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Detect the role of tumor markers in the diagnosis of colorectal cancer

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Abstract: Colorectal cancer (CRC) globally represents a significant source of illness and death related to cancer. Even though there is proof of a 90% 5-year survival rate with early-stage diagnosis, fewer than 40% of cases are identified at a localized stage. Despite recent progress in surgical and multimodal therapies, the overall survival rate for advanced CRC patients remains markedly low, it has become possible to develop biomarkers that help with the identification of patient responses for cancer diagnosis, management, and surveillance.

Hence, CEA and CA19.9 biomarkers underwent testing in a patient sample to assess their respective effectiveness, and their p-values were measured, we observed a statistically significant p-value of 0.049 for CEA, indicating its significance. In contrast, CA19.9 yielded a p-value of 0.084, which is considered not statistically significant, CEA and CA19.9 exhibit a positive correlation with a coefficient of 0.403. And the P-value is statistically significant at 0.001.

keywords: colorectal cancer, biomarkers, CEA, CA19.9.

1. Introduction

Colorectal cancer (CRC) is the most common cancer in the gastrointestinal tract, accounting for 13% of all malignant tumors. . Globally, colorectal cancer is thought to be the second most common cause of death from cancer, affecting both men and women equally. The majority of colorectal cancers are rare diseases with a sequenced carcinogenesis process, meaning that mutations gradually accumulate throughout 10 to 15 years [1-2].

Colorectal cancer risk factors encompass genetic elements, such as the sequential accumulation of mutations in adenomatous polyposis coli (APC), Kirsten-ras (K-ras), and p53, contributing to chromosomal instability-associated carcinogenesis [3-4], The risk of CRC significantly rises after the age of 50, with men having a higher prevalence compared to women. Additionally, a family history of CRC or adenomatous polyps increases the likelihood of developing CRC [5-6], Other risk factors include smoking, being overweight or obese, alcohol consumption, a diet low in fruits and vegetables coupled with high red and processed meat intake, and the presence of diabetes mellitus, which is associated with an increased susceptibility to various cancers. Physical inactivity has also been identified as a risk factor, with a systematic review revealing an inverse relationship between physical activity and CRC [7-8].

The most prevalent symptoms in the sample were weight loss, blood in stool, change in bowel habits, pain, dry mouth, concerns, lack of energy, Lack of appetite, Constipation, Nausea, and Vomiting

Several methods can diagnose colorectal cancer, colonoscopy may detect cancers at an early stage where there is a higher chance for cure than in those discovered in a more advanced stage, Endoscopy is a name for the common devices that have a light source and

helps to visualize the organ/ body cavity, it is insert from the mouth, Colon capsule endoscopy (CCE) is a minimally invasive, Fecal occult blood test (FOBT), and tumor markers [9-10-11].

A biomarker is a substance that serves as a precisely measurable indicator of a pathological or biological state. It can assist in identifying diseases, predicting prognosis, or anticipating a patient's response to medication when applied in the context of a disease process [12].

The prevalent biomarker for colorectal cancer (CRC) identified in blood is a carcinoembryonic antigen (CEA), which is a high molecular weight glycoprotein present in embryonic tissue and colorectal tumors. Elevated blood CEA levels are associated with various tumors likew colorectal, breast, gastric, lung, ovarian, and pancreatic cancers. It is noteworthy that several nonmalignant conditions, can also lead to an increase in CEA levels [13-14].

A monoclonal antibody called CA19-9 binds to E-Selectin. Serum CA19-9 levels are elevated in both benign and malignant processes. Most cases of pancreatic, stomach, lung, biliary system, and colorectal cancer generate the tumor marker. However, elevated levels of CA19-9 are also seen in patients with endometriosis, bronchiectasis, diabetes mellitus, acute cholangitis, and liver cirrhosis [15].

Presently, guidelines continue to advocate for the inclusion of CEA in conjunction with other screening techniques to assess prognosis, conduct surveillance post-curative resection, and monitor treatments. Nonetheless, using CA19-9 alone for colorectal cancer detection or therapy monitoring is not advised due to its limited sensitivity. according to existing recommendations [16-17].

2. Subjects Materials and methods

The proposal was submitted to the Mansoura Faculty of Medicine Institutional Research Board (MFM-IRB) for approval (ethical code: MS.21.08.1603) then consents were taken from the gastrointestinal surgery center at Mansoura University.

There are 82 participants in this study, 43 are CRC patients and 39 are normal control. For patients, the medical and surgical histories were taken، and all analysis needed has been performed such as (liver function and renal function test, CBC, Na, and k)

Sample collection:

Subject (patient and controls) had 3 ml of whole blood collected and left at room temperature for clotting, serum separated by centrifugation at 2000 rpm for 5 min.

Procedures:

In the gastrointestinal surgery center lab, all samples were taken to measure CEA and CA19.9.

3. Results and Discussion

Table 1: Characterization of malignant and non-malignant groups at the time of testing. Study subjects were characterized according to their age and gender.

	Control group N =39		**CRC group N = 43**		**Test (p)**
	№	**%**	**№**	**%**	
Gender					
Male	27	69	26	60	p=0.649
Female	12	31	17	40	
Age(years)					
Median (Range)	33(25-46)		60(53-67)		U=255.500 p=0.028

As demonstrated in Table 1, the median age for the non-malignant group was 33 years, while for the malignant group, the median age was 60.

The p-value is 0.028 (P>0.05) it’s statically significant.

69% of the non-malignant group are male, while 40% of malignant group is female, the p-value is non-significant.

Table 2: characterization of the patient according to the site of tumor, stage, and grade.

Parameter	**N**	**%**
Primary site Right colon Left colon Rectum	 17 20 **7**	 39 45 16
grade **1** **2** **3**	 4 33 2	 10 85 5
stage **1** **2** **3** **4**	 4 18 12 7	 10 44 29 17

As demonstrated in Table 2, the distribution across primary sites is as follows: 39% in the right part of the colon, 45% in the left colon, and 16% in the rectum., according to grade 85% are in grade 2, and most cases are in stage 2.

Table 3: Comparison of Tumor Marker Levels (CEA and CA19.9) Between Non-Malignant and Malignant Conditions.

variable	Control group Median (IQR)	CRC group Median (IQR)	P-value
CEA N=69	1.71 (1.21-3.54)	2.55 (1.60-6.49)	.049
CA19.9 N=64	4.50 (2.40-6.00)	7.65 (2.00-22.80)	.084

As demonstrated in Table 3 The median CEA levels are higher in the Malignant group compared to the Non-malignant group, as indicated by the median values, this difference is statistically significant, with a p-value of 0.049, The median CA19.9 levels also show a numerical increase in the Malignant group compared to the Non-malignant group, the differences in median CA19.9 levels between the two conditions are not statistically significant, with a p-value of 0.084.

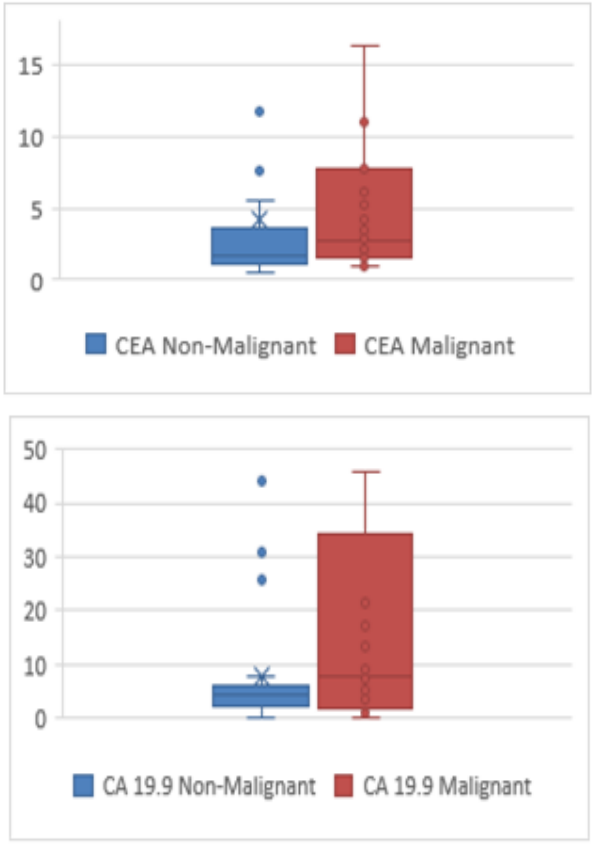

Figure (1):

Table 4: Correlation Matrix of Biomarkers (CEA, CA19.9) in colorectal cancer patients.

	CEA	
	r	P
CA-19.9	0.403	0.001

r* correlation coefficient.

P* Value significant.

CEA and CA19.9 exhibit a positive correlation with a coefficient of 0.403. And the P-value is statistically significant at 0.001.

Conclusion and recommendations:

Colorectal cancer (CRC) stands as a primary contributor to illness and death related to cancer worldwide, many patients are diagnosed too late, in the advanced third and fourth stages of cancer development, leading to higher complications and mortality. Despite advancements in medical science, early detection or secondary prevention is expected to improve treatment effectiveness and prognosis. It has become possible to develop biomarkers that assistance in recognizing patient reactions aids in the diagnosis, treatment, and monitoring of cancer.

CEA & CA19.9 are considered the most effective traditional biomarkers, in this study we found that CEA is statistically significant while CA19.9 is not statistically significant, but there is a positive correlation between CEA & CA19.9 and p-value between them is statistically significant.

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