Clin. Lab. 2018;64:XXX-XXX

ORIGINAL ARTICLE

Identification of Serum Periostin as a Potential Diagnostic and Prognostic Marker for Colorectal Cancer

Dong Dong [1, *], Lufang Zhang [1, *], Li Jia [1], Wei Ji [2], Zhiyong Wang [2], Li Ren [1], Ruifang Niu [2], Yunli Zhou [1]

[*] *These authors contributed equally to this work*
[1] *Department of Laboratory, Tianjin Medical University Cancer Institute and Hospital, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, National Clinical Research Center for Cancer, Tianjin 300060, PR China*
[2] *Public Laboratory, Key Laboratory of Breast Cancer Prevention and Therapy, Tianjin Medical University Cancer Institute and Hospital, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, National Clinical Research Center for Cancer, Tianjin 300060, PR China*

SUMMARY

Background: **Periostin (POSTN) plays an important role in numerous cancers, especially in gastrointestinal malignancy. The objective of this study was to investigate the diagnostic and prognostic role of serum POSTN in colorectal cancer (CRC).**
Methods: **Serum periostin, together with CEA, CA19.9, CA72.4, and CA242 levels were measured in samples from 108 patients with CRC and 56 healthy controls, and their correlation with clinical characteristics was further analyzed. Receiver operating curves (ROC), Kaplan-Meier curves, and log-rank analyses were used to evaluate diagnostic and prognostic significance.**
Results: **Serum POSTN levels were significantly higher in patients with CRC compared with healthy controls ($p < 0.0001$) and associated with clinical stages ($p < 0.001$). ROC analysis revealed that POSTN was a biomarker comparable to CEA, CA19.9, and CA72.4 to distinguish all CRC from healthy controls (AUC = 0.75). Moreover, POSTN retained its diagnostic ability for CEA-negative (AUC = 0.69) and CA19.9-negative CRC patients (AUC = 0.71). Survival analysis revealed that patients with lower serum POSTN had longer overall survival than those with high serum POSTN ($p = 0.0146$).**
Conclusions: **Serum POSTN might be a novel diagnostic and prognostic biomarker for patients with CRC.**
(Clin. Lab. 2018;64:xx-xx. DOI: 10.7754/Clin.Lab.2018.171225)

Correspondence:
Ruifang Niu
Yunli Zhou
Department of Laboratory
Tianjin Medical University Cancer Institute and
Hospital Tianjin's Clinical Research Center for
Cancer, Key Laboratory of Cancer Prevention and
Therapy National Clinical Research Center for Cancer
Huanhuxi Road
Hexi District, Tianjin 300060
PR China
Phone: +86 22 23340123
Email: niuruifang@tjmuch.com (Ruifang Niu)
zhouyunli@tjmuch.com (Yunli Zhou)

Manuscript accepted February 8, 2018

Supplementary Tables and Figures.

Table 1. Sample characteristics and levels of serum markers.

Colorectal cancer	Number	CEA (Mean ± SD)	p-value	CA19.9 (Mean ± SD)	p-value	CA72.4 (Mean ± SD)	p-value	CA242 (Mean ± SD)	p-value
Healthy control	56								
Gender									
Male	29	2.47 ± 2.21	0.550	9.74 ± 5.70	0.567	2.24 ± 2.03	0.734	6.033 ± 5.04	0.479
Female	27	2.79 ± 1.70		10.90 ± 9.12		2.10 ± 1.65		5.17 ± 3.87	
Age									
< 60	30	2.32 ± 1.50	0.215	9.52 ± 5.71	0.408	2.12 ± 1.83	0.863	5.76 ± 4.01	0.809
≥ 60	26	2.97 ± 2.38		11.20 ± 9.18		2.20 ± 1.89		5.46 ± 5.07	
Mean	52.1								
Colorectal cancer	108								
Gender									
Male	61	16.22 ± 30.42	0.180	45.44 ± 130.78	0.936	12.16 ± 39.52	0.154	25.39 ± 83.46	0.842
Female	47	48.44 ± 157.98		47.58 ± 144.78		24.68 ± 48.57		28.85 ± 96.52	
Age									
< 60	52	46.89 ± 152.51	0.141	48.39 ± 138.56	0.883	15.51 ± 31.20	0.635	27.36 ± 93.10	0.959
≥ 60	56	14.79 ± 29.02		44.49 ± 135.58		19.55 ± 53.31		26.47 ± 85.80	
Mean	58.6								
Tumor location									
Colon	58	32.35 ± 133.38	0.829	61.62 ± 182.85	0.183	22.23 ± 53.62	0.222	36.29 ± 118.55	0.210
Rectum	50	27.80 ± 70.82		28.68 ± 33.73		12.25 ± 28.50		16.00 ± 26.63	
Differentiation degree									
Well	11	8.93 ± 9.62	0.554	29.83 ± 35.04	0.742	17.78 ± 35.86	0.987	17.98 ± 20.12	0.903
Moderate	77	37.43 ± 126.78		52.86 ± 159.81		17.96 ± 44.03		29.25 ± 103.78	
Poor	20	14.27 ± 35.39		30.49 ± 36.92		16.15 ± 49.27		22.74 ± 34.50	
Clinical stage									
I, II	49	5.55 ± 7.61	0.019	14.23 ± 13.82	0.015	2.98 ± 1.96	0.001	6.23 ± 5.47	0.017
III, IV	59	50.75 ± 144.01		73.06 ± 180.46		29.76 ± 56.78		44.06 ± 117.96	

Table 2. Performances of individual biomarkers and various panel models for diagnosis of early-stage CRC.

	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Healthy vs. early-stage (I, II)					
POSTN	0.68 (0.57 - 0.78)	81.63	53.57	60.61	76.92
CEA	0.68 (0.57 - 0.78)	71.43	67.86	66.04	73.08
CA19.9 *	0.60 (0.49 - 0.71)	67.35	53.57	55.94	65.22
CA72.4	0.66 (0.56 - 0.77)	79.59	51.79	59.10	74.36
CA242 *	0.52 (0.41 - 0.63)	57.14	51.79	50.91	58.00
POSTN + CEA	0.72 (0.62 - 0.81)	91.84	44.64	59.21	86.21
POSTN + CA72.4	0.71 (0.61 - 0.81)	61.22	73.21	66.66	68.33
POSTN + CEA + CA72.4	0.73 (0.64 - 0.83)	81.63	57.14	62.50	78.04

*** - demonstrated poor discriminatory performance, and left out of subsequent analyses.**

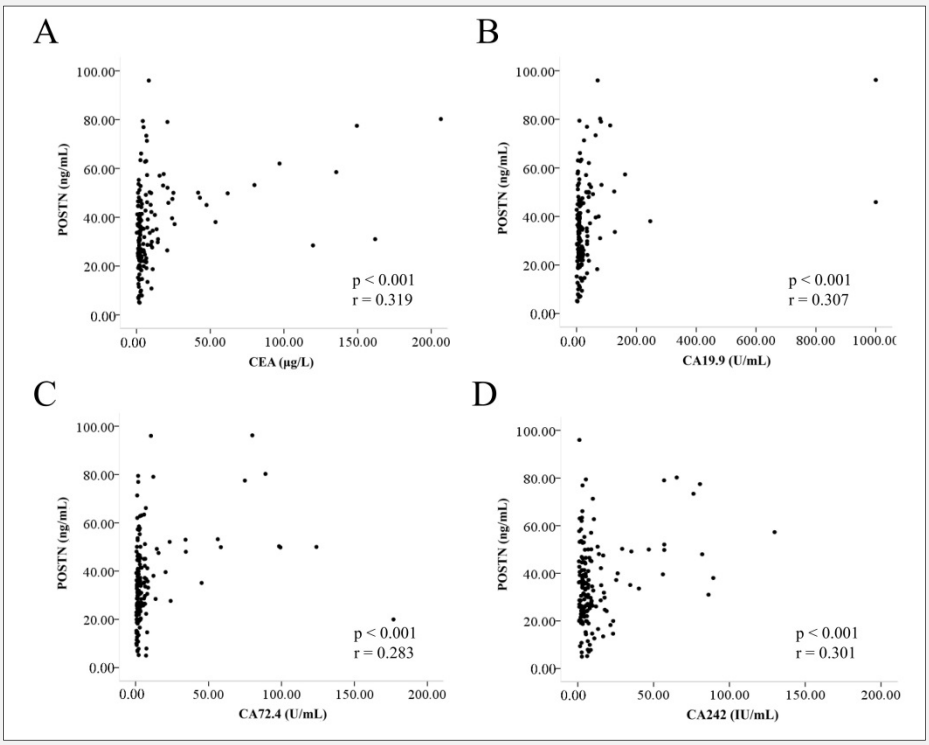

Figure 1. Correlations of serum CEA, CA19.9, CA72.4, CA242 levels and serum POSTN levels.

As shown in A - D, there is no correlation between serum POSTN and CEA (correlation coefficient, 0.319; p < 0.001), CA19.9 (correlation coefficient, 0.307; p < 0.001), CA74.2 (correlation coefficient, 0.283; p < 0.001) or CA242 (correlation coefficient, 0.301; p < 0.001) levels.

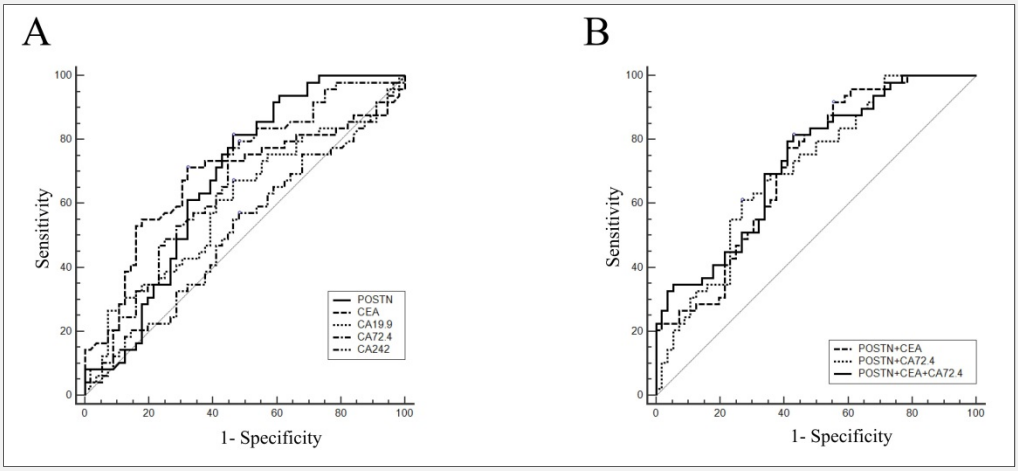

Figure 2. POSTN, CEA, CA19.9, and CA72.4 help to differentiate early versus late-stage CRC.

A, performances of POSTN, CEA, CA19.9, CA72.4, and CA242 as individual markers. ROC curves for POSTN, CEA, CA19.9, CA72.4 and CA242 for discriminating early-stage CRC with healthy controls; B, performances of various marker panels. ROC curves for POSTN + CEA, POSTN + CA72.4, POSTN + CA19.9, and POSTN + CEA + CA19.9 + CA72.4 multiple marker panels for discriminating early-stage CRC from healthy controls.