Supplementary Table 1 Baseline characteristics of CA 19-9 false negative and true negative groups

variables	CA19-9 positive A		CA19-9 false negative B		p value*	CA19-9 true negative C		p value+
	n=219		n=35			n=17		
Age (years)								
<65	133	60.7%	23	65.7%	0.574	11		0.746
≥65	86	39.3%	12	34.3%		6		
Sex								
Male	147	67.1%	20	57.1%	0.248	11		0.838
Female	72	32.9%	15	42.9%		6		
ECOG								
0-1	171	78.1%	30	85.7%	0.302	15		0.537
≥2	48	21.9%	5	14.3%		2		
Stage								
locally advanced	15	6.8%	4	11.4%	0.310	3	17.6%	0.129
metastatic	204	93.2%	31	88.6%		14	82.4%	
Differntiation								
Well to moderately	142	64.8%	27	77.1%	0.152	8	47.1%	0.142
Poorly	77	35.2%	8	22.9%		9	52.9%	
Biliary stent								
yes	28	12.8%	2	5.7%	0.395	0	0.0%	0.234
no	191	87.2%	33	94.3%		17	100.0%	
Chemotherapy								

	A		B		P value*	C		P value+
Gemcitabine	72	32.9%	11	31.4%	0.953	3	17.6%	0.487
Gemcitabine/Elrotinib	87	39.7%	16	45.7%		7	41.2%	
Gemcitabine/Nab-paclitaxel	31	14.2%	4	11.4%		4	23.5%	
Gemcitabine/Fluoropyridimine	24	11.0%	3	8.6%		3	17.6%	
FOLFIRINOX	5	2.3%	1	2.9%		0	0.0%	
No. of metastatic sites								
0-2	180	82.2%	34	97.1%	**0.023**	15	88.2%	0.744
3-	39	17.8%	1	2.9%		2	11.8%	
Liver metastasis								
yes	106	48.4%	11	31.4%	0.061	5	41.7%	0.131
no	113	51.6%	24	68.6%		12	70.6%	
pretreatment NLR								
< 2.60	97	44.3%	26	74.3%	**0.001**	7	41.2%	0.803
≥ 2.60	122	55.7%	9	25.7%		10	58.8%	
post-treatment NLR								
< 2.62	106	48.4%	27	77.1%	**0.002**	10	58.8%	0.408
≥ 2.62	113	51.6%	8	22.9%		7	41.2%	
CA 19-9　(U/ml)								
≤ 37	0		35	100.0%		17	100.0%	
> 37	219		0	0.0%		0	0.0%	
CEA (ng/ml)								
≤ 5	133	60.7%	28	80.0%	**0.028**	14	82.4%	0.117
> 5	86	39.3%	7	20.0%		3	17.6%	

*P value from Chi-square test or Fisher's exact test for categorical variables, A and B
+P value from Chi-square test or Fisher's exact test for categorical variables, A and C

Supplementary Table 2 Baseline characteristics according to pre-treatment NLR

	NLR <2.60		NLR ≥ 2.60		pre-treatment NLR
	n=130		n=141		p value*
Age (years)					
<65	81	62.3%	86	61.0%	0.824
≥65	49	37.7%	55	39.0%	
Sex					
Male	81	62.3%	97	68.8%	0.261
Female	49	37.7%	44	31.2%	
ECOG					
0-1	108	83.1%	108	76.6%	0.185
≥2	22	16.9%	33	23.4%	
Stage					
locally advanced	11	8.5%	11	7.8%	0.842
metastatic	119	91.5%	130	92.2%	
Differntiation					
Well to moderately	93	71.5%	84	59.6%	**0.039**
Poorly	37	28.5%	57	40.4%	
Biliary stent					
yes	12	9.2%	18	12.8%	0.354
no	118	90.8%	123	87.2%	
Chemotherapy					
Gemcitabine single	38	29.2%	48	34.0%	0.395

Others	92	70.8%	93	66.0%	
No. of metastatic sites					
0-2	115	88.5%	114	80.9%	0.084
3-	15	11.5%	27	19.1%	
post-treatment NLR					
< 2.62	95	73.1%	47	33.3%	**< 0.001**
≥ 2.62	35	26.9%	94	66.7%	
CA 19-9 (U/ml)					
≤ 37	43	33.1%	19	13.5%	**< 0.001**
> 37	87	66.9%	122	86.5%	
CEA (ng/ml)					
≤ 5	91	70.0%	85	60.3%	0.094
> 5	39	30.0%	56	39.7%	

*P value from Chi-square test or Fisher's exact test for categorical variables.

Supplementary Table 3 The association of the first response evaluation and CA 19-9 response (A), the first response evaluation and post-treatment NLR (B)

A.

	Decline of CA 19-9 < 18%		*Decline of CA 19-9 ≥18%*		
	n = 114		n = 105		
	n	%	n	%	*p* value*
1st Response					0.001
CR/PR	9	7.9%	45	42.9%	
SD	42	36.8%	50	47.6%	
PD	63	55.3%	10	9.5%	

*P value from linear-by-linear association test

CR ; complete response, PR ; partial response, SD ; stable disease, PD ; progressive disease

B.

	Post-treatment NLR < 2.62		*Post-treatment NLR ≥2.62*		
	n = 143		n = 128		
	n	%	n	%	*p* value*
1st Response					0.001
CR/PR	47	32.9%	18	14.1%	
SD	75	52.4%	46	35.9%	
PD	21	14.7%	64	50.0%	

*P value from linear-by-linear association test

CR ; complete response, PR ; partial response, SD ; stable disease, PD ; progressive disease

Supplementary Figure 1 ROC curves of the prognostic factors(pre- and post- treatment NLR, CA 19-9 decline) and 1-year survival.

A. ROC curve of Pre-treatment NLR and 1year survival, and optimal cutpoint to maximize youden index.
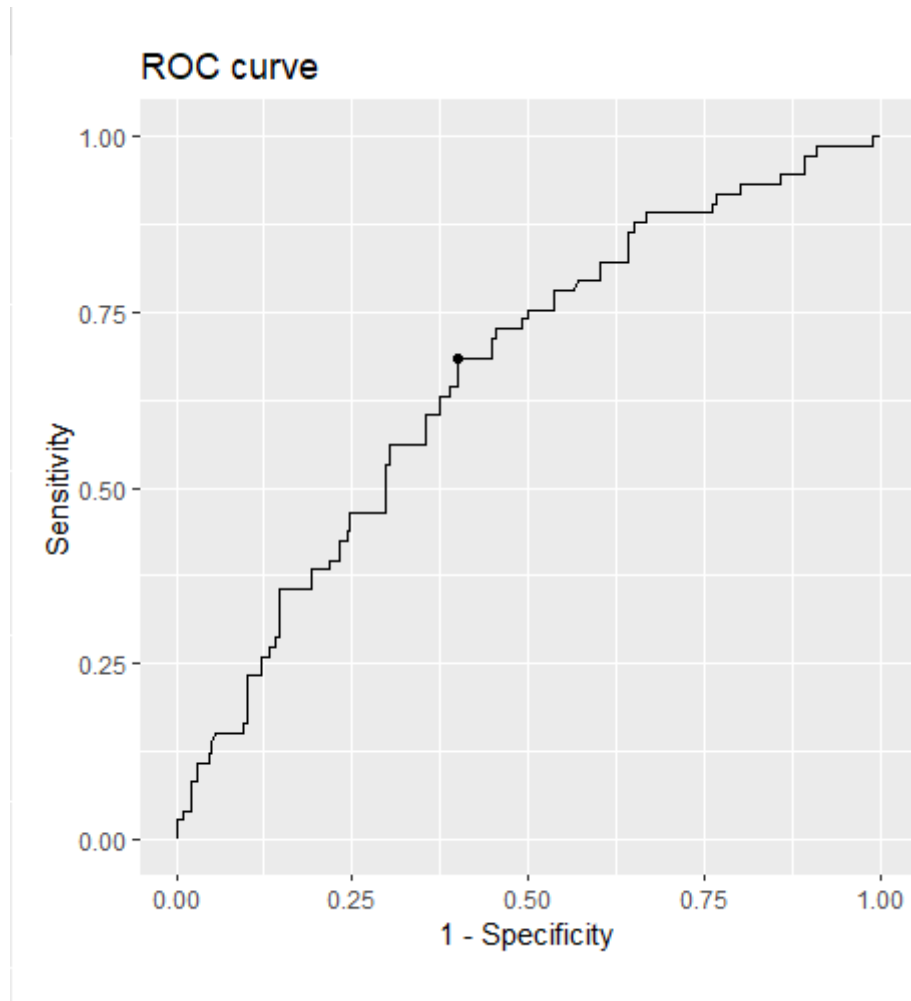
AUC ; 0.66

optimal cutpoint ; 2.60

youden ; 0.285942

outcome ; 1 year survival

sensitivity ;   68.5%

specificity ;   60.1%

B. ROC curve of Post-treatment NLR and 1year survival, and optimal cutpoint to maximize youden index.
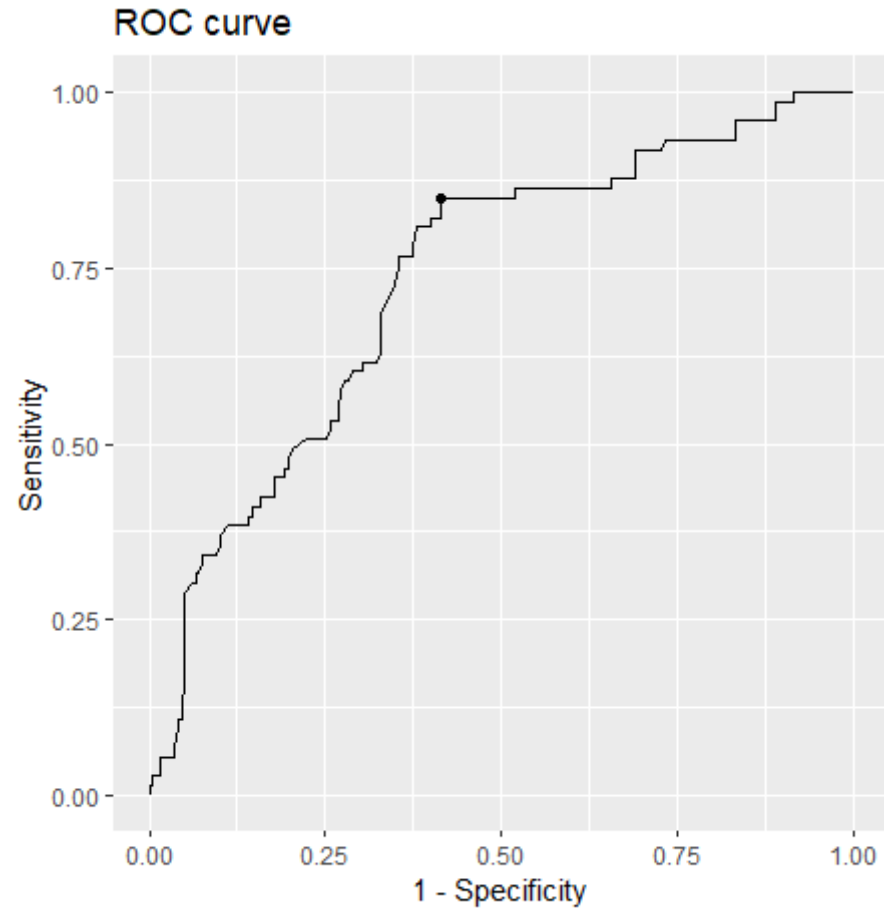
AUC ; 0.73

optimal cutpoint ; 2.62

youden ; 0.435174

outcome ; 1 year survival

sensitivity ;   84.9%

specificity ;   58.6%

ROC curve

C. ROC curve of decline of CA 19-9 and 1-year survival, and optimal cutpoint to maximize youden index.
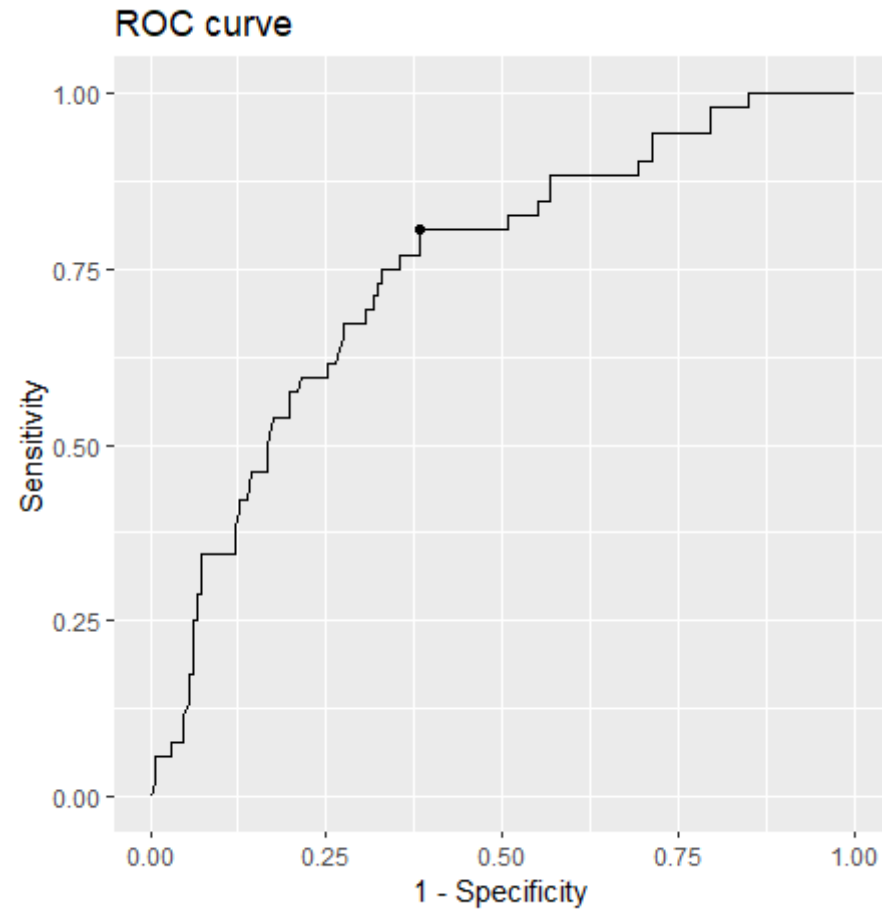
AUC ; 0.75

optimal cutpoint ; -18%

youden ; 0.424459

outcome ; 1-year survival

sensitivity ;　80.8%

specificity ;　61.7%

ROC curve

cutpointr package in R 3.5.3 was used to identify optimal cutting points for each marker.