Int J Clin Exp Med 2015;8(4):6397-6405
www.ijcem.com /ISSN:1940-5901/IJCEM0004841

Original Article

Associations between tumor markers and the risk of colorectal polyp recurrence in Chinese people

Jing Tong, Ying Wang, Bing Chang, Dai Zhang, Bingyuan Wang

Department of Gastroenterology, The First Affiliated Hospital of China Medical University, 155 North Nanjing Street, Shenyang 110001, People's Republic of China

Received December 14, 2014; Accepted March 26, 2015; Epub April 15, 2015; Published April 30, 2015

Abstract: Colorectal cancer primarily arises from the polyps of the colon. Early identification of the recurrence of colorectal polyps represents the best opportunity to prevent the occurrence of colorectal cancer. Thus, the high risk of recurrence is the primary problem. The aim of this study was to examine the associations between tumor markers (CEA and CA19-9) and colorectal polyp recurrence in Chinese people. The risk of colorectal polyp recurrence was studied in 156 subjects (113 males and 43 females, 58.654±11.447 years old) who underwent colonoscopy and polypectomy for the first time between January 2011 and August 2014 at the First Affiliated Hospital of China Medical University, Shenyang, Liaoning, China. All subjects underwent colonoscopies within 6-12 months. Between the colorectal polyp recurrence group and the no recurrence group, the CEA and CA19-9 levels were significantly different, and the trend analyses were consistent with increased risks of recurrence with increasing CEA and CA19-9 levels among the males and patients with single polyps, multiple polyps and proximal colon polyps. The recurrence of colorectal polyps was significantly associated with increased CEA and CA19-9 levels.

Keywords: CEA, CA19-9, polypectomy, colorectal polyp, recurrence

Introduction

Colorectal cancer (CRC) is the fourth most common fatal cancer following lung, stomach, and liver cancers. The majority of colorectal cancers arise from adenomatous polyps. Colorectal polyps are common in the general population. The estimated prevalence is 30-50% after the age of 65 years [1-3]. The removal of polyps is associated with a reduced risk of CRC [4, 5]. However, patients with removed polyps remain at high risk of developing new polyps or cancers, which justifies follow-up with repeated colonoscopies [6]. The clinical characteristics of patients at high risk for polyp recurrence are controversial.

Some studies have reported that recurrent polyps tend to involve multiple, small, tubular polyps that are more likely to be in the proximal colon compared to baseline polyps [7]. In some studies, serum triglyceride [8-11] and cholesterol [12-14] levels have been positively related to an increased risk of colorectal polyps, while several investigators have reported insignificant or even inverse relationships between serum lipids and colorectal polyps [15-17]. Most of the research on polyp recurrence and the associated risk factors has not considered the carcinoembryonic antigen (CEA) or the carbohydrate antigen 19-9 (CA19-9) levels. Therefore, the aim of this investigation was to examine whether the recurrence rate of colorectal polyp is associated with CEA and CA19-9 levels.

Patients and methods

The subjects (N=156) were patients who had undergone endoscopic polypectomy in our hospital from January 2011 to August 2014. There were 113 men (average age, 58.876±11.914 years) and 43 women (average age, 58.070± 10.225 years). The inclusion criteria were as follows: patients with complete and available medical records, and patients who had undergone endoscopy in the 6-12 months after endoscopic polypectomy. Written informed consent was obtained from all patients.

Risk factors

Blood samples were collected from the participating patients at the initial diagnosis and 6-12

Table 1. Comparisons of demographic and clinical characteristics among the two groups

Baseline characteristics	*Colorectal polyp Recurrence (105)*	*Colorectal polyp No Recurrece (51)*	*P value*
Age (years)	58.57±11.87	58.82±10.64	0.898
Sex			0.007
Male (n)	69	44	
Female (n)	36	7	
Smoking status (n)			0.610
Never	68	37	
Former	9	3	
Current	28	11	
Drinking status (n)			0.695
Never	86	44	
Former	6	3	
Current	13	4	
Positive family history (colorectal cancer) (n)	18	4	0.117
Num			0.006
Single (n)	23	22	
Multiple (n)	82	29	
Size (n)			0.499
≤0.5 cm	28	13	
0.5-1.0 cm	44	26	
≥1.0 cm	33	12	
Pathological types			0.103
Hyperplasia polyp (n)	7	5	
Tubular adenoma (n)	44	29	
Tubulovillous adenoma (n)	54	17	
Site			0.005
The distal part of colon (n)	15	6	
The proximal part of colon (n)	51	38	
Both right and left polyp (n)	39	7	
Total cholesterol (mmol/L)	4.572±0.881	4.528±0.824	0.761
Triglycerides (mmol/L)	1.194±0.564	1.396±1.410	0.328
Urinary nitrogen (mmol/L)	323.152±77.856	327.765±72.095	0.723
CEA (ng/ml)	2.771±1.905	1.882±0.951	0.000
CA199 (ng/ml)	10.549±7.971	8.071±4.494	0.014

Table 2. The results of binary logistic regression analysis to colorectal polyp recurrence

	β	*SE*	*Wald*	*P value*	*OR*	*95.0% CI*	
						Lower	Upper
Sex	-1.327	0.508	6.835	0.009	0.265	0.098	0.717
Num	-1.375	0.435	9.984	0.002	0.253	0.108	0.593
Site	-0.414	0.329	1.586	0.208	0.661	0.347	1.259
CEA (ng/ml)	-0.550	0.197	7.797	0.005	0.577	0.392	0.849
CA199 (ng/ml)	-0.078	0.035	4.820	0.028	0.925	0.863	0.992

months after endoscopic polypectomy. The serum levels of blood urinary nitrogen, total plasma cholesterol, and plasma triglycerides were measured using a multichannel analyzer (Roche Hitachi 737; Boehringer Mannheim Diagnostics, USA). The CEA and CA19-9 levels were measured with an immunometric chemiluminecent assay kit (Beckman Co, USA).

Statistical analyses

The data are expressed as the mean ± the SD or as counts. The statistical analyses were per-

Table 3. Compare CEA and CA19-9 levels in recurrence group with no recurrence group

Baseline characteristics	*CEA ng/ml Recurrence (105)*	*CEA ng/ml No recurrence (51)*	*P value*	*CA199 ng/ml Recurrence (105)*	*CA199 ng/ml No recurrence (51)*	*P value*
Sex						
Male	2.547±1.435	1.950±0.935	0.016	10.394±7.447	8.079±4.653	0.044
Female	3.202±2.547	1.454±1.009	0.084	10.845±8.995	8.017±3.624	0.421
Num						
Single	3.047±1.733	1.976±0.948	0.014	17.356±10.199	8.837±4.943	0.001
Multiple	2.694±1.953	1.811±0.963	0.022	12.112±8.663	7.490±4.115	0.000
Location						
The distal part of colon	2.699±1.966	1.802±1.140	0.311	11.463±8.797	7.897±3.401	0.353
The proximal part of colon	2.569±1.717	1.859±0.944	0.015	13.476±10.233	8.460±4.883	0.003
Both right and left polyp	3.063±2.118	2.076±0.950	0.236	13.671±8.085	6.107±2.476	0.000

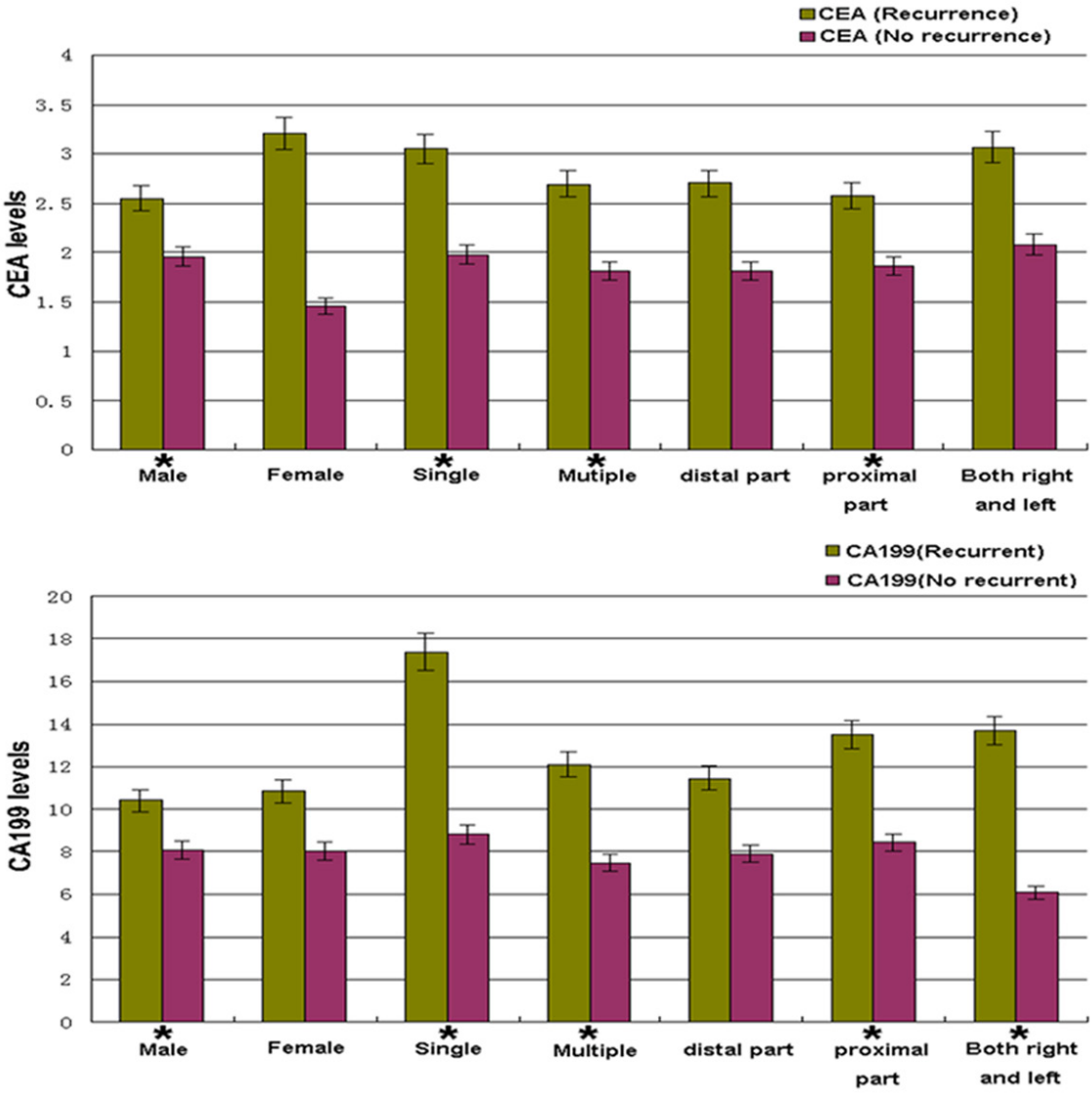

Figure 1. Compare CEA and CA19-9 levels in recurrence group with no recurrence group. Tested with independent-samples T-test (P<0.05).

formed using SPSS version 19.0 (SPSS Inc., USA), and the level of statistical significance was defined as P<0.05. Tests for several independent samples were used to explore the

Table 4. Compare CEA and CA199 levels of pre-polypectomy with post-polypectomy in recurrent group

Baseline characteristics	*CEA ng/ml pre-polypectomy (105)*	*CEA ng/ml post-polypectomy (105)*	*P value*	*CA199 ng/ml pre-polypectomy (105)*	*CA199ng/ml post-polypectomy (105)*	*P value*
Total	2.771±1.905	2.649±1.825	0.522	13.261±9.230	13.129±10.219	0.838
Sex						
Male	2.547±1.435	2.529±1.490	0.912	10.394±7.447	9.588±6.073	0.036
Female	3.202±2.547	2.878±2.344	0.492	10.845±8.995	10.079±8.155	0.128
Num						
Single	3.047±1.733	3.023±1.912	0.950	17.356±10.199	16.002±8.158	0.229
Multiple	2.694±1.953	2.543±1.797	0.497	12.112±8.663	12.324±10.634	0.783
Location						
The distal part of colon	2.699±1.966	3.023±2.445	0.404	11.463±8.797	11.367±7.930	0.882
The proximal part of colon	2.569±1.717	2.544±1.911	0.912	13.476±10.233	12.224±7.085	0.086
Both right and left polyp	3.063±2.118	2.641±1.426	0.292	13.671±8.085	14.991±13.810	0.359

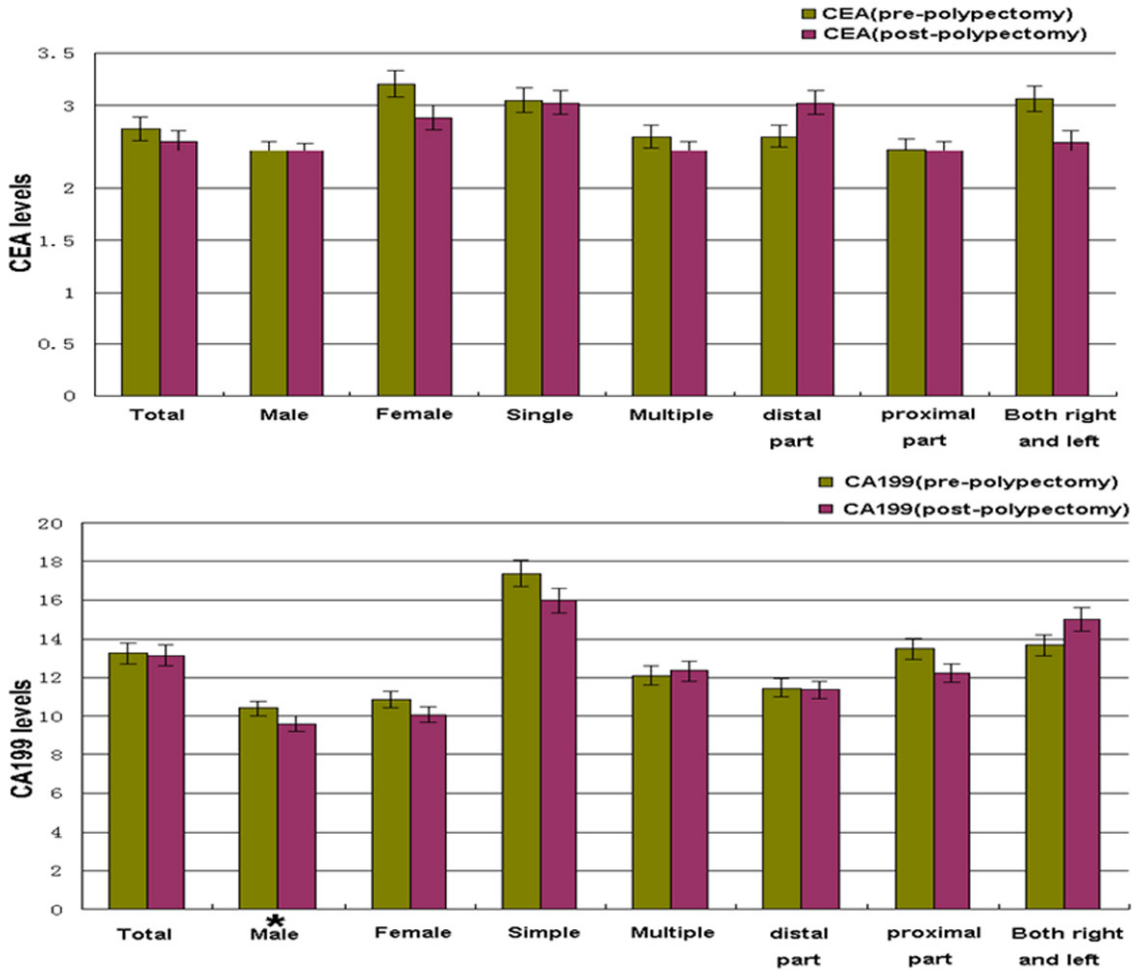

Figure 2. Compare CEA and CA199 levels of pre-polypectomy with post-polypectomy in recurrent group. *Tested with paired-samples T-test (P<0.05).

associations between the risk of polyp recurrence and age, sex, smoking status, drinking status, polyp number, pathological types, site, and CEA, CA19-9, total cholesterol, triglycerides and urinary nitrogen levels. Paired-samples T-test to compare CEA and CA199 levels of pre-polypectomy with post-polypectomy in recurrent group or no recurrent group. Binary

Table 5. Compare CEA and CA199 levels of pre-polypectomy with post-polypectomy in no recurrent group

Baseline characteristics	*CEA ng/ml pre-polypectomy (51)*	*CEA ng/ml post-polypectomy (51)*	*P value*	*CA199 ng/ml pre-polypectomy (51)*	*CA199 ng/ml Post-polypectomy (51)*	*P value*
Total	1.882±0.951	1.671±0.794	0.030	8.071±4.494	7.488±4.108	0.034
Sex						
Male	1.950±0.935	1.771±0.795	0.085	8.079±4.653	7.578±4.096	0.060
Female	1.454±1.009	1.044±0.432	0.179	8.017±3.624	6.923±4.466	0.368
Num						
Single	1.976±0.948	1.783±0.892	0.125	8.837±4.943	7.963±4.435	0.048
Multiple	1.811±0.963	1.587±0.714	0.123	7.490±4.115	7.127±3.882	0.309
Location						
The distal part of colon	1.802±1.140	1.362±0.545	0.162	7.897±3.401	7.005±0.938	0.186
The proximal part of colon	1.859±0.944	1.701±0.858	0.182	8.460±4.883	7.726±4.354	0.019
Both right and left polyp	2.076±0.950	1.777±0.586	0.123	6.107±2.476	6.611±4.223	0.609

logistic regression analysis was used to determine the factors associated with colorectal polyp recurrence in the entire population.

Results

Baseline characteristics

All of the patients were divided into two groups based on colorectal polyps as observed by endoscopic polypectomy at 6-12 months; i.e., recurrence and no recurrence groups. The 156 patients were evaluated at baseline and found to be eligible for the present analysis. The demographic characteristics of these patients are summarized in **Table 1**. **Table 1** illustrates the significant differences between the polyp recurrence group and the no recurrence group in terms of sex, polyp number, polyp site, and the CEA and CA19-9 values. Thus, we then analyzed the differences in the CEA and CA19-9 levels between the two groups.

The relationship of colorectal polyp recurrence and other factors

In the binary logistic regression analysis, in which colorectal polyp recurrence were taken as a dependent variable and age, sex, smoking status, drinking status, positive family history, polyp number, Pathological type, polyp size, polyp site, total cholesterol, triglycerides, urinary nitrogen, CEA, and CA199 were taken as covariate, we found that there were risk factors associated with the recurrence of colorectal polyps, which included CEA (OR=0.577; 95% CI: 0.392-0.849, P<0.05) and CA199 (OR=0.925; 95% CI: 0.863-0.992, P<0.05) (**Table 2**).

The associations between the risk of colorectal polyp recurrence and the CEA and CA19-9 values

Table 3 and **Figure 1** show that the CEA and CA19-9 levels were statistically significantly different between the two groups. The results of the trend analyses were consistent with increased risks of recurrence with increasing CEA and CA19-9 levels among the males and those with single polyps, multiple polyps and polyps in the proximal colon. In terms of the males (P<0.05) and those with single polyps (P<0.05), multiple polyps (P<0.05) and polyps in the proximal colon (P<0.05), the CEA levels in the polyp recurrence group were significantly greater than those in the no recurrence group. In terms of the males (P<0.05) and those with single polyps (P=0.001), multiple polyps (P<0.001), polyps in the proximal colon (P<0.05) and polyps on both the right and left sides (P<0.001), the CA19-9 levels in polyp recurrence group were statistically increased compared to the no recurrence group.

Comparison of the CEA and CA19-9 levels before and after polypectomy in the recurrence group

Table 4 and **Figure 2** show the CEA and CA19-9 levels before and after the polypectomies were marginally significantly different in the recurrent group, and only in the male recurrent group were the CA19-9 levels significantly different before and after polypectomy (P<0.05).

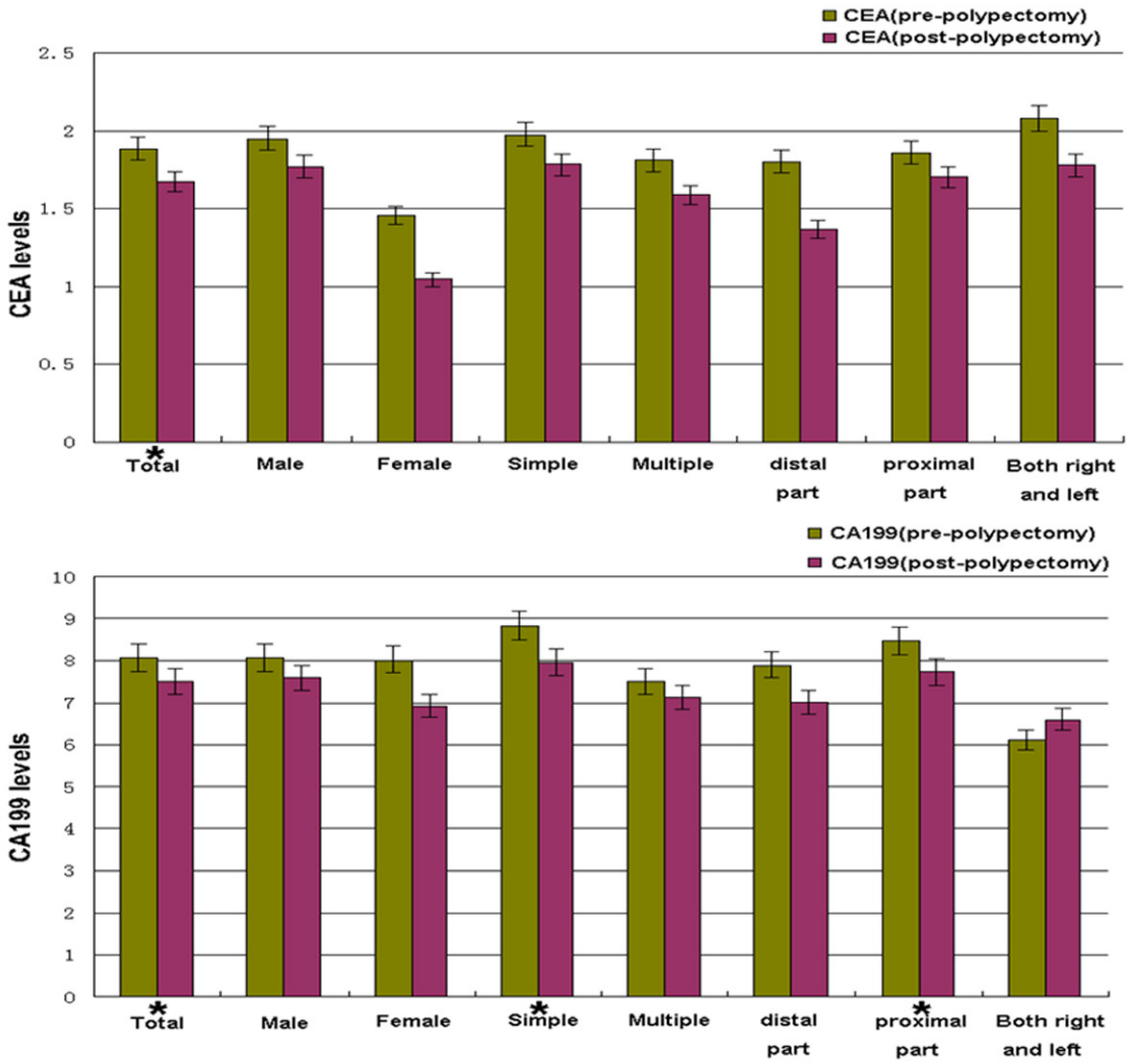

Figure 3. Compare CEA and CA199 levels of pre-polypectomy with post-polypectomy in no recurrent group. *Tested with paired-samples T-test (P<0.05).

Comparison of the CEA and CA19-9 levels before and after polypectomy in the no recurrence group

Table 5 and **Figure 3** show that in total the pre- and post-polypectomy CEA and CA19-9 levels were significantly different in the no recurrence group and that the CEA and CA19-9 levels before and after polypectomy were almost but not significantly different in subgroups. Among those with single polyps and those with polyps in the proximal part of the colon in the no recurrence group, the CA19-9 levels were significantly different before and after polypectomy (P<0.05).

Discussion

The sequence from adenomas to carcinomas is a slow, multistep process, and only a small proportion of adenomas (approximately 3 to 5%) develop into carcinomas after 10 years [18]. The primary prevention of colorectal cancer is limited because the causes of this ailment remain unclear. Secondary or tertiary prevention, i.e., the removal of precancerous lesions or early cancers, might be more useful for reducing mortality due to colorectal cancer. Thus, the high risk of recurrence becomes the primary problem. In this study, the mean follow-up period was 10.3 months (range 6-12), and

the recurrence rate was 67.3%, which is generally higher than the 22-50% that has been reported in previous studies [6, 7, 19-28]. The predictors of colorectal polyp recurrence have not been well established. The reported risk factors for recurrence include multiple polyps [6, 7, 19-28], large polyps [22, 24, 25, 27], severe dysplasia [19, 25], tubulovillous/villous adenomas [19, 25, 28], and polyps in the proximal colon [24, 26]. In our study, the recurrence of colorectal polyp was related to serum CEA and CA19-9 concentrations.

The majority of studies have reported highly significant differences in tumor markers between normal populations, populations with adenomatous polyps, and populations with CRC [29]. However, we evaluated the associations between tumor markers and the risk of colorectal polyp recurrence. Our study revealed increased risks of colorectal polyp recurrence based on sex, polyp number, polyp location, CEA, and CA19-9. The mechanisms underlying the associations between tumor markers and colorectal polyps and the roles of these markers in the prediction of colorectal polyp recurrence are unclear. We analyzed these issued based primarily on two points. First, CEA is a product of columnar and goblet cells in the normal colon and colonic cancer cells and has a half-life of 3-11 days. The serum levels of CEA might increase 4.5 to 8 months before the development of cancer symptoms. Therefore, CEA monitoring is the most cost-effective indicator of the disease [30]. In some studies, CEA levels have been positively related to colorectal polyps in patients who smoke [31]. CA19-9 is an antigen that was originally isolated from human colorectal carcinomas and is identified with a monoclonal antibody designed against CA19-9. CA19-9 could be an inexpensive screening tool that might aid early diagnoses in populations at risk for cancer. Secondly, the monitoring of serum CEA and CA19-9 levels have been widely used for non-malignant conditions [32]. For example, ageing, chronic renal failure, hypothyroidism, cigarette smoking, chronic obstructive pulmonary disease, obesity, fatty liver disease, cholecystolithiasis, chronic hepatitis B and abdominal pain might be associated with alterations in serum CEA or CA 19-9 levels [33-40]. In this study, we analyzed the correlations between the risk for colorectal polyp recurrence and the serum levels of total cholesterol, triglyceride, and urinary nitrogen. Most studies have shown that triglyceride levels are positively related to an increased risk of colorectal polyps [41, 42], and some studies have shown that cholesterol levels are positively related to an increased risk of colorectal polyps. Our research analyzed the risk factors for colorectal polyp recurrence after polypectomy and revealed that colorectal polyp recurrence was not related to total cholesterol, triglycerides, or urinary nitrogen.

The current study provides new evidence linking tumor markers to the risk of colorectal polyp recurrence after polypectomy and confirmed the lack of associations of total cholesterol, triglycerides, and urinary nitrogen with colorectal polyp recurrence. To better understand the role of tumor markers in the prediction of colorectal polyp recurrence, additional detailed studies are needed to clarify the effects of both systemic and local CEA and CA19-9 levels on colorectal polyp recurrence.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jing Tong, Department of Gastroenterology, The First Affiliated Hospital of China Medical University, 155 North Nanjing Street, Shenyang 110001, People's Republic of China. Tel: +86-24-83282554; E-mail: realll30@126.com

References

[1] Rickert RR, Auerbach O, Garfinkel L, Hammond EC, Frasca JM. Adenomatous lesions of the large bowel: an autopsy survey. Cancer 1979; 43: 1847-1857.

[2] Eide TJ, Stalsberg H. Polyps of the large intestine in Northern Norway. Cancer 1978; 42: 2839-48.

[3] Vatn MH, Stalsberg H. The prevalence of polyps of the large intestine in Oslo: an autopsy study. Cancer 1982; 49: 819-825.

[4] Jorgensen OD, Kronborg O, Fenger C. The Funen Adenoma Follow-up Study. Incidence and death from colorectal carcinoma in an adenoma surveillance program. Scand J Gastroenterol 1993; 28: 869-874.

[5] Citarda F, Tomaselli G, Capocaccia R, Barcherini S, Crespi M. Efficacy in standard clinical practice of colonoscopic polypectomy in reducing colorectal cancer incidence. Gut 2001; 48: 812-815.

[6] Bonithon-Kopp C, Piard F, Fenger C, Cabeza E, O'Morain C, Kronborg O, Faivre J. Colorectal adenoma characteristics as predictors of recurrence. Dis Colon Rectum 2004; 47: 323-333.
[7] Martinez ME, Sampliner R, Marshall JR, Bhattacharyya AK, Reid ME, Alberts DS. Adenoma characteristics as risk factors for recurrence of advanced adenomas. Gastroenterology 2001; 120: 1077-1083.
[8] Bird CL, Ingles SA, Frankl HD, Lee ER, Longnecker MP, Haile RW. Serum lipids and adenomas of the left colon and rectum. Cancer Epidemiol Biomarkers Prev 1996; 5: 607-612.
[9] Park SK, Joo JS, Kim DH, Kim YE, Kang D, Yoo KY. Association of serum lipids and glucose with the risk of colorectal adenomatous polyp in men: a case-control study in Korea. J Korean Med Sci 2000; 15: 690-695.
[10] Otani T, Iwasaki M, Ikeda S, Kozu T, Saito H, Mutoh M, Wakabavashi K, Tsuqane S. Serum triglycerides and colorectal adenoma in a case-control study among cancer screening examinees (Japan). Cancer Causes Control 2006; 17: 1245-1252.
[11] Manus B, Adang RP, Ambergen AW, Bragelmann R, Armbrecht U, Stockbrugger RW. The risk factor profile of recto-sigmoid adenomas: a prospective screening study of 665 patients in a clinical rehabilitation centre. Eur J Cancer Prev 1997; 6: 38-43.
[12] Bayerdorffer E, Mannes GA, Richter WO, Ochsenkuhn T, Seeholzer G, Kopcke W, Wiebecke B, Paumqartner G. Decreased high-density lipoprotein cholesterol and increased low-density cholesterol levels in patients with colorectal adenomas. Ann Intern Med 1993; 118: 481-487.
[13] Meance S, Boutron-Ruault MC, Myara A, Gerhardt MF, Marteau P, Lavergne A, Franchisseur C, Bouley C. Fecal primary bile acids and serum cholesterol are associated with colorectal adenomas. Dig Dis Sci 2003; 48: 1751-1757.
[14] Mannes GA, Maier A, Thieme C, Wiebecke B, Paumgartner G. Relation between the frequency of colorectal adenoma and the serum cholesterol level. N Engl J Med 1986; 315: 1634-1638.
[15] Chung YW, Han DS, Park YK, Son BK, Paik CH, Lee HL, Jeon YC, Sohn JH. Association of obesity, serum glucose and lipids with the risk of advanced colorectal adenoma and cancer: a case-control study in Korea. Dig Liver Dis 2006; 38: 668-672.
[16] Kono S, Ikeda N, Yanai F, Yamamoto M, Shigematsu T. Serum lipids and colorectal adenoma among male self-defence officials in northern Kyushu, Japan. Int J Epidemiol 1990; 19: 274-278.
[17] Kono S, Imanishi K, Shinchi K, Yanai F. Serum lipids and left-sided adenomas of the large bowel: an extended study of self-defense officials in Japan. Cancer Causes Control 1993; 4: 117-121.
[18] Eide TJ. Natural history of adenomas. World J Surg 1991; 15: 3-6.
[19] van Stolk RU, Beck GJ, Baron JA, Haile R, Summers R. Adenoma characteristics at first colonoscopy as predictors of adenoma recurrence and characteristics at follow-up. The Polyp Prevention Study Group. Gastroenterology 1998; 115: 13-18.
[20] Matek W, Guggenmoos-Holzmann I, Demling L. Follow-up of patients with colorectal adenomas. Endoscopy 1985; 17: 175-181.
[21] Kellokumpu I, Husa A. Colorectal adenomas: morphologic features and the risk of developing metachronous adenomas and carcinomas in the colorectum. Scand J Gastroenterol 1987; 22: 833-841.
[22] Winawer SJ, Zauber AG, O'Brien MJ, Ho MN, Gottlieb L, Sternberg SS, Waye JD, Bond J, Schapiro M, Stewart ET, Panish J, Ackroyd F, Kurtz RC, Shike M. Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. The National Polyp Study Workgroup. N Engl J Med 1993; 328: 901-906.
[23] Neugut AI, Jacobson JS, Ahsan H, Santos J, Garbowski GC, Forde KA, Treat MR, Waye J. Incidence and recurrence rates of colorectal adenomas: a prospective study. Gastroenterology 1995; 108: 402-408.
[24] Fornasarig M, Valentini M, Poletti M, Carbone A, Bidoli E, Sozzi M, Canizzaro R. Evaluation of the risk for metachronous colorectal neoplasms following intestinal polypectomy: a clinical, endoscopic and pathological study. Hepatogastroenterology 1998; 45: 1565-1572.
[25] Yang G, Zheng W, Sun QR, Shu XO, Li WD, Yu H, Shen GF, Shen YZ, Potter JD, Zheng S. Pathologic features of initial adenomas as predictors for metachronous adenomas of the rectum. J Natl Cancer Inst 1998; 90: 1661-1665.
[26] Noshirwani KC, van Stolk RU, Rybicki LA, Beck GJ. Adenoma size and number are predictive of adenoma recurrence: implications for surveillance colonoscopy. Gastrointest Endosc 2000; 51: 433-437.
[27] Avidan B, Sonnenberg A, Schnell TG, Leya J, Metz A, Sontag SJ. New occurrence and recurrence of neoplasms within 5 years of a screening colonoscopy. Am J Gastroenterol 2002; 97: 1524-1529.
[28] Henry LG, Condon RE, Schulte WJ, Aprahamian C, DeCosse JJ. Risk of recurrence of colon polyps. Ann Surg 1975; 182: 511-515.

[29] Mead R, Duku M, Bhandari P, Cree IA. Circulating tumour markers can define patients with normal colons, benign polyps, and cancers. Br J Cancer 2011; 105: 239-245.
[30] Flamen P, Hoekstra OS, Homans F, Van Cutsem E, Maes A, Stroobants S, Peeters M, Penninckx F, File L, Bleichrodt RP, Mortelmans L. Unexplained rising carcinoembryonic antigen (CEA) in the postoperative surveillance of colorectal cancer: the utility of positron emission tomography (PET). Eur J Cancer 2001; 37: 862-869.
[31] Shahangian S, Fritsche HA, Hughes JI. Carcinoembryonic antigen in serum of patients with colorectal polyps: correlation with histology and smoking status. Clin Chem 1991; 37: 651-655.
[32] McLaughlin R, O'Hanlon D, Kerin M, Kenny P, Grimes H, Given HF. Are elevated levels of the tumour marker CA19-9 of any clinical significance?–an evaluation. Ir J Med Sci 1999; 168: 124-126.
[33] Fukuda I, Yamakado M, Kiyose H. Influence of smoking on serum carcinoembryonic antigen levels in subjects who underwent multiphasic health testing and services. J Med Syst 1998; 22: 89-93.
[34] Amino N, Kuro R, Yabu Y, Takai SI, Kawashima M, Morimoto S, Ichihara K, Miyai K, Kumahara Y. Elevated levels of circulating carcinoembryonic antigen in hypothyroidism. J Clin Endocrinol Metab 1981; 52: 457-462.
[35] Bulut I, Arbak P, Coskun A, Balbay O, Annakkaya AN, Yavuz O, Gülcan E. Comparison of serum CA 19.9, CA 125 and CEA levels with severity of chronic obstructive pulmonary disease. Med Princ Pract 2009; 18: 289-293.
[36] Witherspoon LR, Shuler SE, Alyea K, Husserl FE. Carcinoembryonic antigen: assay following heat compared with perchloric acid extraction in patients with colon cancer, non-neoplastic gastrointestinal diseases, or chronic renal failure. J Nucl Med 1983; 24: 916-921.
[37] Herbeth B, Bagrel A. A study of factors influencing plasma CEA levels in an unselected population. Oncodev Biol Med 1980; 1: 191-198.
[38] Graziani G, Cucchiari D, Podesta MA, Quagliuolo V, Montanelli A. Abdominal pain and increased CA19-9. Clin Chem 2013; 59: 1678-1679.
[39] Tong Y, Song Z, Zhu W. Study of an elevated carbohydrate antigen 19-9 concentration in a large health check-up cohort in China. Clin Chem Lab Med 2013; 51: 1459-1466.
[40] Lee JY, Lee DC, Lee JW. Serum carcinoembryonic antigen is associated with non-alcoholic fatty liver disease in healthy Korean non-smokers. Clin Chem Lab Med 2013; 51: 1499-1504.
[41] Tabuchi M, Kitayama J, Nagawa H. Hypertriglyceridemia is positively correlated with the development of colorectal tubular adenoma in Japanese men. World J Gastroenterol 2006; 12: 1261-1264.
[42] Liao KF, Lai HC, Lai SW, Cheng KC, Lin CH. Association between rectosigmoid adenomas and cardiovascular risk factors: a hospital-based, cross-sectional study. Ann Acad Med Singapore 2009; 38: 630-636.