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Relationship between Plasma Calcium and Carcino Embryonic Antigen among Colorectal Cancer patients

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Abstract

Background: Colorectal cancer (CRC) is one of the leading causes of cancer-related morbidity and mortality worldwide. Carcinoembryonic antigen (CEA) is widely used as a tumor marker in CRC for diagnosis, prognosis, and monitoring response to therapy. Alterations in plasma calcium levels are frequently observed in malignancies and may reflect tumor burden or paraneoplastic phenomena. This study aimed to evaluate the relationship between plasma calcium levels and CEA among patients with CRC.

Methods: A cross-sectional analytical study was conducted among 100 histopathologically confirmed CRC patients attending a tertiary care hospital for 01 Year. Demographic, clinical, and laboratory data were collected. Plasma total calcium and serum CEA were measured at diagnosis prior to treatment. Patients were categorized based on CEA levels and calcium status. Statistical analysis included Pearson's correlation, independent t-test, ANOVA, and multivariate linear regression.

Results: The mean age of participants was 58.6 ± 12.4 years, with a male predominance (60%). Elevated CEA (>5 ng/mL) was observed in 68% of patients, while hypercalcemia (>10.5 mg/dL) was present in 18%. A statistically significant positive correlation was found between plasma calcium and CEA levels ($r = 0.42$, $p < 0.001$). Patients with metastatic disease had significantly higher mean calcium and CEA levels compared to non-metastatic patients ($p < 0.001$). Multivariate analysis demonstrated that plasma calcium remained independently associated with CEA after adjusting for age, sex, and tumor stage ($\beta = 0.38$, $p = 0.002$).

Conclusion: Plasma calcium levels show a significant positive association with CEA among CRC patients. Monitoring calcium alongside CEA may provide additional prognostic information, particularly in advanced disease.

Keywords: Colorectal cancer, plasma calcium, carcinoembryonic antigen, tumor markers, hypercalcemia

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Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second leading cause of cancer-related deaths globally. According to World Health Organization, CRC accounts for millions of new cases annually, with increasing incidence in developing countries[1].

Carcinoembryonic antigen (CEA) is a glycoprotein involved in cell adhesion, first described in 1965 by Phil Gold and Samuel O. Freedman. Although not specific for CRC, CEA remains one of the most widely used biomarkers for prognosis, recurrence detection, and treatment monitoring[2].

Disturbances in calcium metabolism are common in malignancy. Hypercalcemia of malignancy may result from tumor secretion of parathyroid hormone-related peptide (PTHrP), osteolytic metastases, or dysregulated vitamin D metabolism. While hypercalcemia is more commonly associated with breast cancer, lung cancer, and multiple myeloma, it may also occur in advanced CRC, particularly with bone metastases[3-4].

Calcium is essential for intracellular signaling cascades, apoptosis, and cell division. The development of tumors may be aided by dysregulated calcium homeostasis. According to experimental research, the amount of calcium outside the cell affects the adherence and migration of tumor cells [5].

There is little information on the direct correlation between plasma calcium and CEA levels in patients with colorectal cancer (CRC), despite the well-established functions of CEA and calcium in oncology. Gaining knowledge of this link could help us better understand the prognosis and disease burden [6]. The objective of this study was to assess the correlation between CEA and plasma calcium in 100 patients with colorectal cancer and investigate its relevance to metastasis and tumor stage.

Materials and Methods

A hospital-based cross-sectional analytical study was conducted at a tertiary care teaching hospital for 01 year.

Study Population

One hundred patients aged ≥18 years with histopathologically confirmed colorectal adenocarcinoma were enrolled. Patients with known primary hyperparathyroidism, chronic kidney disease stage IV/V, vitamin D intoxication, or on calcium supplements were excluded.

Sample Size

A sample size of 100 was calculated based on an anticipated moderate correlation ($r = 0.3$), 95% confidence level, and 80% power.

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Data Collection

Data were collected using a structured proforma including:

- Demographic variables (age, sex)
- Clinical features
- Tumor characteristics (site, stage, metastasis)
- Laboratory parameters (plasma calcium, serum CEA)

Tumor staging was performed according to the TNM classification system.

Laboratory Analysis

- Plasma total calcium was measured using the o-cresolphthalein complexone method.
- Serum CEA was measured by chemiluminescent immunoassay.
- Hypercalcemia: >10.5 mg/dL
- Elevated CEA: >5 ng/mL

Statistical Analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± SD. Categorical variables were expressed as frequency and percentage. Pearson's correlation assessed the relationship between calcium and CEA. Independent t-test and ANOVA compared means across groups. Multivariate regression identified independent predictors of CEA. A p-value <0.05 was considered statistically significant.

Results

Table 1: Baseline Demographic and Clinical Characteristics (n = 100)

Variable	Frequency (%) / Mean ± SD
Age (years)	58.6 ± 12.4
<50 years	22 (22%)
50–65 years	48 (48%)
>65 years	30 (30%)
Male	60 (60%)
Female	40 (40%)
Colon cancer	62 (62%)
Rectal cancer	38 (38%)
Stage I	10 (10%)
Stage II	28 (28%)
Stage III	34 (34%)
Stage IV	28 (28%)
Metastasis present	30 (30%)

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Table 2: Distribution of Plasma Calcium and CEA Levels

Parameter	Mean ± SD	Normal n (%)	Elevated n (%)
Plasma Calcium (mg/dL)	9.82 ± 0.96	82 (82%)	18 (18%)
Serum CEA (ng/mL)	14.6 ± 18.2	32 (32%)	68 (68%)

Among hypercalcemic patients, 16 (88.9%) had elevated CEA levels.

Table 3: Comparison of Calcium and CEA by Tumor Stage

Stage	Calcium (mg/dL) Mean ± SD	CEA (ng/mL) Mean ± SD
I	9.12 ± 0.44	3.8 ± 1.6
II	9.45 ± 0.63	6.2 ± 3.4
III	9.96 ± 0.78	14.9 ± 8.7
IV	10.68 ± 1.02	32.4 ± 24.5
p-value	<0.001	<0.001

Both calcium and CEA levels increased significantly with advancing stage.

Table 4: Correlation and Regression Analysis

Variable	r-value	p-value
Calcium vs CEA	0.42	<0.001

Multivariate Linear Regression (Dependent Variable: CEA)

Predictor	β Coefficient	p-value
Plasma Calcium	0.38	0.002
Age	0.09	0.28
Sex	0.05	0.46
Stage	0.41	<0.001

Discussion

This study demonstrated a significant positive correlation between plasma calcium and CEA levels among CRC patients[7]. Elevated calcium levels were more common in advanced-stage disease and in patients with metastasis.

The observed hypercalcemia prevalence (18%) is comparable to previous oncology studies reporting 10–20% prevalence in advanced cancers. Although CRC is not classically associated with hypercalcemia, metastatic disease may contribute via osteolytic activity or humoral factors[8-9].

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CEA is widely recognized as a prognostic marker in CRC. Our finding that CEA levels increase progressively from stage I to IV aligns with previous studies demonstrating its correlation with tumor burden and survival outcomes[10].

The moderate correlation (r = 0.42) suggests that while related, calcium and CEA reflect partially independent biological processes. Multivariate regression confirmed that calcium independently predicts elevated CEA even after adjusting for stage[11-12].

Potential mechanisms linking calcium and tumor activity include:

1. Increased osteoclastic bone resorption in metastatic disease
2. PTHrP-mediated hypercalcemia
3. Calcium-mediated intracellular signaling promoting tumor progression

Our findings suggest that plasma calcium measurement may complement CEA in assessing disease severity.

- Combined assessment may improve prognostic stratification
- Hypercalcemia may indicate advanced disease
- Routine calcium monitoring is inexpensive and accessible

Limitations

- Cross-sectional design limits causal inference
- Total calcium measured instead of ionized calcium
- Single-center study
- Lack of PTHrP measurements

Future longitudinal studies are recommended to assess predictive value for survival and recurrence.

Conclusion

There is a significant positive association between plasma calcium and CEA levels in colorectal cancer patients. Elevated calcium is more prevalent in advanced stages and correlates with tumor burden. Combined monitoring of plasma calcium and CEA may enhance clinical assessment and prognostication in CRC.

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ISSN: 0975-3583, 0976-2833 VOL15, ISSUE2, 2024

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