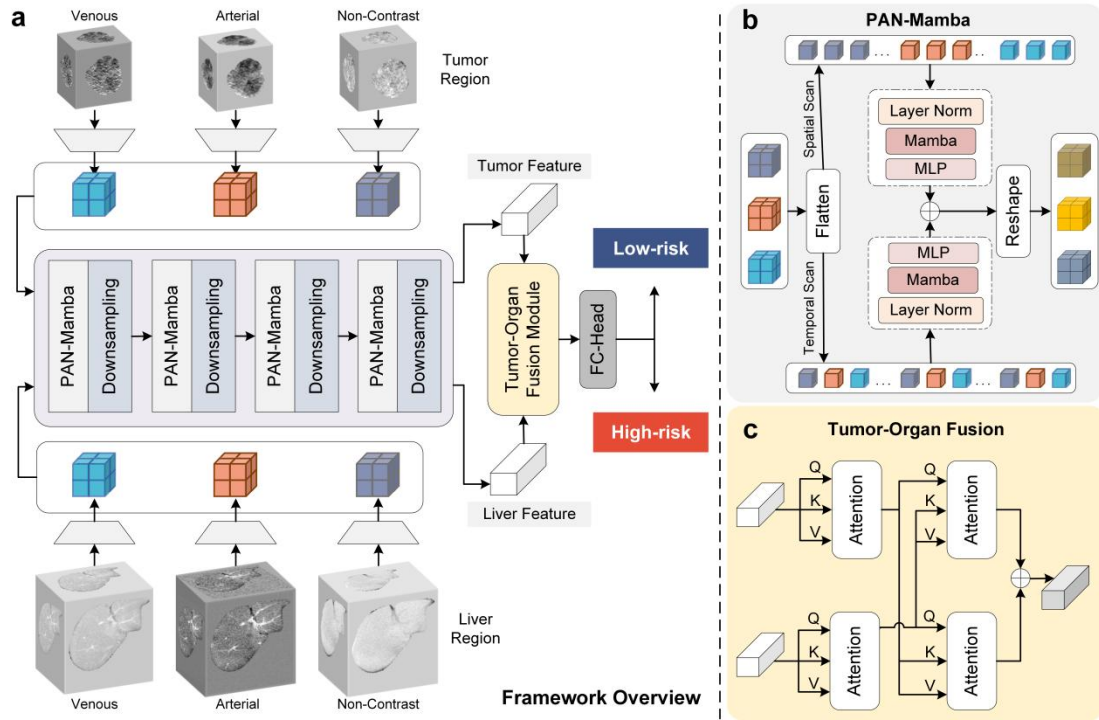
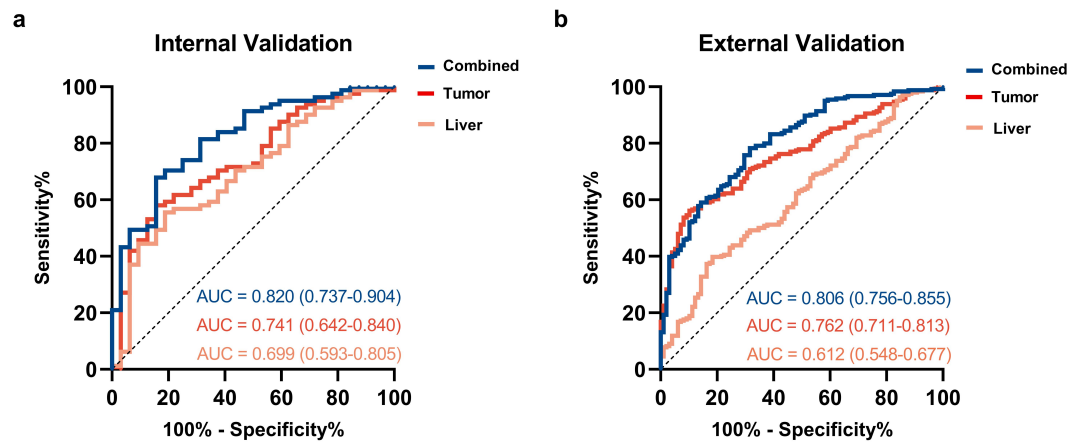




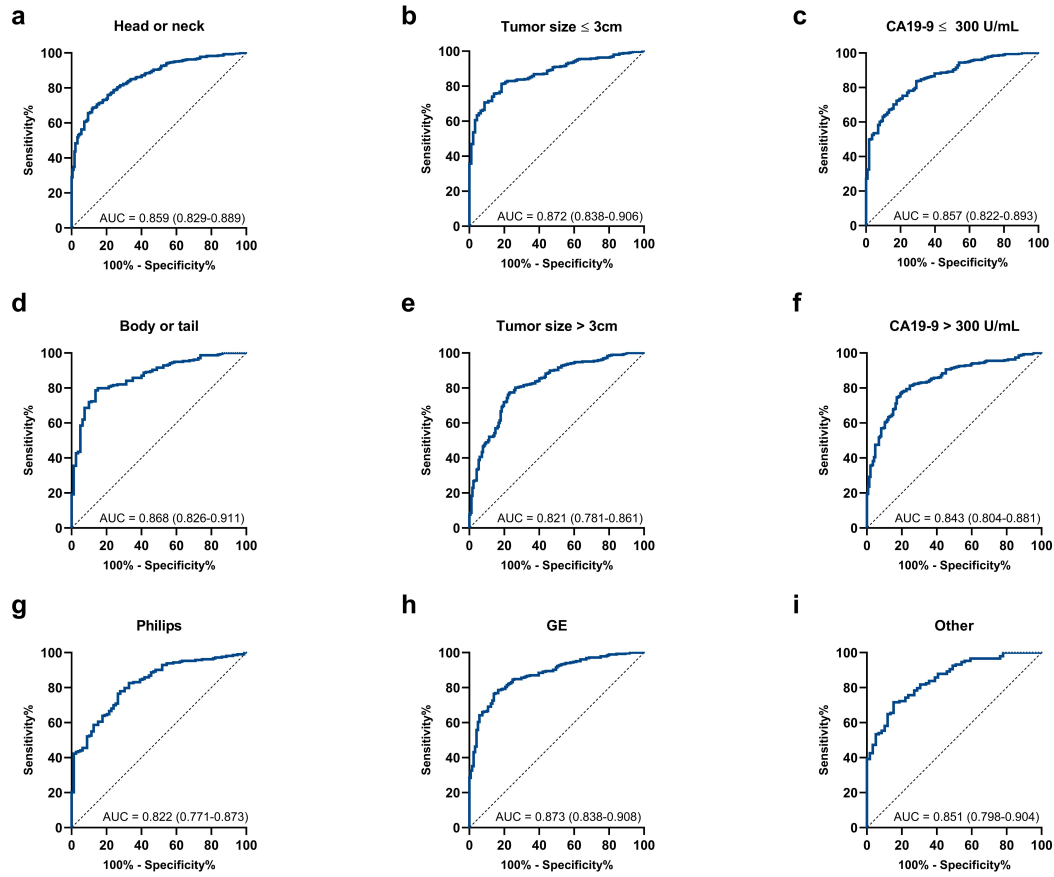
Supplementary Fig. 1 | The architecture of our proposed Mamba network. The model consists of three modules: (a) Multi-phase feature extraction; (b) PAN-Mamba modules; (c) Tumor-Organ Fusion module. Created in Microsoft Visio. Z, G. (2026).



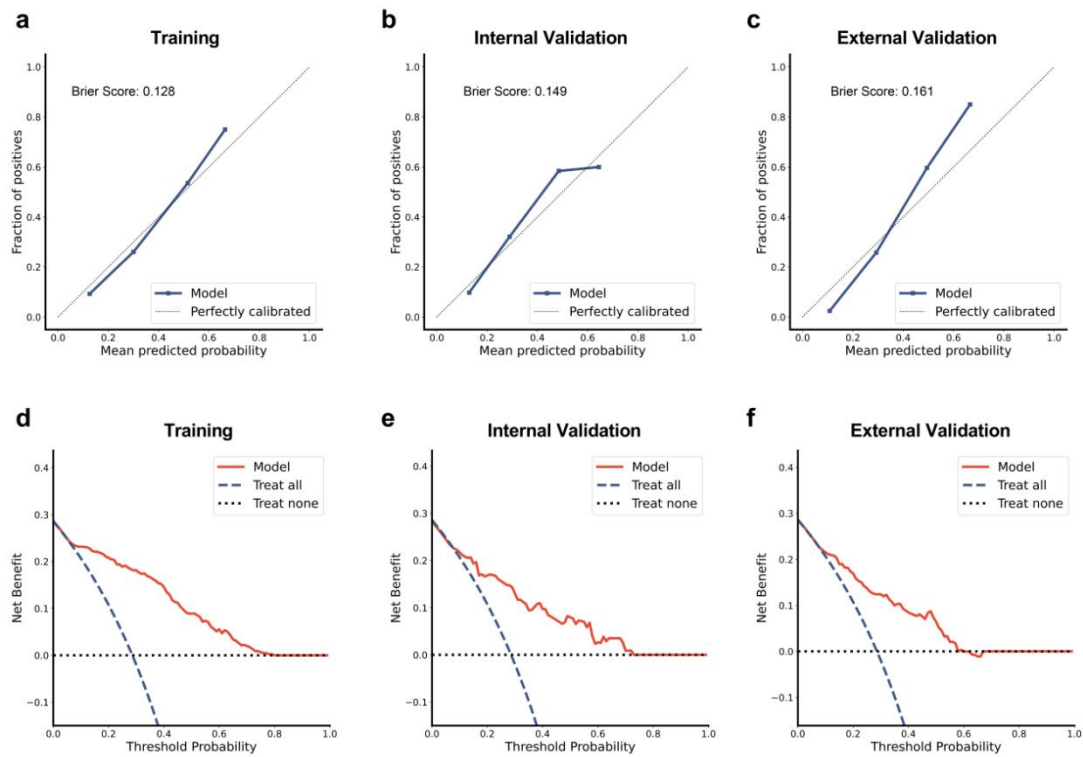
Supplementary Fig. 2 | Training loss and accuracy. Plots showing the improvement in model accuracy in the training cohort with an increase in each epoch.



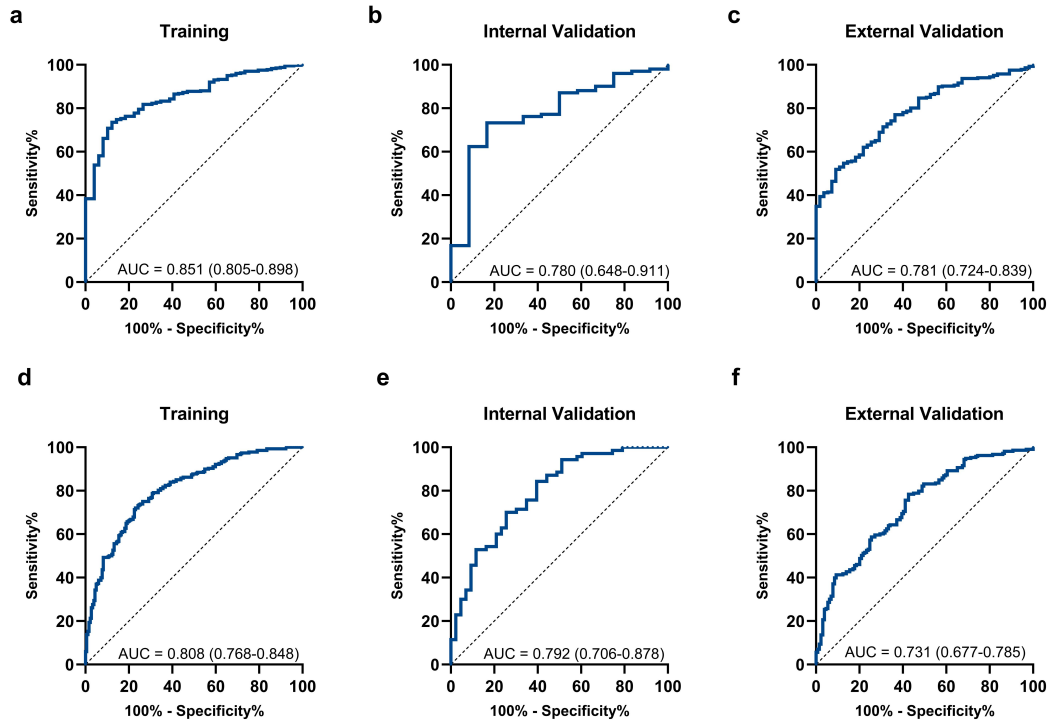
Supplementary Fig. 3 | Ablation analyses comparing tumor-only, liver-only, and combined models. Receiver operating characteristic curves in internal validation (n = 113; a) and external validation cohort (n = 342; b). Values in parentheses represent 95% CIs for the AUC.



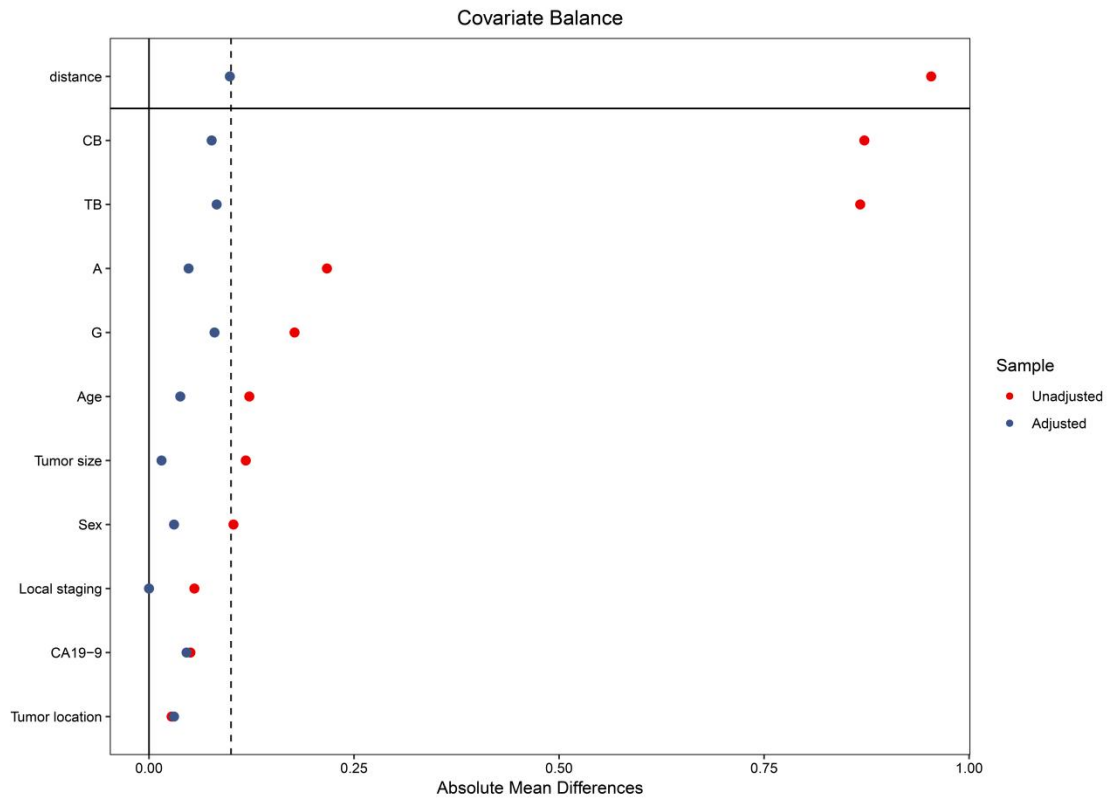
Supplementary Fig. 4 | The performance of Mamba-based model to predict the early liver metastases in different subgroups. Receiver operating characteristic curves in different subgroups defined by tumor location (n = 905; a and d), tumor size (n = 905; b and e), CA19-9 levels (n = 905; c and f) and different scanner vendors (n = 905; g-i). Values in parentheses represent 95% CIs for the AUC.



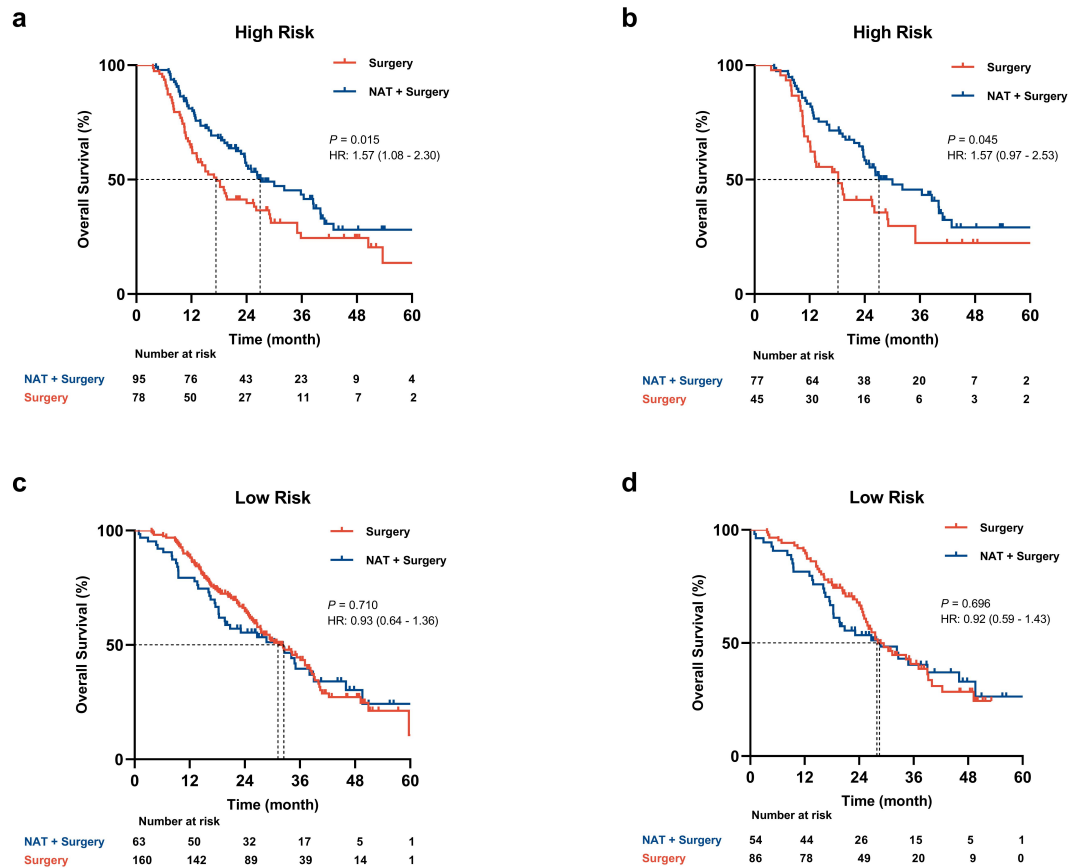
Supplementary Fig. 5 | Calibration curves and decision curve analysis. The calibration curves for the Mamba-based model in the training and validation cohorts ($n = 905$; a-c). The decision curve analysis for the Mamba-based model in the training and validation cohorts ($n = 905$; d-f).



Supplementary Fig. 6 | The performance of Mamba-based model to predict the liver metastases development in shorter-term and longer-term. (a-c) Predictive performance for short-term liver metastases (≤ 3 months; $n = 116$). (d-f) Predictive performance for longer-term liver metastases (≤ 12 months; $n = 354$). Values in parentheses represent 95% CIs for the AUC.



Supplementary Fig. 7 | Covariate balance before and after propensity score matching. Absolute standardized mean differences for clinical variables comparing patients who received NAT followed by surgery versus those who underwent upfront surgery, before matching (NAT + surgery: n = 158; upfront surgery: n = 238) and after matching (NAT + surgery: n = 131; upfront surgery: n = 131). NAT, neoadjuvant therapy.



Supplementary Fig. 8 | Sensitivity analysis of Mamba-based model predicts benefit from neoadjuvant chemotherapy. Kaplan-Meier curves of landmark OS for patients who received or did not receive NAT in different risk groups stratified by the model. The findings in the total cohort ($n = 396$; a, c) versus the results in the cohort after propensity score matching ($n = 262$; b, d). Survival differences were analyzed using the log-rank test, statistical significance was determined using two-sided tests; OS, overall survival; NAT, neoadjuvant therapy.

Supplementary Table 1 | The clinicopathological characteristics of patients in training and validation cohorts

Characteristics	Training cohort			Internal validation cohort			External validation cohort		
	ELM (-)	ELM (+)	p value	ELM (-)	ELM (+)	p value	ELM (-)	ELM (+)	p value
	(n = 321)	(n = 129)		(n = 81)	(n = 32)		(n = 244)	(n = 98)	
Sex			0.815			0.999			0.126
Female	125 (38.9)	48 (37.2)		34 (42.0)	14 (43.8)		111 (45.5)	35 (35.7)	
Male	196 (61.1)	81 (62.8)		47 (58.0)	18 (56.2)		133 (54.5)	63 (64.3)	
Age (years)			0.024			0.746			0.960
≤ 65	146 (45.5)	43 (33.3)		36 (44.4)	16 (50.0)		127 (52.0)	52 (53.1)	
> 65	175 (54.5)	86 (66.7)		45 (55.6)	16 (50.0)		117 (48.0)	46 (46.9)	
Tumor location			0.999			0.999			0.005
Head or neck	220 (68.5)	88 (68.2)		57 (70.4)	22 (68.8)		130 (53.3)	69 (70.4)	
Body or tail	101 (31.5)	41 (31.8)		24 (29.6)	10 (31.2)		114 (46.7)	29 (29.6)	
Local staging			0.001			0.368			0.908
Resectable	290 (90.3)	102 (79.1)		69 (85.2)	25 (78.1)		213 (87.3)	86 (87.8)	
Borderline resectable	31 (9.7)	27 (20.9)		12 (14.8)	7 (21.9)		31 (12.7)	12 (12.2)	
Tumor size (cm)			2.00×10^{-6}			0.485			0.011
≤ 3	184 (57.3)	41 (31.8)		38 (46.9)	12 (37.5)		136 (55.7)	39 (39.8)	
> 3	137 (42.7)	88 (68.2)		43 (53.1)	20 (62.5)		108 (44.3)	59 (60.2)	
CA19-9 (U/mL)			0.016			0.068			0.012
≤ 300	196 (61.1)	62 (48.1)		50 (61.7)	13 (40.6)		133 (54.5)	38 (38.8)	
> 300	125 (38.9)	67 (51.9)		31 (38.3)	19 (59.4)		111 (45.5)	60 (61.2)	
Differentiation			5.26×10^{-4}			0.069			4.30×10^{-5}
Well	189 (58.9)	52 (40.3)		45 (55.6)	11 (34.4)		131 (53.7)	28 (28.6)	
Poor	132 (41.1)	77 (59.7)		36 (44.4)	21 (65.6)		113 (46.3)	70 (71.4)	
Nerve infiltration	261 (81.3)	104 (80.6)	0.972	62 (76.5)	23 (71.9)	0.783	193 (79.1)	85 (86.7)	0.138
Lymphovascular invasion	88 (27.4)	45 (34.9)	0.145	25 (30.9)	9 (28.1)	0.953	65 (26.6)	47 (48.0)	2.41×10^{-4}
Resection margin			0.453			0.318			0.002
R0	304 (94.7)	125 (96.9)		79 (97.5)	30 (93.8)		236 (96.7)	85 (86.7)	
R1	17 (5.3)	4 (3.1)		2 (2.5)	2 (6.2)		8 (3.3)	13 (13.3)	
LNM	105 (32.7)	50 (38.8)	0.266	29 (35.8)	14 (43.8)	0.569	95 (38.9)	59 (60.2)	0.001

Except where indicated, data are numbers of patients, with percentages in parentheses. Categorical variables were compared using the chi-square (χ^2) test; Fisher's exact test was applied when expected cell counts were < 5. Statistical significance was determined using two-sided tests; ELM, early liver metastases, CA19-9, carbohydrate antigen 19-9, R0, negative surgical margin, R1, positive surgical margin, LNM, Lymph node metastases.

Supplementary Table 2 | Univariable and multivariable Cox regression analysis of progression-free survival and overall survival of patients with upfront surgery

Characteristics	PFS				OS			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
ELM (Low risk vs High risk)	1.93 (1.67, 2.23)	3.64×10^{-19}	1.93 (1.67, 2.25)	4.24×10^{-18}	1.96 (1.67, 2.30)	2.49×10^{-16}	1.89 (1.61, 2.23)	3.04×10^{-14}
Sex (Female vs Male)	1.09 (0.94, 1.25)	0.249			1.19 (1.01, 1.39)	0.040	1.20 (1.02, 1.41)	0.030
Age (years, ≤ 65 vs > 65)	1.13 (0.99, 1.31)	0.076	1.16 (1.01, 1.34)	0.039	1.28 (1.09, 1.50)	0.002	1.34 (1.14, 1.57)	3.00×10^{-4}
Tumor location (Head or neck vs Body or tail)	0.86 (0.74, 0.99)	0.041	0.78 (0.66, 0.91)	0.001	0.78 (0.60, 0.92)	0.004	0.73 (0.61, 0.87)	4.00×10^{-4}
Local staging (Resectable vs Borderline resectable)	1.65 (1.36, 2.02)	6.88×10^{-7}	1.54 (1.25, 1.89)	3.61×10^{-5}	1.64 (1.32, 2.05)	9.07×10^{-6}	1.57 (1.25, 1.97)	1.00×10^{-4}
Tumor size (cm, ≤ 3 vs > 3)	1.64 (1.42, 1.89)	5.59×10^{-12}	1.33 (1.14, 1.55)	2.00×10^{-4}	1.48 (1.27, 1.74)	1.10×10^{-6}	1.25 (1.05, 1.48)	0.012
CA19-9 (U/mL, ≤ 300 vs > 300)	1.40 (1.22, 1.61)	2.44×10^{-6}	1.26 (1.09, 1.45)	0.002	1.31 (1.11, 1.53)	0.001	1.16 (0.98, 1.35)	0.096
Differentiation (Well vs Poor)	1.38 (1.20, 1.59)	6.06×10^{-6}	1.33 (1.15, 1.54)	1.00×10^{-4}	1.42 (1.21, 1.66)	1.70×10^{-5}	1.30 (1.10, 1.53)	0.002
Nerve infiltration	1.18 (0.99, 1.41)	0.065	1.00 (0.83, 1.21)	0.980	1.05 (0.87, 1.28)	0.612		
Lymphovascular invasion	1.49 (1.28, 1.74)	2.11×10^{-7}	1.35 (1.15, 1.60)	3.00×10^{-4}	1.36 (1.15, 1.62)	4.00×10^{-4}	1.19 (0.99, 1.43)	0.063
Resection margin	1.46 (1.07, 1.99)	0.018	1.17 (0.85, 1.60)	0.336	1.29 (0.91, 1.81)	0.149		
TNM ($\leq$ IIa vs $\geq$ IIb)	1.36 (1.18, 1.57)	2.41×10^{-5}	1.13 (0.97, 1.32)	0.120	1.48 (1.26, 1.74)	1.48×10^{-6}	1.27 (1.07, 1.51)	0.006

Univariate and multivariate Cox regression analyses were performed. Statistical significance was determined using two-sided tests; PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; ELM, early liver metastases; CA19-9, carbohydrate antigen 199.

Supplementary Table 3 | The clinical heterogeneity between the development and NAT+surgery cohorts

Characteristics	Training cohort (n = 450)	NAT + Surgery cohort (n = 158)	p value
Age (years)			0.015
≤ 65	189 (42.0)	97 (61.4)	
> 65	261 (58.0)	61 (38.6)	
Sex			0.010
Female	173 (38.4)	80 (50.6)	
Male	277 (61.6)	78 (49.4)	
Tumor location			0.005
Head or neck	308 (68.4)	88 (55.7)	
Body or tail	142 (31.6)	70 (44.3)	
Local staging			0.068
Resectable	392 (87.1)	130 (82.3)	
Borderline resectable	58 (12.9)	28 (17.7)	
Tumor size (cm)			0.020
≤ 3	225 (50.0)	62 (39.2)	
> 3	225 (50.0)	96 (60.8)	
CA19-9 (U/mL)			0.040
≤ 300	258 (57.3)	75 (47.5)	
> 300	192 (42.7)	83 (52.5)	

Except where indicated, data are numbers of patients, with percentages in parentheses. Categorical variables were compared using the chi-square (χ^2) test. Statistical significance was determined using two-sided tests; NAT, neoadjuvant therapy; CA19-9, carbohydrate antigen 19-9.

Supplementary Table 4 | The baseline preoperative clinical characteristics based on surgical approach, before and after propensity score matching

Characteristics	Total cohort			Propensity score matched cohort		
	NAT + Surgery (n = 158)	Upfront surgery (n = 238)	p value	NAT + Surgery (n = 131)	Upfront surgery (n = 131)	p value
Age (years)						
≤ 65	97 (61.4)	117 (49.2)	0.022	72 (55.0)	77 (58.8)	0.618
> 65	61 (38.6)	121 (50.8)		59 (45.0)	54 (41.2)	
Sex						
Female	80 (50.6)	96 (40.3)	0.055	67 (51.1)	63 (48.1)	0.711
Male	78 (49.4)	142 (59.7)		64 (48.9)	68 (51.9)	
Tumor location						
Head or neck	88 (55.7)	126 (52.9)	0.663	69 (52.7)	73 (55.7)	0.710
Body or tail	70 (44.3)	112 (47.1)		62 (47.3)	58 (44.3)	
Local staging						
Resectable	130 (82.3)	209 (87.8)	0.164	112 (85.5)	112 (85.5)	0.999
Borderline resectable	28 (17.7)	29 (12.2)		19 (14.5)	19 (14.5)	
Total bilirubin (μmol/L) ^b	13.05 (9.00, 21.30)	15.10 (10.00, 61.60)	0.004	13.20 (9.10, 20.83)	12.30 (9.13, 21.83)	0.530
Direct bilirubin (μmol/L) ^b	4.95 (3.50, 10.10)	5.60 (3.90, 47.50)	0.007	5.10 (3.53, 9.50)	4.60 (3.50, 8.43)	0.564
Albumin (g/L) ^b	42.45 (38.30, 45.50)	43.95 (40.40, 46.40)	0.008	42.70 (38.48, 46.10)	43.30 (40.03, 46.00)	0.682
Globulin (g/L) ^b	25.40 (23.00, 27.60)	26.20 (23.80, 28.50)	0.026	25.40 (23.20, 27.83)	25.60 (23.53, 28.10)	0.533
Tumor size (cm)						
≤ 3	62 (39.2)	126 (52.9)	0.010	57 (43.5)	59 (45.0)	0.901
> 3	96 (60.8)	112 (47.1)		74 (56.5)	72 (55.0)	
CA19-9 (U/mL)						
≤ 300	75 (47.5)	125 (52.5)	0.378	64 (48.9)	70 (53.4)	0.537
> 300	83 (52.5)	113 (47.5)		67 (51.1)	61 (46.6)	

Except where indicated, data are numbers of patients, with percentages in parentheses. Categorical variables were compared using the chi-square (χ^2) test, continuous variables were compared using the Mann-Whitney U test. Statistical significance was determined using two-sided tests; NAT, neoadjuvant therapy; CA19-9, carbohydrate antigen 19-9; ^a mean ± standard deviation, ^b medians (interquartile range).

Supplementary Table 5 | The clinicopathological characteristics between patients undergoing radiotranscriptomic analysis and the overall cohort

Characteristics	Total cohort (n = 342)	Radiotranscriptomic cohort (n = 62)	p value
Age (years) ^a	64.79 ± 9.35	63.15 ± 9.50	0.204
Sex			0.405
Female	146 (42.7)	30 (48.4)	
Male	196 (57.3)	32 (51.6)	
Tumor location			0.623
Head or neck	199 (58.2)	34 (54.8)	
Body or tail	143 (41.8)	28 (45.2)	
Tumor size (cm) ^b	3.00 (2.40, 3.70)	3.05 (2.60, 3.70)	0.412
CA19-9 (U/mL)			0.640
≤ 300	171 (50.0)	29 (46.8)	
> 300	171 (50.0)	33 (53.2)	
Total bilirubin (μmol/L) ^b	15.00 (9.70, 84.20)	14.70 (8.40, 56.50)	0.320
Direct bilirubin (μmol/L) ^b	5.50 (3.80, 68.80)	5.35 (3.40, 42.50)	0.350
Albumin (g/L) ^b	43.30 (39.72, 46.10)	43.85 (39.90, 46.40)	0.769
Globulin (g/L) ^b	25.80 (23.60, 28.20)	25.60 (23.50, 27.80)	0.534
Differentiation			0.967
Well	159 (46.5)	29 (46.8)	
Poor	183 (53.5)	33 (53.2)	
T stage			0.549
T1	80 (23.4)	11 (17.7)	
T2	213 (62.3)	40 (64.5)	
T3 or T4	49 (14.3)	11 (17.7)	
TNM stage			0.470
≤ IIa	188 (55.0)	31 (50.0)	
≥ IIb	154 (45.0)	31 (50.0)	
Nerve infiltration	278 (81.3)	51 (82.3)	0.856
Lymphovascular invasion	112 (32.7)	15 (24.2)	0.182
Resection margin			0.228
R0	321 (93.9)	55 (88.7)	
R1	21 (6.1)	7 (11.3)	
LNM	154 (45.0)	31 (50.0)	0.470

Except where indicated, data are numbers of patients, with percentages in parentheses. Categorical variables were compared using the chi-square (χ^2) test, continuous variables were compared using the Mann-Whitney U test or Student's t test. Statistical significance was determined using two-sided tests; CA19-9, carbohydrate antigen 19-9; R0, negative surgical margin; R1, positive surgical margin; LNM, lymph node metastases. ^a mean ± standard deviation, ^b medians (interquartile range).