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Measurement Of Tumor Markers In The Diagnosis Of Colorectal Carcinoma

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Abstract

Current clinical practice in oncology has a growing impetus on early diagnosis, proper prognostication and (of late) screening for malignancy in asymptomatic groups. Serum CEA has been the most sensitive diagnostic tool in asymptomatic patients for early diagnosis of recurrent disease in CRC and its use is proposed in several international guidelines. CA19-9 marker is associated with the presence of various solid tumors including CRC and preoperative rise in several serum nucleic acid markers has proven to predict both prognosis and metastasis in CRC.

Objective: The aim of the study was evaluate the diagnostic significance of tumor markers Carcinoembryonic antigen (CEA) and CA 19-9 in patients with colorectal cancer.

Material and Methods: In this study clinically diagnosed 116 colorectal cancer patients were studied. Colorectal cancer patients were diagnosed by clinically and histopathologically.

Results: ROC curve showed sensitivity of CEA 56% and specificity 71 % at optimal cutoff 5 ng/ml at confidence interval (CI) 95 % followed by CA 19-9 which showed sensitivity 28 % and specificity 97% at optimal cut off 37 U/mL at CI 95 %

Conclusion: In patients with CRC all single STMs show low sensitivity and specificity, while the simultaneous measurement of a panel of STMs may increase the diagnostic accuracy. Although, CEA is a well-known tumor marker for CRC, and we found a 75% sensitivity of CEA for CRC, the detection of serum CEA levels has not proven to be sufficiently sensitive for detection of primary CRC, especially early stage CRC.

Keywords: Carcinoembryonic Antigen, CA 19-9, Colorectal Cancer Patients

Introduction

The natural laws that govern the world of biology have seen the evolution of organisms of convoluted acclimation for their survival. For the preservation of homeostasis, all the organisms; single- celled to complex tissues has integrated[1]. The laws of natural selection have been executed courtly, desultory. The organisms generally can not only be allowed by the natural selection to accrue propitious acclimation, but it has been observed that the unflinching laws of biology allow microevolution among individual cells. At the rudimentary levels, cancer is the product of applied natural selection. Unrestrained division of those cells will procreate which can overcome the encumbering boundaries and sustain the opportunity to develop further aberrations that stimulate excrescence, survival, migration and invasion to establishment in, distant organs[1]. Moreover the enormous challenges for successful treatment of cancers are due to misuse of normal development and homeostatic. Current clinical practice in oncology has a growing impetus on early diagnosis, proper prognostication and (of late) screening for malignancy in asymptomatic groups. Serum CEA has

been the most sensitive diagnostic tool in asymptomatic patients for early diagnosis of recurrent disease in CRC and its use is proposed in several international guidelines. The carcinoembryonic antigen (CEA) is the most commonly used tumor marker in patients with colorectal cancer[2]. It is used as an early diagnostic index for recurrence during follow-up after radical surgery has been well established by several authors. CA19-9 marker is associated with the presence of various solid tumors including CRC and preoperative rise in several serum nucleic acid markers has proven to predict both prognosis and metastasis in CRC. Several serum tumor markers (STMs) have been proposed for the diagnosis of CRC, but their detection should be combined to increase accuracy[3]. Detection of colon cancer at early stages is critical for curative treatment intervention. Prediction of survival is another feature requested for tumor markers and elevated levels of both CEA and CA 19-9 have also been reported to be associated with poor prognosis in CRC

Subjects and Methods:

Subject:

This case study was carried out on 116 subjects in the Department of Biochemistry and department of gastroenterology Sher-I- Kashmir institute of medical sciences, Srinagar, Jammu & Kashmir. India. This is one of the largest tertiary care hospital in state of Jammu & Kashmir. Our study was case study including patients attending to regional Onco-logic Center as in the outpatient clinic. The included subjects in this study were 69 males (69%) and 31 females (31%), their ages were between 20-70 years. Ethical clearance was obtained from the ethical committee. Written informed consents were taken from all participants in this study.

Methods

CRC patients included in the study were subjected to the following: Clinical examinations. Radiological investigations include: Abdominal ultrasound and CT, and lower gastrointestinal endoscopy (colonoscopy) and biopsy taking of colorectal cancer tissue for histopathological examinations to confirm the diagnosis. 5 ml blood samples were collected using aseptic techniques. Serum was separated from the blood by allowing it to complete clot and centrifuged at 3000 rpm for 10 minutes. Serum was stored at -80°C until analysis time. Serum of each sample was evaluated for CEA and CA 19-9 tumor markers.

Results: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor and all calculations were carried out in Statistica.10 (Dell Tech-nologies, Round Rock, Texas, USA), as well as in the softwareSPSS.v.25. Continuous variables were summarized in the form of means and standard deviations. Receiver Operating Curve (ROC) was applied for sensitivity and specificity. Overall, 68 (58.63%) men and 48 (41.37%) women were studied. ROC curve showed sensitivity of CEA 56% and specificity 71 % at optimal cutoff 5 ng/ml at confidence interval (CI) 95 % followed by CA 19-9 which showed sensitivity 28 % and specificity 97% at optimal cut off 37 U/mL at CI 95 %.

Table1: ROC analysis of CEA marker in evaluation of Colorectal Carcinoma		
CEA	**Value**	**95% CI**
Sensitivity	56	34.9-75.6
Specificity	71	61.0-80.4
AUC	0.613	0.523 – 0.706
Optimal Cutoff	5	-
Table2: ROC analysis of CA19-9 marker in evaluation of Colorectal Carcinoma		
CA19-9	**Value**	**95% CI**
Sensitivity	28	12.1-49.4

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Specificity	97	92.3-99.7
AUC	0.625	0.530 to 0.713
Optimal Cutoff	37	-

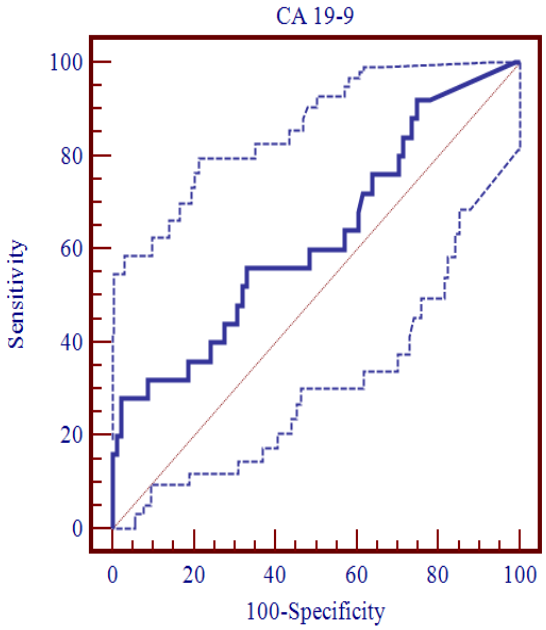

Figure 1: ROC of CA 19-9

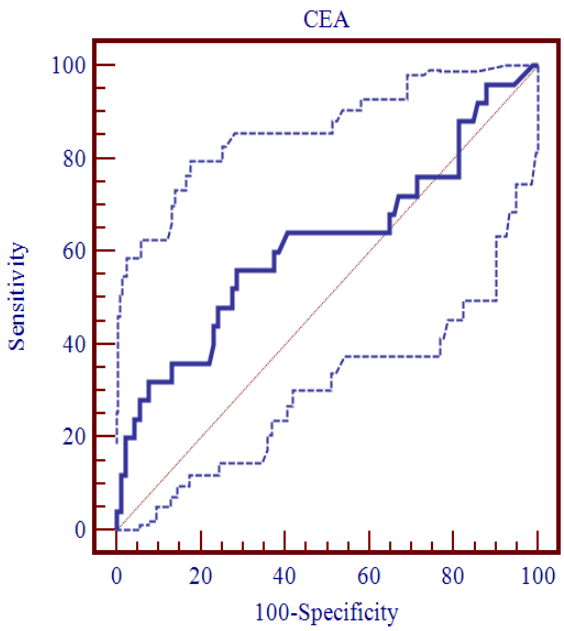

Figure 2: ROC of CEA

Discussion

Sequential accumulation of genetic alterations over time leads to gradual development of colorectal cancer. In 1970s, based on histological and epidemiological studies the preponderance of colorectal carcinoma was believed to originate from pre-malignant adenomatous polyps[4]. A current view is that the familial cases may be a quite heterogeneous group, in which modest-to-moderate predisposition to colorectal carcinoma is possibly conferred by an undetermined number of potentially common genetic variations[5]. Battery of markers is used to confirm the diagnosis of various types of cancers. CEA is one of the most widely used tumor markers, especially for patients with CRC[3]. Thus, the elevation of serum tumor marker levels in human serum can be useful for early diagnosis of cancer[6]. The early detection of colorectal cancer (CRC) significantly improves the prognosis of patients and is a key factor to reduce the mortality from CRC. In the present study the sensitivity and specificity of CEA, markers is 56% and 71 %(Table 1). The results were similar to the findings of Kuusela et al (1991)[7], Von Kleist's et al (1996)[8], Wang et al (1985)[9], Eskelinen et al (1994)[10], Paganuzzi et al (1994)[11]. Our results are in accordance with U ward et al (1993)[12] as they concluded that, sensitivity of CEA was 74% and specificity was 100% and appeared to be the most useful marker which was elevated in 80% of the patients with colorectal cancer. Our finding of increase in sensitivity of CEA in colorectal cancer patients is similar with the observation of various authors Filella Xavier et al (1991)[13], N Wild et al (2010)[14], Fernandes et al (2005)[15] found that CEA showed the best sensitivity. In our study, the sensitivity of CA19-9 marker was 28% and specificity was 97% (Table 2)which are similar to the results of Spila et al (2001)[16], Carpelan et al (2002)[17] , Huber et al (2010)[18]. Our results are supported by Von kleist et al (1996)[8] as they concluded that sensitivity for CA 19-9 was 33% and specificity was 96%. The sensitivity (28%) of CA 19-9 was lesser than the sensitivity of CEA (56%)

Conclusion:

In patients with CRC all single STMs show low sensitivity and specificity, while the simultaneous

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measurement of a panel of STMs may increase the diagnostic accuracy. Although, CEA is a well known tumor marker for CRC, and we found 56% sensitivity and 71% specificity of CEA for CRC, the detection of serum CEA levels has not proven to be sufficiently sensitive for detection of primary CRC, especially early stage CRC.

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