

Combined Features Based on Preoperative Controlling Nutritional Status Score and Circulating Tumour Cell Status Predict Prognosis for Colorectal Cancer Patients Treated with Curative Resection

Chaogang Yang^{1,2,3*}, Chen Wei^{1,2,3*}, Shuyi Wang^{1,2,3*}, Song Han⁴, Dongdong Shi^{1,2,3}, Chunxiao Zhang^{1,2,3}, Xiaobin Lin^{1,2,3}, Rongzhang Dou^{1,2,3}, Bin Xiong^{1,2,3}

1. Department of Gastrointestinal Surgery & Department of Gastric and Colorectal Surgical Oncology, Zhongnan Hospital of Wuhan University, Wuhan 430071, China;
2. Hubei Key Laboratory of Tumor Biological Behaviors, Wuhan 430071, China;
3. Hubei Cancer Clinical Study Center, Wuhan 430071, China;
4. Department of Circulating Tumor Cells, YZY Medical Technological company, Wuhan 430075, China.

*These authors contributed equally to this work.

Corresponding author: Dr. Bin Xiong, MD. Email: binxiong1961@whu.edu.cn; Tel.:+862767813152

Table S1. The demographics and clinicopathological characteristics of 160 CRC patients

Items	Value
Age (Mean \pm SD, years)	58.4 \pm 11.8
Gender [n (%)]	
Male	90 (56.3)
Female	70 (43.7)
BMI (kg/m ²)	
<18.5	69 (43.1)
\geq 18.5, <25.0	70 (43.8)
\geq 25.0	21 (13.1)
Tumour location	
Colon	93 (58.1)
Rectal	67 (41.9)
Tumour size (cm)	
<3	91 (56.9)
\geq 3	69 (43.1)
Histopathological type	
Well	38 (23.8)
Moderate	55 (34.4)
Poor	67 (41.8)
Depth of tumour invasion	
T1	4 (2.5)
T2	20 (12.5)
T3	62 (38.8)
T4	74 (46.2)
Lymph node metastasis	
N0	52 (32.5)
N1	53 (33.1)
N2	34 (21.3)
N3	21 (13.1)
pTNM stage	
I	13 (8.1)
II	78 (48.8)
III	69 (43.1)
Lymphatic vessel invasion	
Negative	96 (60.0)
Positive	64 (40.0)
Nerve invasion	
Negative	98 (61.2)
Positive	62 (38.8)
Severe complication	
Absence	136 (85.0)
Presence	24 (15.0)
Adjuvant chemotherapy	
No	78 (48.8)
Yes	82 (51.2)
Preoperative CEA (ng/ml)	
<5	111 (69.4)
\geq 5	49 (30.6)
Preoperative CA125 (U/ml)	
<35	123 (76.9)
\geq 35	37 (23.1)
Preoperative CA199 (U/ml)	
<37	115 (71.9)
\geq 37	45 (28.1)
Preoperative CONUT score	
Low	86 (53.8)
High	74 (46.2)
Preoperative CTC	
Negative	43 (26.9)
Positive	117 (73.1)
Preoperative CONUT-CTC score	
0	34 (21.3)
1	61 (38.1)
2	65 (40.6)

Notes: CRC, colorectal cancer; BMI, body mass index; TNM, tumour-node-metastasis; CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CA199; carbohydrate antigen 199; CONUT, controlling nutritional status; CTC, circulating tumour cell.

Table S2. Analyses of factors regarding recurrence-free survival of CRC patients

Variables	No.	No. of recurrence (%)	Median RFS (Range)	χ^2 value	<i>P</i> value
Gender				0.261	0.609
Male	90	40 (44.4)	31.3 (28.9-33.7)		
Female	70	28 (40.0)	31.9 (29.3-34.4)		
Age (years)				2.184	0.139
<60	83	41 (49.4)	30.6 (28.2-33.0)		
≥60	77	27 (35.1)	33.2 (30.6-35.8)		
BMI (kg/m ²)				2.920	0.232
<18.5	69	35 (50.7)	30.4 (27.8-33.1)		
≥18.5, <25.0	70	22 (31.4)	33.7 (31.0-36.4)		
≥25.0	21	11 (52.4)	30.3 (25.9-34.6)		
Tumour location				1.840	0.175
Colon	93	35 (37.6)	32.8 (30.4-35.1)		
Rectal	67	33 (49.3)	30.4 (27.8-33.1)		
Tumour size (cm)				0.170	0.680
<3	91	38 (41.8)	32.1 (29.8-34.4)		
≥3	69	30 (43.5)	30.9 (28.3-33.5)		
Histopathological type				4.044	0.044*
Well-moderate	93	35 (37.6)	33.2 (31.0-35.5)		
Poor	67	33 (49.3)	29.5 (26.7-32.3)		
Depth of tumour invasion				4.927	0.026*
T1-T2	24	3 (12.5)	38.6 (33.8-40.1)		
T3-T4	136	65 (47.8)	31.0 (29.1-32.9)		
Lymph node metastasis				16.630	<0.001*
N0-1	105	33 (31.4)	34.4 (32.4-36.5)		
N2-3	55	35 (53.8)	26.9 (24.1-29.6)		
pTNM stage				28.486	<0.001*
I-II	91	23 (25.3)	36.1 (34.0-38.1)		
III	69	45 (65.2)	26.5 (24.1-28.7)		
Lymphatic vessel invasion				11.099	0.001*
Negative	96	31 (32.3)	34.3 (32.2-36.5)		
Positive	64	37 (57.8)	28.3 (25.5-31.1)		
Nerve invasion				7.980	0.005*
Negative	98	33 (33.7)	33.9 (31.7-36.0)		
Positive	62	35 (56.5)	28.8 (26.0-31.8)		
Severe complication				0.989	0.320
Absence	136	54 (39.7)	32.2 (30.2-34.1)		
Presence	24	14 (58.3)	29.8 (25.7-33.9)		
Adjuvant chemotherapy				6.542	0.011*
No	78	24 (30.8)	34.4 (31.9-36.8)		
Yes	82	44 (53.7)	29.6 (27.2-32.1)		
Preoperative CEA (ng/ml)				2.754	0.097
<5	111	43 (38.7)	32.7 (30.6-34.8)		
≥5	49	25 (51.0)	29.5 (30.0-33.5)		
Preoperative CA125 (U/ml)				2.632	0.105
<35	123	47 (38.2)	32.6 (30.5-34.6)		
≥35	37	21 (56.8)	28.4 (25.4-31.5)		
Preoperative CA199 (U/ml)				2.340	0.126
<37	115	43 (37.4)	32.6 (30.5-34.8)		
≥37	45	25 (55.6)	29.4 (26.4-32.3)		
Preoperative CONUT score				18.491	<0.001*
Low	86	24 (27.9)	35.5 (33.3-37.6)		
High	74	44 (59.5)	27.7 (25.2-30.3)		
Preoperative CTC				19.318	<0.001*
Negative	43	5 (11.6)	39.2 (37.0-41.4)		
Positive	117	63 (53.8)	29.3 (27.3-31.4)		
Preoperative CONUT-CTC score				32.850	<0.001*
0	34	4 (11.8)	39.2 (36.8-41.7)		
1	61	21 (34.4)	34.2 (31.6-36.9)		
2	65	43 (66.2)	25.7 (23.4-28.1)		
Overall	160	68 (42.5)	31.8 (30.0-33.5)	-	-

Notes: * indicates $P < 0.05$. CRC, colorectal cancer; BMI, body mass index; TNM, tumour-node-metastasis; CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CA199, carbohydrate antigen 199; CONUT, controlling nutritional status; CTC, circulating tumour cell; RFS, recurrence-free survival.

Table S3. Analyses of factors regarding cancer-specific survival of CRC patients

Variables	No.	No. of death (%)	Median CSS (Range)	χ^2 value	<i>P</i> value
Gender				0.178	0.673
Male	90	28 (31.1)	36.3 (34.7-38.0)		
Female	70	19 (27.1)	36.2 (34.4-37.9)		
Age (years)				0.331	0.565
<60	83	27 (32.5)	36.2 (34.5-37.9)		
≥60	77	20 (26.0)	36.9 (35.0-38.8)		
BMI (kg/m ²)				3.645	0.162
<18.5	69	28 (40.6)	35.3 (33.4-37.2)		
≥18.5, <25.0	70	13 (18.6)	38.1 (36.2-39.9)		
≥25.0	21	6 (28.8)	36.1 (35.3-37.8)		
Tumour location				1.610	0.204
Colon	93	23 (24.7)	37.2 (35.6-38.9)		
Rectal	67	24 (35.8)	35.7 (33.7-37.6)		
Tumour size (cm)				1.192	0.275
<3	91	24 (26.4)	37.2 (35.6-38.8)		
≥3	69	23 (33.3)	35.1 (33.2-37.0)		
Histopathological type				4.116	0.042*
Well-moderate	93	23 (24.7)	37.6 (36.0-39.1)		
Poor	67	24 (35.8)	34.9 (32.8-37.0)		
Depth of tumour invasion				2.115	0.146
T1-T2	24	3 (12.5)	38.9 (35.8-42.1)		
T3-T4	136	44 (32.4)	36.2 (34.8-37.5)		
Lymph node metastasis				14.264	<0.001*
N0-1	105	21 (20.0)	38.2 (36.8-39.7)		
N2-3	55	26 (47.3)	33.1 (31.1-35.1)		
pTNM stage				26.981	<0.001*
I-II	91	12 (13.2)	39.5 (38.2-40.8)		
III	69	35 (50.7)	32.7 (30.9-34.5)		
Lymphatic vessel invasion				14.131	<0.001*
Negative	96	17 (17.7)	38.7 (37.3-40.1)		
Positive	64	30 (46.9)	33.7 (31.7-35.8)		
Nerve invasion				6.674	0.010*
Negative	98	21 (21.4)	37.8 (36.2-39.4)		
Positive	62	26 (41.9)	34.7 (32.7-36.7)		
Severe complication				0.177	0.674
Absence	136	38 (27.9)	36.6 (35.2-38.0)		
Presence	24	9 (37.5)	35.8 (32.7-38.8)		
Adjuvant chemotherapy				10.209	0.001*
No	78	12 (15.4)	38.9 (37.3-40.5)		
Yes	82	35 (42.7)	34.7 (33.0-36.5)		
Preoperative CEA (ng/ml)				0.240	0.624
<5	111	32 (28.8)	36.7 (35.2-38.2)		
≥5	49	15 (30.6)	36.0 (33.7-38.3)		
Preoperative CA125 (U/ml)				2.615	0.106
<35	123	31 (25.2)	37.0 (35.6-38.5)		
≥35	37	16 (43.2)	34.2 (32.2-36.3)		
Preoperative CA199 (U/ml)				1.830	0.176
<37	115	29 (25.2)	37.0 (35.5-38.5)		
≥37	45	18 (40.0)	34.9 (32.9-36.9)		
Preoperative CONUT score				25.222	<0.001*
Low	86	12 (14.0)	39.4 (38.4-40.8)		
High	74	35 (47.3)	33.2 (31.2-35.1)		
Preoperative CTC				12.485	<0.001*
Negative	43	2 (4.7)	41.1 (40.0-42.3)		
Positive	117	45 (38.5)	35.2 (33.7-36.7)		
Preoperative CONUT-CTC score				32.805	<0.001*
0	34	1 (2.9)	41.5 (40.6-42.4)		
1	61	12 (19.8)	38.8 (37.2-40.3)		
2	65	34 (52.3)	31.8 (30.0-37.8)		
Overall	160	47 (29.4)	36.5 (35.3-37.8)	-	-

Notes: *indicates $P < 0.05$. CRC, colorectal cancer; BMI, body mass index; TNM, tumour-node-metastasis; CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CA199, carbohydrate antigen 199; CONUT, controlling nutritional status; CTC, circulating tumour cell; CSS: cancer-specific survival.

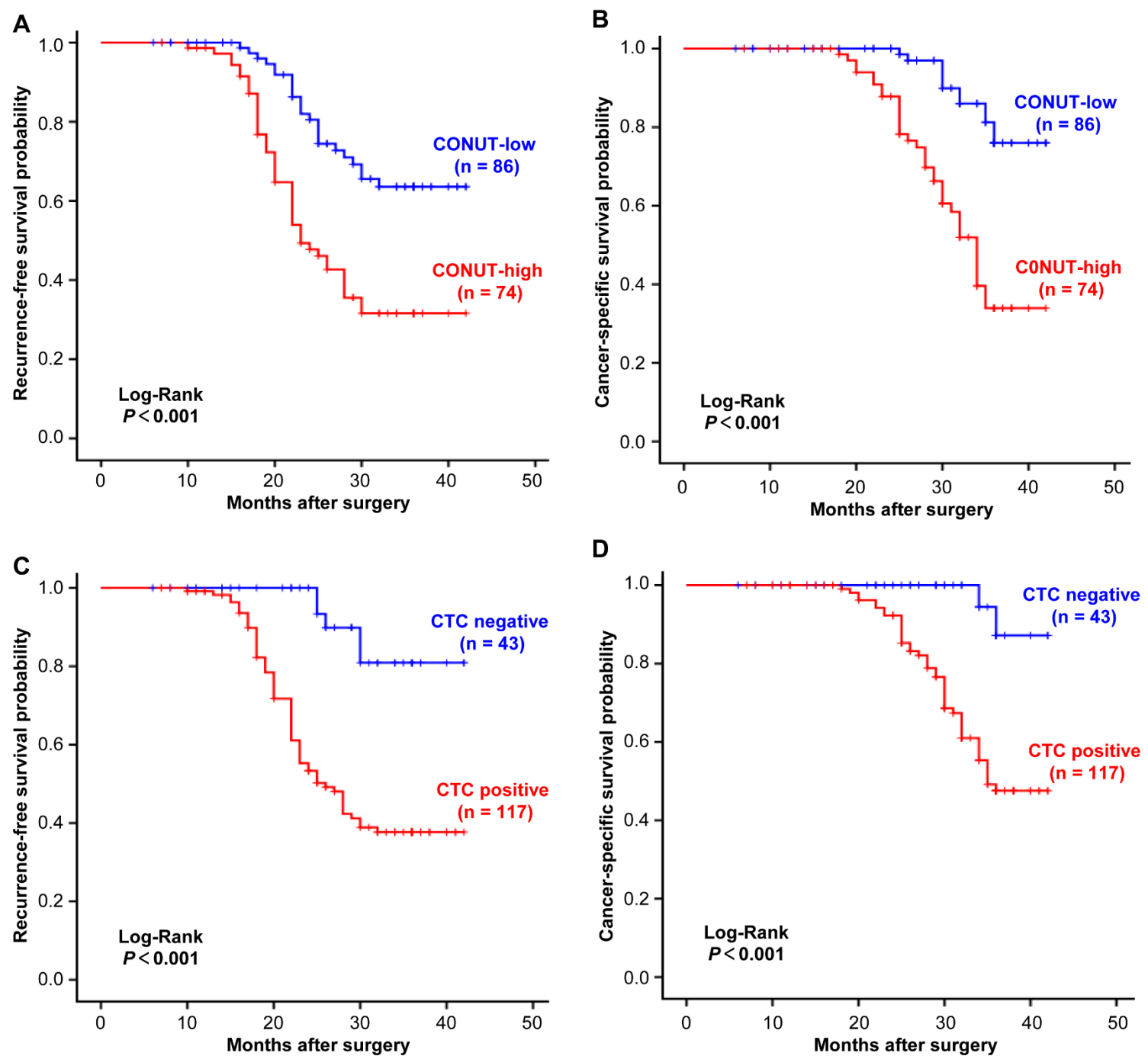


Figure S1. Kaplan-Meier curves for CRC patients in the different preoperative CONUT score or CTC status groups. A-B. Recurrence-free survival and cancer-specific survival in preoperative CONUT-low and-high score groups, respectively. C-D. Recurrence-free survival and cancer-specific survival in preoperative CTC negative and positive groups, respectively. Abbreviation: CRC, colorectal cancer; CONUT, controlling nutritional status; CTC, circulating tumour cell.