

Appendix 1

The relationship between perioperative laboratory parameters and prognosis

Table S2 shows the comparison of perioperative laboratory results between the textbook outcome (TO) group and the non-textbook outcome (non-TO) group. The following laboratory parameters did not show statistically significant differences between the two groups preoperatively and on the first day following surgery: albumin, percentage of neutrophils, percentage of lymphocytes, NLR, monocyte-to-lymphocyte ratio (MLR), and lymphocyte-to-monocyte ratio (LMR) ($P>0.05$). However, significant differences were observed on the third day following surgery, with the TO group having a lower percentage of neutrophils [TO:non-TO =78.8% (62.7%, 95.4%):83.1% (67.9%, 92.9%), $P=0.003$], a higher percentage of lymphocytes [TO:non-TO =10.3% (4.15%, 32.4%):9.70% (2.40%, 22.8%), $P=0.049$], and a lower NLR [TO:non-TO =8.20 (2.78, 39.8): 10.3 (4.15, 32.4), $P=0.04$]. This might suggest that patients in the non-TO experienced more severe stress and inflammatory responses postoperatively, leading to a certain degree of immunosuppression.

Given the widespread reporting of postoperative NLR being associated with poor prognosis in malignant tumors, postoperative stress, and inflammatory response, we further investigated the impact of NLR on the long-term prognosis of PDAC patients. This study further examined the relationship between NLR on the third day following surgery with both DFS and OS. Utilizing the Youden index (7.49) for the optimal discrimination of OS as the criterion for dichotomizing, 108 PDAC patients were classified into NLR*-high group ($n=66$) and NLR*-low NLR ($n=42$). There were significant differences in baseline prognostic data between the two groups regarding age, TNM staging, and tumor differentiation degree ($P<0.05$, Table S3). Propensity scoring match (PSM) was carried out to adjust for these confounders in both groups, considering factors such as age, the TNM stage, and differentiation (Table S4). However, there was no significant difference in DFS and OS associated with NLR, both before and after PSM.

In summary, this study indicates that patients with more complications (non-TO group) may experience more intense postoperative stress and inflammation. However, in this cohort, no significant association was observed between postoperative NLR and long-term outcomes (Figure S1A-S1D), but patients with lower NLR had relatively better OS compared to those with higher NLR (Figure S1B,S1D).

Table S1 All baseline characteristics of PDAC patients with or without achieving textbook outcomes following PD

Characteristics	Non-textbook outcome group (n=42)	Textbook outcome group (n=69)	P value
Preoperative characteristics			
Gender			>0.99
Female	19 (45.2%)	30 (43.5%)	
Male	23 (54.8%)	39 (56.5%)	
Age (years)	62.7 (12.3)	60.2 (9.32)	0.28
BMI (kg/m ²)	22.1 (3.34)	21.7 (2.70)	0.45
ASA			0.04
1	3 (7.1%)	7 (10.1%)	
2	13 (31.0%)	30 (43.5%)	
3	22 (52.4%)	32 (46.4%)	
4	4 (9.5%)	0 (0%)	
CCI			0.64
<5	12 (28.6%)	24 (34.8%)	
≥5	30 (71.4%)	45 (65.2%)	
Resectability			0.83
Resectable	32 (76.2%)	50 (72.5%)	
Borderline	10 (23.8%)	19 (27.5%)	
CA125 (U/mL)	17.5 [3.48, 68.0]	16.4 [3.40, 207]	0.15
CA199 (U/mL)	222 [0.600, 4370]	181 [0.600, >10000]	0.35
CA724 (U/mL)	1.90 [0.400, 36.9]	2.60 [0.500, 79.4]	0.13
Smoke			0.78
No	34 (81.0%)	53 (76.8%)	
Yes	8 (19.0%)	16 (23.2%)	
Drink			0.22
No	38 (90.5%)	55 (79.7%)	
Yes	4 (9.5%)	14 (20.3%)	
Hypertension			>0.99
No	32 (76.2%)	52 (75.4%)	
Yes	10 (23.8%)	17 (24.6%)	
Diabetes			>0.99
No	30 (71.4%)	48 (69.6%)	
Yes	12 (28.6%)	21 (30.4%)	
Jaundice			0.87
No	13 (31.0%)	19 (27.5%)	
Yes	29 (69.0%)	50 (72.5%)	
PT [^] (s)	12.2 (1.46)	11.7 (1.10)	0.07
APTT [^] (s)	26.1 (4.20)	25.1 (2.98)	0.20
ALT [^] (U/L)	80.0 [3.00, 490]	79.0 [10.0, 563]	0.57
AST [^] (U/L)	49.0 [13.0, 462]	55.0 [12.0, 484]	0.45
Total bilirubin [^] (μmol/L)	74.5 [8.40, 396]	102 [5.30, 342]	0.65
Albumin [^] (g/L)	35.5 (4.48)	36.5 (5.65)	0.33
Hb [^] (g/L)	119 (19.1)	118 (19.3)	0.81
RBC [^] (10 ¹² /L)	4.01 (0.627)	3.96 (0.690)	0.69
PLT [^] (10 ⁹ /L)	223 [92.0, 453]	250 [90.0, 469]	0.38
RDW [^] (%)	46.8 (5.83)	47.9 (7.72)	0.43
WBC [^] (10 ⁹ /L)	7.01 (2.40)	7.13 (2.92)	0.81
Neutrophils [^] (%)	68.3 [36.7, 93.1]	66.4 [37.9, 91.2]	0.96
Lymphocyte [^] (%)	20.3 [3.30, 44.4]	21.4 [3.00, 48.9]	0.81
Monocyte [^] (%)	7.55 [3.60, 15.3]	7.30 [3.70, 17.3]	0.64
NLR [^]	3.24 [0.830, 25.9]	3.19 [0.780, 30.4]	0.64
MLR [^]	0.390 [0.130, 2.85]	0.380 [0.160, 1.70]	0.73
PLR [^]	186 [67.5, 435]	187 [59.8, 485]	0.48
Preoperative biliary drainage			
Normal*	13 (31.0%)	20 (29.0%)	>0.99
None*	12 (28.6%)	20 (29.0%)	
ERCP	4 (9.5%)	6 (8.7%)	
PTCD	13 (31.0%)	23 (33.3%)	
Postoperative characteristics			
PT [#] (s)	13.5 (1.58)	13.0 (1.39)	0.14
APTT [#] (s)	34.7 (26.1)	28.5 (5.15)	0.13
ALT [#] (U/L)	103 [15.0, 2210]	122 [19.0, 1670]	0.70
AST [#] (U/L)	86.0 [15.0, 4470]	93.0 [20.0, 1610]	0.57
Total bilirubin [#] (μmol/L)	67.2 [8.50, 305]	80.5 [7.20, 331]	0.51
Albumin [#] (g/L)	29.7 (4.49)	30.9 (5.57)	0.20
Hemoglobin [#] (g/L)	111 (20.9)	112 (20.0)	0.78
RBC [#] (10 ¹² /L)	3.66 (0.645)	3.69 (0.694)	0.79
PLT [#] (10 ⁹ /L)	210 [78.0, 453]	198 [88.0, 437]	0.73
RDW [#] (%)	50.1 (6.76)	49.0 (5.82)	0.40
WBC [#] (10 ⁹ /L)	11.9 (4.15)	12.4 (4.48)	0.57
Neutrophils [#] (%)	88.8 [68.6, 94.1]	88.2 [67.7, 94.5]	0.68
Lymphocyte [#] (%)	5.85 [1.00, 26.2]	6.00 [2.00, 22.1]	0.96
Monocyte [#] (%)	4.85 [2.00, 12.9]	5.40 [1.70, 11.9]	0.35
NLR [#]	15.1 [2.62, 88.5]	14.6 [3.06, 46.1]	0.23
MLR [#]	0.810 [0.160, 4.40]	0.880 [0.120, 3.08]	0.75
PLR [#]	310 [68.5, 2020]	303 [64.2, 877]	0.14
PT* (s)	13.2 (2.03)	12.5 (1.39)	0.054
APTT* (s)	31.9 (6.92)	28.0 (5.52)	0.002
ALT* (U/L)	54.5 [8.00, 4340]	54.0 [10.0, 1100]	0.23
AST* (U/L)	37.0 [11.0, 3750]	34.0 [9.00, 873]	0.19
Total bilirubin* (μmol/L)	41.9 [9.80, 306]	47.1 [7.20, 299]	0.54
Albumin* (g/L)	32.7 (5.92)	33.0 (3.87)	0.77
Hemoglobin* (g/L)	97.5 (17.9)	102 (17.4)	0.19
RBC* (10 ¹² /L)	3.28 (0.609)	3.40 (0.646)	0.33
PLT* (10 ⁹ /L)	178 [78.0, 416]	196 [29.0, 349]	0.52
RDW* (%)	49.6 (5.61)	48.8 (5.69)	0.49
WBC* (10 ⁹ /L)	11.7 (4.41)	11.0 (4.94)	0.46
Neutrophils* (%)	83.6 [67.9, 93.1]	78.8 [62.7, 95.4]	<0.001
Lymphocyte* (%)	7.65 [2.70, 17.4]	9.70 [2.40, 22.8]	0.02
Monocyte* (%)	5.80 [1.00, 12.5]	7.20 [2.10, 17.8]	0.03
NLR*	10.8 [4.15, 33.5]	8.20 [2.78, 39.8]	0.02
MLR*	0.820 [0.100, 2.48]	0.740 [0.230, 4.03]	0.48
PLR*	216 [68.5, 705]	197 [27.0, 992]	0.56
AMY POD [#] (U/L)	118 [8.00, 1980]	99.0 [15.0, 1390]	0.56
DFA POD [#] (U/L)	450 [3.00, 36100]	211 [11.0, 13300]	0.046
DFA POD* (U/L)	184 [6.00, 65000]	83.0 [6.00, 15100]	0.005
Intraoperative characteristics			
Operation duration (hours)	7.00 [3.60, 12.0]	6.00 [2.15, 12.0]	0.13
Operation type			
L	17 (40.5%)	27 (39.1%)	0.80
L→O	7 (16.7%)	9 (13.0%)	
O	15 (35.7%)	30 (43.5%)	
R	3 (7.1%)	3 (4.3%)	
Vascular gestures			
None**	32 (76.2%)	50 (72.5%)	0.86
PV	4 (9.5%)	5 (7.2%)	
SMA	1 (2.4%)	2 (2.9%)	
SMV	5 (11.9%)	12 (17.4%)	
Pancreatic anastomosis			
Duct-to-mucosa	34 (81.0%)	55 (79.7%)	>0.99
End-to-end	8 (19.0%)	14 (20.3%)	
Estimated blood loss (mL)	200 [20.0, 16000]	150 [20.0, 4800]	0.38
Blood transfusion (mL)	400 [200, 7100]	800 [200, 2400]	0.71
None***	23 (54.8%)	37 (53.6%)	
Pancreatic texture			
Hard	21 (50.0%)	55 (79.7%)	0.002
Soft	21 (50.0%)	14 (20.3%)	
Dilated main pancreatic duct diameter (cm)	0.27 [0.11, 0.67]	0.34 [0.15, 0.81]	0.02
Dilated bile duct diameter (cm)	0.9 [0.5, 1.5]	0.9 [0.2, 3.5]	0.21
Pathologic characteristics			
TNM (AJCC 8th)			
I	6 (14.3%)	12 (17.4%)	0.85
II	7 (16.7%)	13 (18.8%)	
III	29 (69.0%)	44 (63.8%)	
Differentiation degree			
Low	11 (26.2%)	16 (23.2%)	0.93
Medium	29 (69.0%)	50 (72.5%)	
Well	2 (4.8%)	3 (4.3%)	
Tumor size (cm)	3.00 [1.40, 6.40]	3.00 [1.00, 10.3]	0.65
Resected lymph nodes	15.5 [5.00, 37.0]	16.0 [3.00, 50.0]	0.32
Positive lymph nodes	1.00 [0, 22.0]	1.00 [0, 20.0]	0.84
Proportion of positive lymph nodes	0.07 [0, 0.81]	0.08 [0, 1.00]	0.77
Prognostic characteristics			
DFS time (days)	283 [31, 2090]	426 [34, 2060]	0.23
Missing	3 (7.1%)	0 (0%)	
OS time (days)	541 [123, 2100]	759 [173, 2060]	0.28
Missing	3 (7.1%)	0 (0%)	
LOS (days)	22 [4, 97]	12 [6, 37]	<0.001
LOFAT (days)	69 [39, 135]	47 [26, 87]	<0.001
Missing	4	0	
PATc	6 [1, 16]	8 [1, 22]	0.08
Missing	4	0	
CPAT (PATc ≥6)			
No	13 (33.3%)	15 (21.7%)	0.28
Yes	26 (66.7%)	54 (78.3%)	
Death	3	0	

Data are presented as n (%), mean (standard deviation) and median [minimum, maximum]. [^], preoperative level; [#], postoperative first day level; *, postoperative day 3 level. Missing: absence value. PDAC, pancreatic ductal adenocarcinoma; PD, pancreaticoduodenectomy; BMI, body mass index; ASA, American Society of Anesthesiologists; CCI, Charlson comorbidity index; CA125/199/724, carbohydrate antigen 125/199/724; PT, prothrombin time; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; RDW, red blood cell distribution width; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; AMY, serum amylase; DFA, drainage fluid amylase; POD, postoperative day; MLR, monocytes/lymphocyte ratio; Normal*, no jaundice; None*, no preoperative biliary drainage; None**, no vascular reconstruction; None***, no blood transfusion; ERCP, endoscopic retrograde cholangiopancreatography; PTCD, percutaneous transhepatic cholangial drainage; L, laparoscopic surgery; O, open surgery; L→O, laparoscopic surgery transit open; R, robotic surgery; PV, portal vein; SMV, superior mesenteric vein; SMA, superior mesenteric artery; TNM (AJCC 8th), TNM stage of American Joint Committee on Cancer (eighth edition); DFS, disease-free survival; OS, overall survival; LOS, length of postoperative hospital stay; LOFAT, length of time to the first adjuvant therapy; PATc, postoperative adjuvant therapy cycles; CPAT, completed postoperative adjuvant therapy.

Table S2 Comparison of laboratory parameters in the TO group and non-TO group

Characteristics	Non-textbook outcome group (n=39)	Textbook outcome group (n=69)	P value
Albumin [^] (g/L)	35.6 [23.6, 45.0]	36.5 [22.6, 48.5]	0.32
Neutrophils [^] (%)	67.9 [36.7, 93.1]	66.4 [37.9, 91.2]	0.91
Lymphocyte [^] (%)	20.1 [3.30, 44.4]	21.4 [3.00, 48.9]	0.93
NLR [^]	3.25 [0.830, 25.9]	3.19 [0.780, 30.4]	0.91
MLR [^]	0.410 [0.13, 2.85]	0.38 [0.16, 1.70]	0.98
PLR [^]	190 [67.5, 435]	187 [59.8, 485]	0.59
Albumin [#] (g/L)	30.2 [19.1, 41.1]	30.7 [18.2, 50.7]	0.64
Neutrophils [#] (%)	88.9 [75.4, 94.1]	88.2 [67.7, 94.5]	0.41
Lymphocyte [#] (%)	5.70 [1.00, 18.4]	6.00 [2.00, 22.1]	0.46
NLR [#]	15.2 [4.10, 88.5]	14.6 [3.06, 46.1]	0.43
MLR [#]	0.82 [0.28, 4.40]	0.88 [0.12, 3.08]	0.89
PLR [#]	314 [68.5, 2020]	303 [64.2, 877]	0.25
Albumin [*] (g/L)	32.4 [26.2, 62.7]	33.0 [23.7, 41.1]	0.42
Neutrophils [*] (%)	83.1 [67.9, 92.9]	78.8 [62.7, 95.4]	0.003
Lymphocyte [*] (%)	8.10 [2.80, 17.4]	9.70 [2.40, 22.8]	0.049
NLR [*]	10.3 [4.15, 32.4]	8.20 [2.78, 39.8]	0.04
MLR [*]	0.79 [0.10, 2.48]	0.74 [0.23, 4.03]	0.58
PLR [*]	208 [68.5, 705]	197 [27.0, 992]	0.29

Data are presented as medium [minimum, maximum]. [^], preoperative level; [#], postoperative first day level; ^{*}, postoperative day 3 level. TO, textbook outcomes; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; MLR, monocytes/lymphocyte ratio.

Table S3 Baseline data of the high and low NLR groups on the third postoperative day before PSM

Characteristics	NLR*-high (n=66)	NLR*-low (n=42)	P value
Age (<65/≥65 years)	34 (51.5%)/32 (48.5%)	31 (73.8%)/11 (26.2%)	0.04
Gender (female/male)	29 (43.9%)/37 (56.1%)	18 (42.9%)/24 (57.1%)	>0.99
CA199 (<200/≥200 U/L)	35 (53.0%)/31 (47.0%)	21 (50.0%)/21 (50.0%)	0.91
Resectability (resectable/borderline)	46 (69.7%)/20 (30.3%)	33 (78.6%)/9 (21.4%)	0.43
pT stage			0.78
1	6 (9.1%)	3 (7.1%)	
2	22 (33.3%)	18 (42.9%)	
3	30 (45.5%)	16 (38.1%)	
4	8 (12.1%)	5 (11.9%)	
pN stage			0.79
0	25 (37.9%)	18 (42.9%)	
1	25 (37.9%)	16 (38.1%)	
2	16 (24.2%)	8 (19.0%)	
TNM (AJCC 8 th)			0.03
I	7 (10.6%)	11 (26.2%)	
II	16 (24.2%)	4 (9.5%)	
III	43 (65.2%)	27 (64.3%)	
Differentiation			0.02
Poor	10 (15.2%)	15 (35.7%)	
Medium	54 (81.8%)	24 (57.1%)	
Well	2 (3.0%)	3 (7.1%)	
Perineural invasion (no/yes)	6 (9.1%)/60 (90.9%)	4 (9.5%)/38 (90.5%)	>0.99
Adipose tissue invasion (no/yes)	11 (16.7%)/55 (83.3%)	11 (26.2%)/31 (73.8%)	0.34
Vascular cancer thrombus (no/yes)	28 (42.4%)/38 (57.6%)	18 (42.9%)/24 (57.1%)	>0.99
Initial recurrence site			0.54
Abdominal or retroperitoneal metastasis	8 (12.1%)	6 (14.3%)	
hepatic metastases	27 (40.9%)	10 (23.8%)	
Local recurrence	9 (13.6%)	9 (21.4%)	
Lung metastases	8 (12.1%)	5 (11.9%)	
Multiple metastasis	6 (9.1%)	4 (9.5%)	
None	8 (12.1%)	8 (19.0%)	
CPAT (PATc ≥6) (no/yes)	20 (30.3%)/46 (69.7%)	8 (19.0%)/34 (81.0%)	0.28
Textbook outcomes (no/yes)	29 (43.9%)/37 (56.1%)	10 (23.8%)/32 (76.2%)	0.055

Data are presented as n (%). *, postoperative day 3 level. NLR, neutrophil/lymphocyte ratio; pT stage, pathological T stage; pN stage, pathological N stage; TNM (AJCC 8th), TNM stage of American Joint Committee on Cancer (eighth edition); CA199, carbohydrate antigen 199; PATc, postoperative adjuvant therapy cycles; CPAT, completed postoperative adjuvant therapy; PSM, propensity scoring match.

Table S4 Baseline data of the high and low NLR groups on the third postoperative day after PSM

Characteristics	NLR [*] -high (n=30)	NLR [*] -low (n=30)	P value
Age (<65/≥65 years)	21 (70.0%)/9 (30.0%)	19 (63.3%)/11 (36.7%)	0.78
Gender (female/male)	13 (43.3%)/17 (56.7%)	15 (50.0%)/15 (50.0%)	0.80
CA199 (<200/≥200 U/L)	15 (50.0%)/15 (50.0%)	15 (50.0%)/15 (50.0%)	>0.99
Resectability (resectable/borderline)	17 (56.7%)/13 (43.3%)	23 (76.7%)/7 (23.3%)	0.17
pT stage			0.70
1	5 (16.7%)	3 (10.0%)	
2	10 (33.3%)	13 (43.3%)	
3	10 (33.3%)	11 (36.7%)	
4	5 (16.7%)	3 (10.0%)	
pN stage			0.42
0	11 (36.7%)	15 (50.0%)	
1	10 (33.3%)	10 (33.3%)	
2	9 (30.0%)	5 (16.7%)	
TNM (AJCC 8 th)			0.81
I	7 (23.3%)	9 (30.0%)	
II	4 (13.3%)	3 (10.0%)	
III	19 (63.3%)	18 (60.0%)	
Differentiation			0.96
Poor	8 (26.7%)	7 (23.3%)	
Medium	21 (70.0%)	22 (73.3%)	
Well	1 (3.3%)	1 (3.3%)	
Perineural invasion (no/yes)	2 (6.7%)/28 (93.3%)	1 (3.3%)/29 (96.7%)	>0.99
Adipose tissue invasion (no/yes)	6 (20.0%)/24 (80.0%)	7 (23.3%)/23 (76.7%)	>0.99
Vascular cancer thrombus (no/yes)	12 (40.0%)/18 (60.0%)	14 (46.7%)/16 (53.3%)	0.79
Initial recurrence site			0.86
Abdominal or retroperitoneal metastasis	4 (13.3%)	6 (20.0%)	
hepatic metastases	12 (40.0%)	8 (26.7%)	
Local recurrence	5 (16.7%)	4 (13.3%)	
Lung metastases	4 (13.3%)	5 (16.7%)	
Multiple metastasis	2 (6.7%)	2 (6.7%)	
None	3 (10.0%)	5 (16.7%)	
CPAT (PATc ≥6) (No/Yes)	9 (30.0%)/21 (70.0%)	5 (16.7%)/25 (83.3%)	0.36
Textbook outcomes (No/Yes)	14 (46.7%)/16 (53.3%)	9 (30.0%)/21 (70.0%)	0.29

Data are presented as n (%). *, postoperative day 3 level. NLR, neutrophil/lymphocyte ratio; pT stage, pathological T stage; pN stage, pathological N stage; TNM (AJCC 8th), TNM stage of American Joint Committee on Cancer (eighth edition); CA199, carbohydrate antigen 199; PATc, postoperative adjuvant therapy cycles; CPAT, completed postoperative adjuvant therapy; PSM, propensity scoring match.

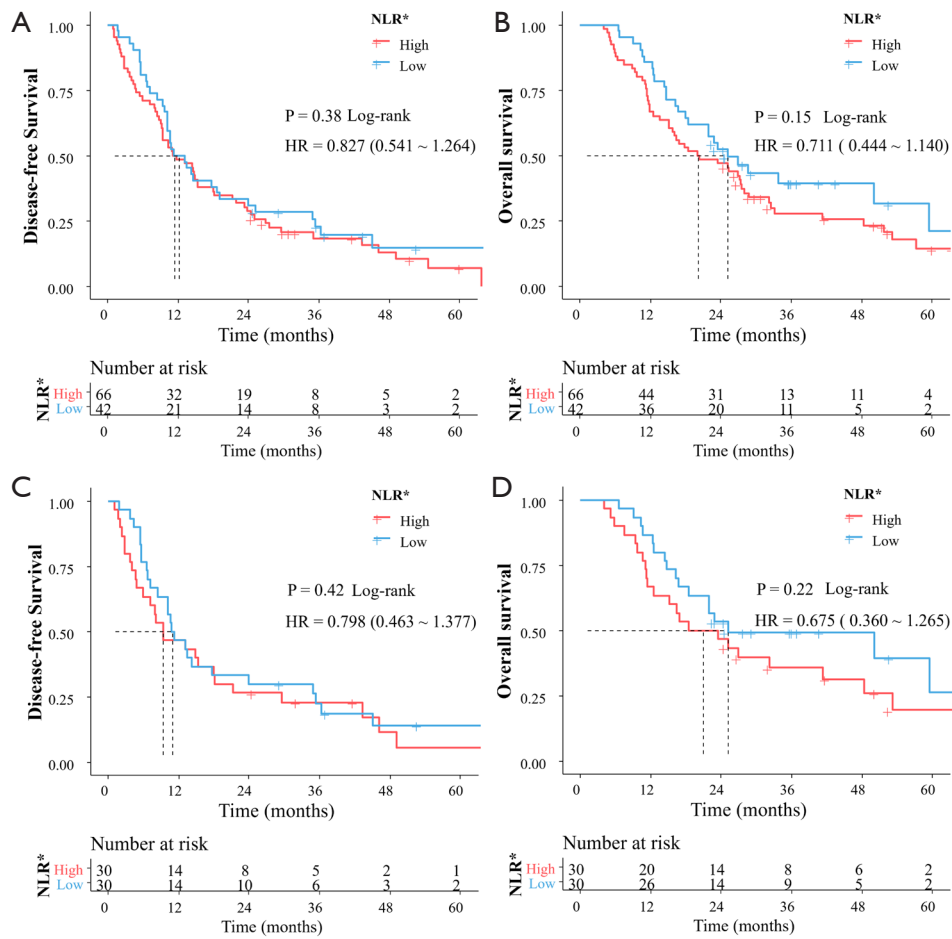


Figure S1 Effect of high and low NLR groups on long-term prognosis on the third postoperative day. (A) Effect of NLR* on DFS before PSM. (B) Effect of NLR* on OS before PSM. (C) Effect of NLR* on DFS after PSM. (D) Effect of NLR* on OS after PSM. *, postoperative day 3 level. NLR, neutrophil/lymphocyte ratio; PSM, propensity scoring match; DFS, disease-free survival; OS, overall survival.