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Increased serum CA125 II, but not CEA, CA19-9, AFP or CA72-4 in colon cancer compared to rectal cancer

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Globally, colorectal cancer is the third most frequent cancer type, with >1.4 million new cases and >690,000 deaths annually [1]. Survival from colorectal cancer is significantly dependent on the stage at diagnosis, with the 5-year rate at ~90% for localized disease, 70% for regional disease and 13% for distantly metastatic disease [2]. Several screening tests, including faecal occult blood test and colonoscopy, are frequently used in the detection of colorectal cancer. However, none are established and well-accepted screening tools due to their invasiveness, high cost or low sensitivity [3]. Therefore, the search for more sensitive, easily detected and representative biomarkers is of great significance for the early diagnosis and monitoring of this disease.

Several biological and clinical hallmarks indicate that rectal cancer is different from colon cancer. The rectum and colon have a different embryological origin, anatomy and function [4]. Consequently, the treatments for primary rectal and colon cancer are different. Primary rectal cancer requires specific surgical treatment: total mesorectal excision, preceded by neoadjuvant radiotherapy or chemoradiotherapy [5]. Despite a substantial rise in survival over the last two decades, the 5-year disease-specific overall survival rate is approximately 59% for colon cancer and 61% for rectal cancer [6]. This indicates that it is very important to explore the difference between colon cancer and rectal cancer.

Tumour markers are widely useful in the management of patients with tumours. Serum carcinoembryonic antigen (CEA) and cancer antigen 19–9 (CA19-9) are the most commonly used indexes in the clinical diagnosis of colorectal cancer, but both are non-specific. CEA is a glycoprotein produced by columnar and goblet cells in the normal colon cells, as well as colonic cancer cells with a half-life of 3–11 days. CA19-9 is also a glycoprotein with high molecular weight, which may be detected in the blood of gastrointestinal cancer patients [7]. We hypothesized different expressions of CEA, CA19-9, alpha-fetoprotein (AFP), cancer antigen 72–4 (CA72-4) and cancer antigen 125 II (CA125 II) between colon cancer and rectal cancer, hoping to provide reference for the different pathogenesis and treatment of these diseases.

Of 219 patients with histopathologically confirmed colorectal cancer, 114 had colon cancer and 105 rectal cancer. There was no significant difference in age and gender between the colon cancer group and rectal cancer group (table 1). Five mL peripheral blood was extracted from a peripheral vein, and serum isolated by centrifugation at 2000× g for 15 min. Serum CA19-9, AFP, CA72-4 and CA125 II levels were determined by radioimmunoassay (Roche Diagnostics, Indianapolis, IN, USA), with a normal upper limit of 37 U/ml, 7 ng/ml, 6.9 U/ml and 35 U/ml, respectively. The serum CEA level was determined by ELISA (Dinabot, Tokyo, Japan), with a normal upper limit of 5 ng/ml. Statistical analysis was performed using IBM SPSS Version 23. Groups were compared using the Mann–Whitney U test and results are presented as median with interquartile range (table 1). $P < 0.05$ was considered to be statistically significant.

Results are shown in table 1 and figure 1a–1e. There were no difference in levels of CEA, CA19-9, AFP or CA72.4, but levels of CA125-II were 26.5% higher in those with colon cancer.

The sensitivity and specificity of serum CEA and CA19-9 expression in colorectal cancer patients is reported as 0.65 and 0.89, indicating that the serum CEA and CA19-9 expression has diagnostic value with moderate sensitivity and good specificity [8]. However, there are few reports on the difference of serum CEA and CA19-9 expression between colon cancer and rectal cancer: we found no statistically significanct difference.

AFP, a glycoprotein, is derived from embryonic endoderm tissue cells. AFP content in foetal serum is high and gradually decreases to the level of adults after birth. The low content of AFP in the adult blood is mainly due to the loss of the ability to synthesize AFP in mature hepatocytes. When transformed, the liver cancer cells can regain the ability to synthesize AFP. Besides liver cancer, malignant tumours from stomach,

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Table 1. Selected characteristics of the study population and different tumour markers expression between colon and rectal cancer.

	Colon Cancer (n = 114)	Rectal Cancer (n = 105)	P
Age (years)	62.0 (11.3)	62.6 (8.7)	0.692
Gender (male/female)	69/45	67/38	0.617
CEA (ng/ml)	4.9 (2.0–11.0)	3.2 (1.9–7.3)	0.140*
CA19-9 (U/ml)	11.9 (6.5–30.5)	11.1 (7.2–22.8)	0.791*
AFP (ng/ml)	1.9 (1.4–3.0)	2.0 (1.4–3.1)	0.615*
CA72-4 (U/ml)	1.8 (1.1–4.5)	1.4 (1.0–3.2)	0.241*
CA125 II (U/ml)	10.5 (7.7–21.6)	8.3 (6.5–11.0)	0.043*

Data mean [standard deviation], median (inter-quartile range) or n

pancreas, and reproductive system are often accompanied by a small amount of increased AFP [9]. According to our data, AFP has no role in differentiating colon cancer from rectal cancer.

CA72-4 is a high molecular weight mucin CEA (>200 kDa), levels being related to tumour size, stage and metastasis. CA72-4 is present in 85–95% of cases of stomach, colon, pancreas, lung and ovarian tumours, but is not expressed by benign tumours, exudates or normal human tissues, and levels vary with environmental and geographical factors [10,11]. However, we found no statistical significance of serum CA72-4 expression between colon cancer and rectal cancer patients. CA125 is a member of the tethered human mucus (MUC) family of large, heavily glycosylated transmembrane proteins that have a diverse range of functions [12]. CA125 levels higher than 35 U/mL are considered abnormal and are associated with 90% of ovarian carcinomas, and are strongly associated with a poor prognosis [13]. Furthermore, CA125 levels are useful indicators of the response to chemotherapy and disease relapse and progression [14]. A cut-off value for the serum CA125 concentration (82.9 U/ml) is predictive of metastasis, which has the potential to serve as a clinically useful indicator of metastasis in ovarian cancer patients [15]. We found increased serum CA125 II levels in colon cancer patients compared to rectal cancer patients, indicating CA125 II might be involved in the biology of colon cancer separately from that of rectal cancer. However, we acknowledge our sample size is modest and look forward to independent confirmation in a large study.

Our data represent an advance in biomedical science in that serum CEA, CA19-9, AFP and CA72-4 levels do not differentiate colon cancer and rectal

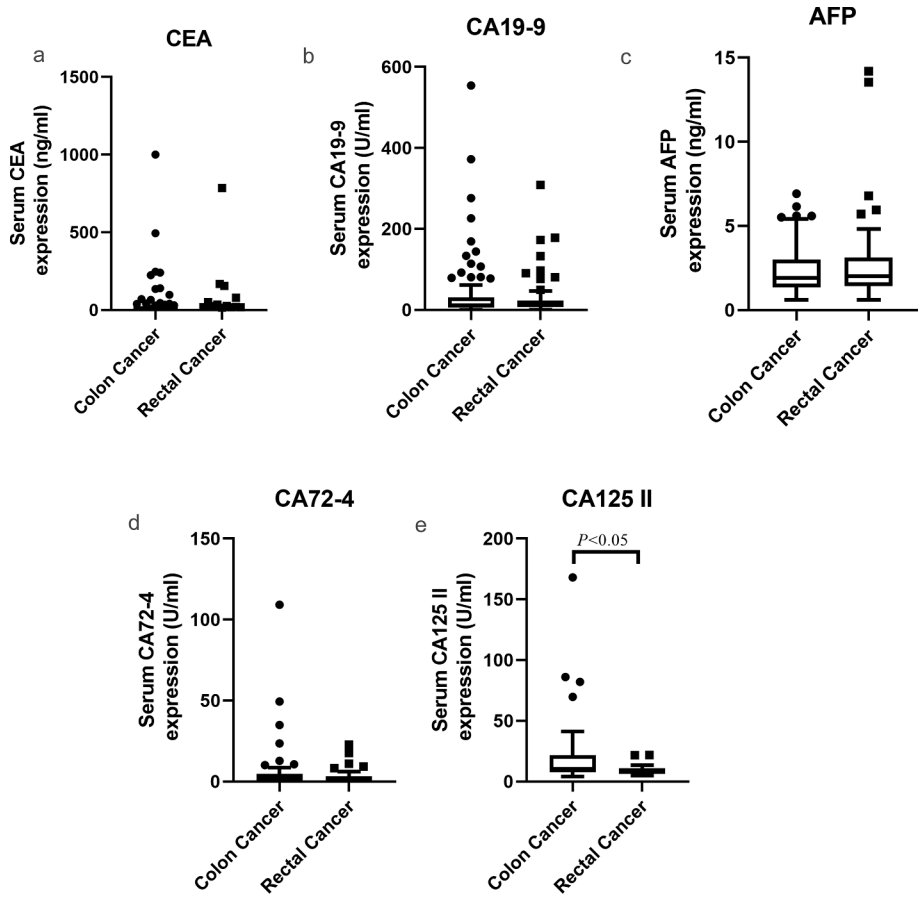

Figure 1. (a) Comparison of serum CEA expression in colon cancer and rectal cancer; (b) Comparison of serum CA19-9 expression in colon cancer and rectal cancer; (c) Comparison of serum AFP expression in colon cancer and rectal cancer; (d) Comparison of serum CA72-4 expression in colon cancer and rectal cancer; (e) Comparison of serum CA125 II expression in colon cancer and rectal cancer.

cancer, whereas serum CA125 II in colon cancer patients is increased statistically compared with rectal cancer patients.

Disclosure statement

No potential conflict of interest was reported by the authors.

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