1		1	
	Aberrant	3.95 (3.04–5.12)	<0.001	3.40 (1.79–6.47)	<0.001
Baseline LDH levels	Physiological	1		1	
	Aberrant	0.86 (0.65–1.14)	0.301	0.80 (0.51–1.26)	0.332
Early treatment period LDH levels	Physiological	1		1	
	Aberrant	2.87 (2.37–3.47)	<0.001	2.55 (1.58–4.13)	<0.001

HR, hazard ratio; BMI, body mass index; ECOG, European Cooperative Oncology Group; NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein; LDH, lactate dehydrogenase.