

Supplementary Online Content

Konishi T, Shimada Y, Hsu M, et al. Association of preoperative and postoperative serum carcinoembryonic antigen and colon cancer outcome. *JAMA Oncol*. Published online December 21, 2017. doi:10.1001/jamaoncol.2017.4420

eTable 1. Patient and Tumor Characteristics

eTable 2. Univariate and Multivariate Analyses of Recurrence Free Survival

eTable 3. Analysis of Sites of Metastatic Recurrence in Relation to CEA Status

eFigure 1. Kaplan-Meier Curves for RFS in Patients With Normal Preoperative, Normalized Postoperative, or Elevated Postoperative CEA Using a Cutoff of 10 ng/mL

eFigure 2. Kaplan-Meier Curves for RFS in Patients With Normal Preoperative, Normalized Postoperative, or Elevated Postoperative CEA, Grouped by TNM Disease Stage

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Patient and tumor characteristics.

Characteristic	All (N=914)	Normal Preoperative CEA (N=715)	Normalized Postoperative CEA (N=142)	Elevated Postoperative CEA (N=57)
Gender, no. (%) of patients				
Male	461 (50.4)	366 (51.2)	68 (47.9)	27 (47.4)
Female	453 (49.6)	349 (48.8)	74 (52.1)	30 (52.6)
Age, years				
Median (IQR)	64 (53-75)	64.0 (52.5, 74.0)	63.0 (54.0, 74.0)	74.0 (60.0, 81.0)
Mean (SD)	63.4 (13.6)	62.9 (13.6)	63.5 (13.4)	70.6 (12.3)
BMI				
Median (IQR)	28.2 (24.7-32.3)	28.4 (24.9, 32.3)	28.3 (24.6, 32.1)	25.2 (23.3, 32.0)
Mean (SD)	28.9 (6.0)	29.0 (6.0)	29.0 (6.2)	27.1 (6.0)
Primary site, no. (%) of patients				
Cecum	158 (17.3)	116 (16.2)	21 (14.8)	21 (36.8)
Ascending	203 (22.2)	164 (22.9)	26 (18.3)	13 (22.8)
Transverse	107 (11.7)	85 (11.9)	16 (11.3)	6 (10.5)
Descending	70 (7.7)	56 (7.8)	8 (5.6)	6 (10.5)
Sigmoid	246 (26.9)	188 (26.3)	52 (36.6)	5 (8.8)
Rectosigmoid	130 (14.2)	106 (14.8)	19 (13.4)	6 (10.5)
Tumor differentiation, no. (%) of patients				
Well	22 (2.4)	17 (2.4)	3 (2.1)	2 (3.5)
Moderate	732 (80.1)	577 (80.7)	115 (81.0)	40 (70.2)
Poor	157 (17.2)	118 (16.5)	24 (16.9)	15 (26.3)
Not available	3 (0.3)	3 (0.4)	0 (0.0)	0 (0.0)
Lymphovascular invasion, no. (%) of patients				
Yes	408 (44.6)	297 (41.5)	76 (53.5)	35 (61.4)
No	493 (53.9)	406 (56.8)	66 (46.5)	21 (36.8)
Unknown	13 (1.4)	12 (1.7)	0 (0.0)	1 (1.8)
Lymph node yield, no.				

Median (IQR)	22 (17-30)	22.0 (16.0, 29.5)	22.5 (18.0, 29.5)	23.0 (17.0, 31.0)
Mean (SD)	24.7 (11.3)	24.7 (11.8)	24.9 (9.5)	23.6 (9.0)
T stage, no. (%) of patients				
T1	144 (15.8)	136 (19.0)	2 (1.4)	6 (10.5)
T2	159 (17.4)	142 (19.9)	11 (7.7)	6 (10.5)
T3	522 (57.1)	386 (54.0)	105 (73.9)	31 (54.4)
T4	89 (9.7)	51 (7.1)	24 (16.9)	14 (24.6)
N stage, no. (%) of patients				
N0	593 (64.9)	480 (67.1)	82 (57.7)	31 (54.4)
N1	225 (24.6)	176 (24.6)	35 (24.6)	14 (24.6)
N2	96 (10.5)	59 (8.3)	25 (17.6)	12 (21.1)
AJCC 7 th ed. stage, no. (%) of patients				
I	245 (26.8)	226 (31.6)	9 (6.3)	10 (17.5)
IIA	318 (34.8)	241 (33.7)	61 (43.0)	16 (28.1)
IIB	22 (2.4)	12 (1.7)	7 (4.9)	3 (5.3)
IIC	8 (0.9)	1 (0.1)	5 (3.5)	2 (3.5)
IIIA	49 (5.4)	47 (6.6)	0 (0.0)	2 (3.5)
IIIB	222 (24.3)	156 (21.8)	49 (34.5)	17 (29.8)
IIIC	50 (5.5)	32 (4.5)	11 (7.7)	7 (12.3)
Preoperative CEA, ng/mL				
Median (IQR)	2.8 (1.9-4.6)	2.4 (1.7, 3.2)	9.4 (6.4, 17.1)	11.5 (8.1, 24.5)
Mean (SD)	5.8 (13.1)	2.5 (1.1)	15.4 (20.8)	22.3 (32.2)
Postoperative CEA, ng/mL				
Median (IQR)	2.5 (1.7-3.7)	2.0 (1.5, 2.7)	2.8 (2.2, 4.1)	7.6 (6.4, 10.1)
Mean (SD)	3.5 (4.5)	2.2 (1.0)	3.0 (1.1)	11.4 (9.6)
Days from surgery to CEA testing				
Median (IQR)	35 (26-49)	37.5 (26.0, 51.8)	31.5 (24.2, 47.8)	40.0 (27.0, 49.0)
Mean (SD)	39.2 (17.7)	40.1 (17.6)	36.5 (17.5)	41.4 (18.0)
Adjuvant chemotherapy, no. (%) of patients				
Yes	375 (41.0)	264 (36.9)	87 (61.3)	24 (42.1)

No	529 (57.9)	443 (62.0)	54 (38.0)	32 (56.1)
Unknown	10 (1.1)	8 (1.1)	1 (0.7)	1 (1.8)

eTable 2. Univariate and multivariate analyses of recurrence free survival

Variable	Univariate			Multivariate		
	% 3-year RFS	95% CI	P	Hazard ratio	95% CI	P
Gender			0.699			
Male	88.8	85.2-91.6				
Female	88.0	84.2-91.0				
Age			0.006			
<65	90.4	87.1-92.9		Ref ^a		
≥65	86.2	82.2-89.5		1.9	1.3-2.8	0.001
BMI			0.318			
<30	89.4	86.2-91.9				
≥30	86.6	82.1-90.2				
Primary site			0.733			
Right colon	88.2	84.6-91.1				
Left colon	88.6	84.9-91.5				
Differentiation			0.095			
Well	100					
Moderate	88.8	86.0-91.1				
Poor	85.1	78.1-90.1				
Lymphovascular invasion			<0.001			
No	93.3	90.4-95.4		Ref		
Yes	82.2	77.7-85.9		1.8	1.2-2.8	0.008
TNM stage			<0.001			
I	98.3	95.5-99.4		Ref		
II	90.9	87.0-93.8		2.7	1.3-6.2	0.007
III	78.3	72.8-82.9		5.7	2.8-13.3	<0.001
CEA group			0.004			
Normal preoperative	89.8	87.0-92.0		Ref		
Normalized postoperative	87.9	80.8-92.6		0.77	0.45-1.3	0.312
Elevated postoperative	74.5	61.4-84.3		2.0	1.1-3.5	0.027
Lymph node yield			0.568			
≥12	88.3	85.8-90.5				
<12	92.1	73.5-98.0				

P values were calculated using the log-rank test for univariate analysis and the Cox proportional hazards model for multivariate analysis.

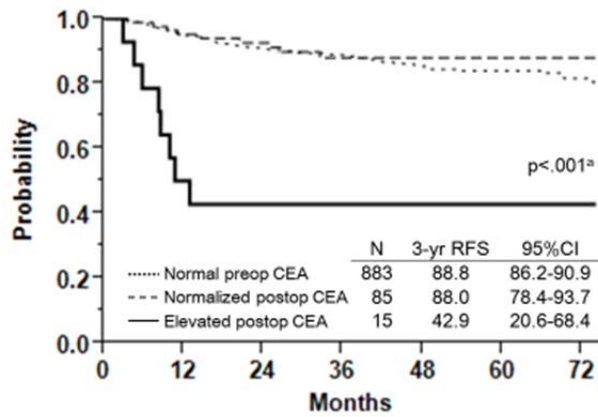
^aRef, reference.

eTable 3. Analysis of sites of metastatic recurrence in relation to CEA status

Recurrence	Normal preoperative CEA		Normalized postoperative CEA		Elevated postoperative CEA		P
	No. (%)	% of CEA group (n=715)	No. (%)	% of CEA group (n=142)	No. (%)	% of CEA group (n=57)	
All sites	64	9.0	17	12.0	13	22.8	
Liver							0.925
Present	31 (48.4)	4.3	8 (47.1)	5.6	7 (53.8)	12.3	
Absent	33 (51.6)	4.6	9 (52.9)	6.3	6 (46.2)	10.5	
Other sites ^a							0.499
Present	44 (68.8)	6.2	10 (58.8)	7.0	7 (53.8)	12.3	
Absent	20 (31.3)	2.8	7 (41.2)	4.9	6 (46.2)	10.5	
M classification							0.762
M1a	39 (60.9)	5.5	12 (70.6)	8.5	8 (61.5)	14.0	
M1b	25 (39.1)	3.5	5 (29.4)	3.5	5 (38.5)	8.8	

P values were calculated using the χ^2 test.

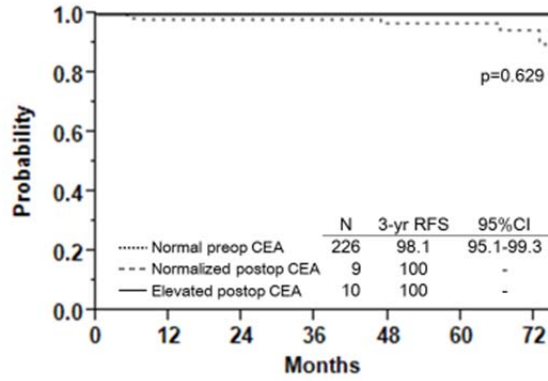
^aLung, n=23; peritoneum, n=21; lymph node, n=18; local, n=6; ovary, n=5; other sites, n=4.



No. at risk							
Normal preop CEA	883	748	545	423	261	164	81
Normalized postop CEA	85	78	66	48	36	19	11
Elevated postop CEA	15	7	4	4	3	2	1

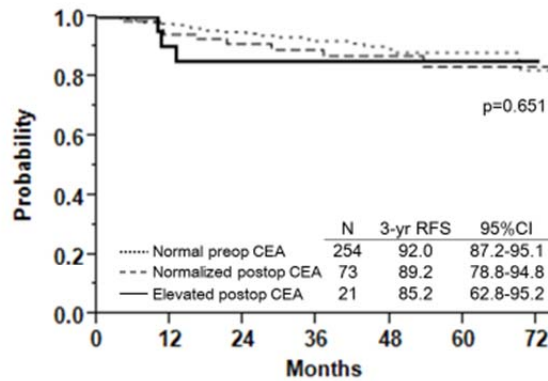
eFigure 1. Kaplan-Meier curves for RFS in patients with normal preoperative, normalized postoperative, or elevated postoperative CEA using a cutoff of 10 ng/mL. ^anormal preoperative CEA vs. elevated postoperative CEA, $p < .001$; normalized postoperative CEA vs. elevated postoperative CEA, $p < .001$. preop CEA, preoperative CEA; postop CEA, postoperative CEA.

A, Stage I



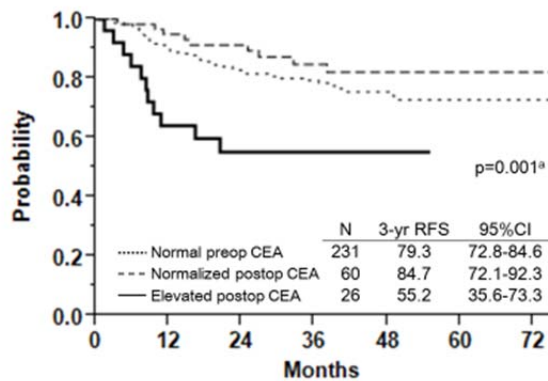
No. at risk	0	12	24	36	48	60	72
Normal preop CEA	226	196	149	116	76	59	25
Normalized postop CEA	9	9	6	6	3	2	2
Elevated postop CEA	10	10	7	5	4	3	3

B, Stage II



No. at risk	0	12	24	36	48	60	72
Normal preop CEA	254	223	171	136	86	47	24
Normalized postop CEA	73	64	55	42	31	17	10
Elevated postop CEA	21	18	15	13	5	3	1

C, Stage III



No. at risk	0	12	24	36	48	60	72
Normal preop CEA	231	187	128	99	57	34	20
Normalized postop CEA	60	55	46	32	24	14	5
Elevated postop CEA	26	16	9	6	3	0	0

eFigure 2. Kaplan-Meier curves for RFS in patients with normal preoperative, normalized postoperative, or elevated postoperative CEA, grouped by TNM disease stage. ^aNormal preoperative CEA vs. elevated postoperative CEA, $p=0.002$; normalized postoperative CEA vs. elevated postoperative CEA, $p=0.001$. preop CEA, preoperative CEA; postop CEA, postoperative CEA.