Accuracy Of Combined Carbohydrate Antigen 242 (CA242) And Carcinoembryonic Antigen (CEA) Examination As A Diagnostic Predictor In Colorectal Cancer Patients at RS Adam Malik

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***Abstract*-** This study is driven by the increasing prevalence of colorectal cancer and the need for rapid, non-invasive, and accurate diagnostic methods. Carbohydrate antigen 242 (CA242) and carcinoembryonic antigen (CEA) is a tumor marker with the potential to serve as a diagnostic predictor for colorectal cancer. An analytical observational study with a cross-sectional design was conducted. The study included 58 subjects, comprising 29 colorectal cancer patients and 29 control subjects. Both groups underwent CEA and CA242 testing using the ELISA method at RS Adam Malik. Data analysis involved non-parametric tests, 2x2 contingency tables, and ROC curve analysis to determine the optimal cut-off value for CA242. At a CA242 cut-off value ≥ 14.250 mg/dL, 18 colorectal cancer cases and 5 control cases were observed. The sensitivity was 68.21%, specificity 62.86%, positive predictive value 74.57%, negative predictive value 78.57%, and overall accuracy was 72.19%. At a CEA cut-off value ≥5.0 mg/dL, 19 colorectal cancer cases and 7 control cases were observed. The sensitivity was 69.25%, specificity 79.75%, positive predictive value 76.98%, negative predictive value 71.90%, and overall accuracy was 74.25% Additionally, the combination of CA242 and CEA improved both sensitivity and specificity, sensitivity was 72.45% and spesitivity was 81.75%, and overall accuracy was 79.65%.The findings indicate that combined CA242 and CEA examination achieves an accuracy of 79.65% as a diagnostic predictor for colorectal cancer at RS Adam Malik. Further studies to combined another marker with CA242 is recommended to validate and strengthen these findings..

Keywords: CA242, CEA, Colorectal Cancer, Diagnostic Accuracy, ELISA, RS Adam Malik

I. INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer worldwide, with over 1.4 million new cases and more than 690,000 deaths annually. In 2020, there were over 1.9 million cases, causing approximately 930,000 deaths globally.[1] According to GLOBOCAN 2020, 1.85 million CRC cases were recorded in developed countries such as China and the United States. However, CRC is increasingly prevalent in developing nations due to lifestyle changes.[2] In Indonesia, CRC incidence reached 12.8% per 100,000 adults in 2020, accounting for 9.5% of cancer-related deaths.[3]

Colonoscopy combined with pathological biopsy remains the most accurate diagnostic method for CRC but is invasive and costly. Alternative non-invasive screening methods, such as fecal occult blood tests, have lower sensitivity and specificity. Early detection is essential for effective management and improved prognosis. Research has explored the potential of exosomes, which contain tumor-derived DNA, RNA, and protein antigens, as diagnostic markers.[4],[5]

Several biomarkers are commonly used for CRC diagnosis, including carcinoembryonic antigen (CEA) and carbohydrate antigens (CA) such as CA19-9, CA125, and CA242.[5] CEA is the most widely used biomarker for diagnosis, disease monitoring, and treatment evaluation. CA19-9, CA125, and CA242 are also valuable in confirming diagnoses and assessing post-treatment responses.[5] Given CRC's heterogeneity, a single biomarker is insufficient for accurate diagnosis. Recent studies show that combining multiple biomarkers improves diagnostic and prognostic accuracy. For example, CEA combined with CA242 significantly enhances sensitivity. Wang et al. demonstrated that analyzing CEA, CA19-9, and CA242 together improves prognostic prediction in surgically treated CRC patients.[5]

CA242 is a glycoprotein linked to tumor-associated carbohydrate antigens and has diagnostic relevance in CRC. Studies suggest that CA242 has similar sensitivity and specificity to CA19-9.[7] It is a sialic acid-containing carbohydrate antigen that can be detected on cell surfaces. CA242 levels correlate with clinical and pathological characteristics of malignant intestinal tumors, including gastric, pancreatic, and colorectal cancers.[5],[8] Higher CA242 levels are observed in advanced-stage CRC and metastatic cases.[6] However, post-treatment CA242 levels decline more rapidly in advanced CRC patients.[9] Research since 1991 has confirmed CA242 detection across all CRC stages. Its post-surgical decline correlates with treatment effectiveness, showing a more pronounced decrease in curatively operated patients. Compared to CEA and CA19-9, CA242 has lower levels in benign neoplasms, making it superior for distinguishing malignant from benign cases.[6]

This study aims to evaluate the accuracy of CA242 testing as a predictor for CRC diagnosis at RS Adam Malik. The findings are expected to clarify CA242's role in CRC detection and provide valuable clinical insights. A better understanding of CA242's diagnostic accuracy may improve early detection and management, ultimately enhancing patient prognosis and reducing mortality rates.

II. METHODS

This study is an analytical observational research with a cross-sectional approach to compare the accuracy of CA242 as a diagnostic predictor in colorectal cancer (CRC) patients at RS Adam Malik, Medan. The study will be conducted from April to March 2025. The sample consists of CRC patients aged >18 years who have undergone biopsy, thoracic imaging, and contrast-enhanced abdominal CT scans. Participants must provide informed consent and agree to CA242 and CEA testing. Exclusion criteria include comorbidities affecting the immune system, liver or kidney dysfunction, metabolic diseases, allergies, lung tumors, pregnancy, breastfeeding, and prior chemotherapy or radiotherapy.

Data collection involves personal information, anamnesis (including symptoms and medical history), and physical examinations. Blood samples will be analyzed for CA242 and CEA using ELISA at the Integrated Laboratory of Universitas Sumatera Utara. Data analysis includes descriptive statistics to assess sample distribution, followed by a 2x2 table analysis for sensitivity and specificity evaluation. The Shapiro-Wilk test determines data normality. One-way ANOVA or Kruskal-Wallis tests will analyze CA242 and CEA levels based on histopathological differentiation. ROC curve analysis will assess CA242's sensitivity and specificity. Statistical analysis will be performed using SPSS version 22.

III. RESULTS

Table 1 presents the characteristics of subjects in this study, which includes colorectal cancer patients and a control group. Each group consists of 29 individuals. The gender distribution is identical in both groups, with 18 males (62.1%) and 11 females (37.9%) in each. A chi-square test showed no significant difference in gender distribution between the colorectal cancer and control groups ($p = 0.786$). Regarding age, the mean age in the colorectal cancer group was 53.21 years with a standard deviation of 11.04 years, while the control group had a mean age of 54.72 years with a standard deviation of 8.36 years. An independent t-test indicated no significant difference in age between the two groups ($p = 0.351$).

For cancer location, most cases were found in the rectum (34.48%), followed by the rectosigmoid (27.59%), descending colon and sigmoid colon (each 13.79%), and the least in the transverse colon (10.34%). Histopathologically, the colorectal cancer group had 15 patients (51.7%) with well-differentiated tumors, 6 patients (20.7%) with moderately differentiated tumors, and 8 patients (27.6%) with poorly differentiated tumors. Cancer staging data showed that the majority of patients were in Stage 3A (31.03%), followed by Stage 2A (20.69%) and Stage 4A (17.24%). Among the colorectal cancer patients, metastasis was found in 8 patients (27.6%), while 21 patients (72.4%) showed no metastasis.

Table 1. Demographic Characteristics of Study Subjects

	Colorectal cancer (n=29)	Control (n=29)	p-value
Gender			
Male	18 (62,1%)	18 (62,1%)	0,786[a]
Female	11 (37,9%)	11 (37,9%)	
Age (years)	53,21±11,04	54,72±8,36	0,351[b]
Cancer Location			
Rectum	10 (34.48%)	-	
Rectosigmoid	8 (27.59%)	-	

Descending colon	4 (13.79%)	-
Transverse colon	3 (10.34%)	-
Sigmoid colon	4 (13.79%)	-
Histopathology		-
Well Differentiated	15 (51,7%)	-
Moderated Differentiated	6 (20,7%)	-
Poorly Differentiated	8 (27,6%)	-
Cancer Stage		-
Stage2A	6 (20.69%)	-
Stage 2B	3 (10.34%)	-
Stage 3A	9 (31.03%)	-
Stage 3B	1 (3.45%)	-
Stage 3C	2 (6.90%)	-
Stage 4A	5 (17.24%)	-
Stage 4B	3 (10.34%)	-
Metastasis		-
Yes	8 (27,6%)	-
No	21 (72,4%)	-

Analysis of CEA and CA242 Levels in Colorectal Cancer Patients

The levels of CEA and CA242 in colorectal cancer patients are presented in Table 2. In this study, the data distribution of CEA and CA242 levels was not normally distributed; therefore, the Mann-Whitney test was used for analysis. Table 4.2 compares the levels of CEA and CA242 between colorectal cancer patients and the healthy control group.

With an equal number of subjects in both groups (n=29), the median CEA level in colorectal cancer patients (6.14; range 1.17–228.0) was significantly higher than in the control group (median 2.30; range 1.14–14.3) with a p-value of 0.005. Similarly, the median CA242 level in colorectal cancer patients (14.90; range 2.70–26.80) was also higher than in the control group (median 2.70; range 1.80–4.50) with a p-value of 0.000, indicating a statistically significant difference.

Table 2. CEA and CA242 Level

Variable	Colorectal Cancer(n=29)	Control (n=29)	p-value
CEA	6,14 (1,17-228,0)	2,30 (1,14-14,3)	0,005
CA242	14,9 (2,70-26,80)	2,70 (1,80-4,50)	0,000

*Mann Whitney

Analysis of CEA and CA242 Levels in Relation to Histopathology and Metastasis in Colorectal Cancer

This study analyzes the differences in CEA and CA242 levels based on histopathological grading and metastasis, as presented in Tables 4.3, 4.4, and 4.5, along with Figures 1, 2, 3, and 4.

Table 3. Differences in CEA and CA242 Levels Based on Histopathological Grade

	Well differentiated	Moderately differentiated	Poorly differentiated	

Variable	Median (min-max)	Median (min-max)	Median (min-max)	p-value
CEA	6,14 (1,17-228,0)	7,0 (1,64-57,8)	7,87 (1,41-55,5)	0,935
CA242	8,40 (2,70-14,3)	13,80 (5,60-19,6)	24,50 (20,8-26,8)	0,384

*****Kruskal Wallis

Table 3 compares CEA and CA242 levels according to histopathological biopsy results (well, moderately, and poorly differentiated). The median CEA level for well-differentiated tumors was 6.14, for moderately differentiated tumors was 7.0, and for poorly differentiated tumors was 7.87, with a p-value of 0.935, indicating no significant difference. Meanwhile, the median CA242 level for well-differentiated tumors was 8.40, for moderately differentiated tumors was 13.80, and for poorly differentiated tumors was 24.50, with a p-value of 0.0384, also indicating no significant difference.

Table 4. Differences in CEA and CA242 Levels Based on Metastasis Occurrence

Variable	Metastasis	Non-Metastasis	p-value
	Median (min-max)	Median (min-max)	
CEA	9,92 (9,92-95,5)	6,14 (1,17-228,0)	0,922
CA242	24,5 (20,8-26,8)	7,60 (2,70-16,2)	0,003

*Mann Whitney

Table 4 presents the comparison of CEA and CA242 levels in patients with and without metastasis. In the metastasis group, the median CEA level was 9.92 (range 9.92–95.5), while in the non-metastasis group, it was 6.14 (range 1.17–228.0), with a p-value of 0.922, showing no significant difference. However, for CA242, the median in the metastasis group was 24.5 (range 20.8–26.8), compared to 7.60 (range 2.70–16.2) in the non-metastasis group, with a p-value of 0.003, indicating a statistically significant difference.

Table 5. Differences in CEA and CA242 Levels Based on Histopathological Grade and Metastasis Occurrence

Variable	Histopathology		Metastasis	
	p	**r**	**p**	**r**
CEA	0,748	-0,062	0,924	-0,018
CA242	0,282	-0,203	0,032	-0,393

*****Spearman

Table 5 presents the statistical analysis measuring the correlation between CEA and CA242 levels with histopathological grading and metastasis. Due to non-normally distributed data, Spearman's test was used. The correlation analysis for histopathology showed a p-value of 0.748 for CEA with a Spearman correlation coefficient (r) of -0.062, indicating no significant correlation. For CA242, the p-value was 0.282 with an r of 0.203, also showing no significant correlation. Regarding metastasis, CEA had a p-value of 0.924 and r of -0.018, indicating no significant correlation. However, for CA242, the p-value was 0.032 with an r of -0.393, demonstrating a significant positive correlation with metastasis occurrence.

Diagnostic Analysis of CEA Levels for Colorectal Cancer

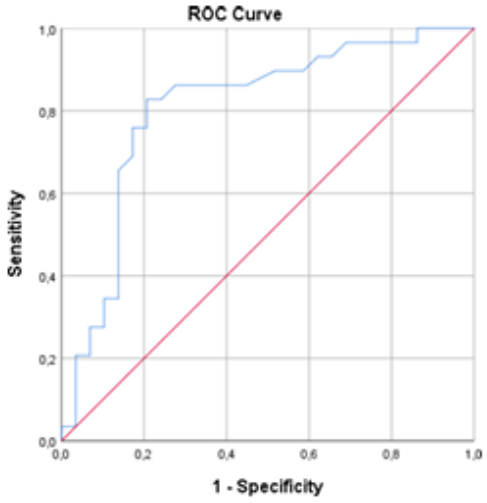
In this study, the cut-off value for CEA levels was set at 5.0 µg/L to detect colorectal cancer. The diagnostic test results for CEA levels are presented in Table 6. At a CEA level of ≥ 5.0 µg/L, there were 19 cases of colorectal cancer and 7 control cases. The sensitivity for detecting colorectal cancer at this threshold was 69.25%, while the specificity was 79.75%. The positive predictive value (PPV) was 76.98%, and the negative predictive value (NPV) was 71.90%.

Table 6. Diagnostic Analysis of CEA for Colorectal Cancer

CEA Level	Colorectal Cancer	Control	Sensitivity	Specificitu	PPV	NPV	Accuracy
≥ 5,0	19	7	69.25%	79.75%	76.98%	71.90%	74.25%
< 5,0	10	22					

Diagnostic Analysis of CA242 Levels for Colorectal Cancer

Figure 1. ROC Curve of CA242 in the Diagnosis of Colorectal Cancer and Coordinates of the Curve of CA242



Test Result Variable(s): CA242

Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
,2000	1,000	1,000
1,2400	1,000	,966
1,7900	1,000	,931
2,7100	1,000	,897
3,2600	1,000	,862
3,8000	,966	,862
4,2400	,966	,828
4,3400	,966	,793
4,5900	,966	,759
5,1550	,966	,724
5,3300	,966	,690
6,4150	,931	,655
6,3900	,931	,621
7,5300	,897	,586
7,7450	,897	,552
8,7000	,897	,517
9,9000	,862	,448
10,3900	,862	,414
11,0900	,862	,379
11,7450	,862	,345
12,4700	,862	,310
15,4050	,759	,172
15,5450	,724	,172
15,8000	,690	,172
16,3500	,655	,148
16,7400	,621	,148
16,8150	,828	,241
16,9800	,828	,207
20,0850	,517	,148
20,5850	,483	,136
20,6200	,448	,136
20,5700	,414	,136
21,3950	,379	,136
21,0450	,345	,136
21,3600	,345	,103
21,6800	,310	,103
22,2200	,276	,103
22,0000	,276	,069
22,5850	,241	,069
22,6200	,207	,069
23,5700	,207	,034
24,3950	,172	,034
25,0450	,138	,034
25,3600	,103	,034

Based on the ROC curve and coordinate points, the highest Youden index was found when the cut-off value for CA242 was set at ≥ 14.250 mg/dL. Sensitivity and specificity analyses for CA242 in diagnosing colorectal cancer are presented in Table 8. At CA242 levels ≥ 14.250 mg/dL, there were 18 cases of colorectal cancer and 5 control cases. Meanwhile, at CA242 levels < 14.250 mg/dL, there were 11 cases of colorectal cancer and 24 control cases. The sensitivity for detecting colorectal cancer at this threshold was 68.21%, while specificity was 62.86%. The positive predictive value (PPV) was 74.57%, and the negative predictive value (NPV) was 78.57%, with an overall accuracy of 72.19%.

Table 7. Diagnostic Analysis of CA242 for Colorectal Cancer

CA242 Level	Colorectal Cancer	Control	Sensitivity	Specificitu	PPV	NPV	Accuracy
≥14,250	18	5	68.21%	62.86%	74.57%	78.57%	72.19%
<14,250	11	24					

Diagnostic Analysis of the Combined Use of CEA and CA242 for Colorectal Cancer

At CEA levels ≥ 5.0 mg/dL and CA242 levels ≥ 14.250 mg/dL, there were 18 cases of colorectal cancer and 4 control cases. The sensitivity for detecting colorectal cancer using this combination of tumor markers was 72.45%, while specificity was 81.75%. The positive predictive value (PPV) was 84.65%, and the negative predictive value (NPV) was 65.80%, with an overall accuracy of 79.65%.

Table 8. Combined Diagnostic Analysis of CEA and CA242 for Colorectal Cancer

Level	Colorectal Cancer	Control	Sensitivity	Specificity	PPV	NPV	Accuracy
CEA ≥ 5,0 CA242 ≥14,250	18	4	72.45%	81.75%	84.65%	65.80%	79.65%

IV. DISCUSSION

This study employs an observational analytic design with a cross-sectional approach. This design was chosen as it allows researchers to measure the prevalence of a condition or characteristic, such as CA242 levels and histopathological differentiation categories in colorectal cancer patients, at a specific point in time. Cross-sectional studies are advantageous as they provide an overview of the relationship between variables without requiring long-term follow-up. Additionally, they are cost-effective and time-efficientcompared to longitudinal studies, which require continuous observation.10

The study included 58 patients, divided into 29 colorectal cancer patients and 29 control patients. Carcinoembryonic antigen (CEA) and carbohydrate antigen 242 (CA242) levels were measured to evaluate their diagnostic capabilities for colorectal cancer. CEA is a tumor marker widely used in colorectal cancer management, particularly for monitoring post-surgical cancer recurrence, as preoperative and postoperative CEA levels are independent predictors of overall survival.11 CEA, a membrane-bound glycoprotein, is

overexpressed in 90–95% of colorectal cancer cases. Its expression correlates with increased Ras activation, affecting cell metabolism by modulating glycoprotein levels and metabolic pathways.12

The gender distribution was equal in both groups, with 18 males (62.1%) and 11 females (37.9%) per group. Chi-square tests showed no significant differences in gender distribution between the colorectal cancer and control groups ($p = 0.786$). The mean age in the colorectal cancer group was 53.21 years (SD 11.04), while in the control group, it was 54.72 years (SD 8.36), with no significant age difference ($p = 0.351$). These findings align with Luo et al.'s study, which also reported a higher male prevalence without statistical significance.5

Regarding tumor location, most cases were found in the rectum (34.48%), rectosigmoid (27.59%), descending colon (13.79%), and sigmoid colon (13.79%), with the least cases in the transverse colon (10.34%). These results align with Luo et al.'s study, where the rectum was the most common tumor site in 193 patients.5 In terms of histopathological differentiation, the colorectal cancer group had 15 well-differentiated cases (51.7%), 6 moderately differentiated cases (20.7%), and 8 poorly differentiated cases (27.6%). In contrast, Luo et al.'s study reported a higher prevalence of moderately differentiated cases (254 patients), followed by poorly differentiated (96 patients) and well-differentiated (8 patients).5

Based on the TNM classification from the American Joint Committee on Cancer Staging, most patients were in Stage 3A (31.03%), followed by Stage 2A (20.69%) and Stage 4A (17.24%). In the colorectal cancer group, 8 patients (27.6%) had metastases, while 21 patients (72.4%) did not. Compared to Luo et al.'s study, where most patients were in early-stage (Stage I+II), this study found more cases in advanced stages. This discrepancy may be due to China's colorectal cancer screening program, which offers biennial screenings for residents aged 50–75.5

CEA and CA242 levels were significantly higher in colorectal cancer patients than in the control group. For CEA, the median level in cancer patients was 6.14 µg/L (range: 1.17–228.0), compared to 2.30 µg/L (range: 1.14–14.3) in the control group ($p = 0.005$). CA242 levels in cancer patients had a median of 8.90 µg/L (range: 2.70–26.8), significantly higher than in the control group (median 2.70 µg/L, range: 1.80–4.50) with $p = 0.000$.

CA242, a tumor marker commonly used for pancreatic carcinoma diagnosis, contains a sialic acid-enriched carbohydrate epitope present as glycoprotein or glycolipid on the cell surface.13 CA242 is strongly overexpressed in pancreatic carcinoma cells and correlates with differentiation level and clinical stage. Unlike CA19-9, CA242 is less affected by cholestasis and benign obstructions, making it a reliable biomarker.13 Studies show that CA242 levels correlate well with CA19-9 and CA50, suggesting its utility in gastrointestinal malignancy diagnosis. Luo et al. (2022) also found elevated CA242 levels in colorectal cancer patients, consistent with this study. However, no correlation was observed between histopathological differentiation and CA242 levels in both studies, likely due to intra-category histopathological variations.4,11,14

This study found a significant difference in CA242 levels between metastatic and non-metastatic groups, suggesting that CA242 can help distinguish metastatic colorectal cancer. CA242 is associated with metastatic risk due to its link with e-selectin, a vascular adhesion molecule mainly found in endothelial cells.25 E-selectin facilitates cancer cell circulation by responding to cytokines like IL-1 and TNF, allowing tumor cells to migrate and metastasize.13,14 CA242 levels significantly correlate with cancer staging and perineural invasion.

Using a cut-off value of 5.0 mg/dL, CEA demonstrated a sensitivity of 69.25% and specificity of 79.75% for colorectal cancer diagnosis, aligning with previous studies. Nicholson et al. systematically reviewed 52 studies and evaluated CEA's diagnostic performance at different cut-offs. At 5 mg/dL, CEA had a sensitivity of 71% and specificity of 88%, whereas at 10 mg/dL, sensitivity was 68% and specificity was 97%.35 Other studies reported a sensitivity of 64% and specificity of 100%, which increased to 90% and 91% when combined with CA125 and CA15-3.11,14

CA242 exhibited a sensitivity of 68.21% and specificity of 62.86% at a cut-off of 14.250 mg/dL, with 74.57% of colorectal cancer patients testing positive. These results differ from prior research, where only 9.50% of colorectal cancer patients tested positive for CA242.5 Combining CEA and CA242 improved diagnostic sensitivity to 72.45% and specificity to 81.75%. Previous studies reported a sensitivity of 69.30% and specificity of 84.60% for the same combination, confirming that combining CEA and CA242 enhances colorectal cancer detection accuracy.15

V. CONCLUSION

The findings indicate that combined CA242 and CEA examination achieves an accuracy of 79.65% as a diagnostic predictor for colorectal cancer at RS Adam Malik. Further studies to combined another marker with CA242 is recommended to validate and strengthen these findings.

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