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ARTICLE

THE RELATIONSHIP BETWEEN TUMOR SIZE PARAMETERS AND CARCINOEMBRYONIC ANTIGEN (CEA) LEVELS IN COLORECTAL ADENOCARCINOMA BASED ON CONTRAST-ENHANCED ABDOMINAL CT SCAN

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ABSTRACT

Colorectal adenocarcinoma is common and deadly worldwide, including Indonesia. CEA is a colorectal cancer marker, while contrast-enhanced abdominal CT scans show tumor area and thickness. Tumor size and CEA levels are debated in medical literature. CEA levels, contrast-enhanced abdominal CT scan area, and colorectal cancer thickness were evaluated in this study. RSUP Prof. Dr. I.G.N.G. Ngoerah conducted this retrospective analytical observational cross-sectional study from January 2018 to July 2023. Colorectal cancer patients with contrast-enhanced abdominal CT images and CEA levels were studied. Statistics included Pearson correlation and multivariate linear regression. Even after controlling for age and sex, tumor area and CEA levels were positively correlated by Pearson correlation (r = 0.513; p = 0.001) and multivariate regression analysis (B = 0.547; 95% CI: 0.246–0.848; p = 0.001). CEA levels did not affect tumor thickness (r = 0.196; p = 0.224). The study revealed no association between CEA and tumor thickness. CEA values strongly correlate with colorectal adenocarcinoma tumor area but not thickness. CEA may be measured by tumor area.

Keywords: Colorectal adenocarcinoma; contrast-enhanced abdominal CT scan; tumor area; tumor thickness; CEA.

АБСТРАКТ

Аденокарцинома толстой кишки является распространенным и смертельно опасным заболеванием во всем мире, включая Индонезию. CEA является маркером рака толстой кишки, а контрастная компьютерная томография брюшной полости показывает площадь и толщину опухоли. Размер опухоли и уровни CEA являются предметом дискуссий в медицинской литературе. В данном исследовании были оценены уровни CEA, площадь контрастной компьютерной томографии брюшной полости и толщина рака толстой кишки. Профессор И.Г.Н.Г. Нгоера провел это ретроспективное аналитическое наблюдательное кросс-секционное исследование с января 2018 года по июль 2023 года. Исследовались пациенты с колоректальным раком, у которых были проведены контрастные КТ-сканирования брюшной полости и определены уровни CEA. Статистические данные включали корреляцию Пирсона и многомерную линейную регрессию. Даже после учета возраста и пола площадь опухоли и уровни CEA положительно коррелировали по корреляции Пирсона (r = 0,513; p = 0,001) и многомерному регрессионному анализу (B = 0,547; 95% ДИ: 0,246–0,848; p = 0,001). Уровни CEA не влияли на толщину опухоли (r = 0,196; p = 0,224). Исследование не выявило связи между CEA и толщиной опухоли. Значения CEA сильно коррелируют с площадью опухоли колоректальной аденокарциномы, но не с ее толщиной. CEA можно измерить по площади опухоли.

Ключевые слова: колоректальная аденокарцинома; контрастная компьютерная томография брюшной полости; площадь опухоли; толщина опухоли; CEA.

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INTRODUCTION

Colorectal adenocarcinoma is one of the most common cancers worldwide, with a steadily increasing incidence largely associated with dietary and lifestyle changes similar to those in developed countries. It has become a major health problem in developing nations, creating an urgent need for early detection to reduce mortality and improve survival rates.[1] Globally, colorectal cancer is the second leading cause of cancer-related death, with an estimated 1.8 million new cases and nearly 900,000 deaths each year.[2]

In Indonesia, colorectal cancer ranks among the top five most prevalent cancers, with cases rising annually. Most patients are diagnosed at advanced stages due to limited early detection facilities, leading to persistently high mortality rates and placing additional strain on the healthcare system.[3]

Radiological modalities play a central role in the diagnosis of colorectal cancer. Conventional methods such as X-ray and fluoroscopy provide limited information, while abdominal ultrasonography is less sensitive for detecting small lesions.[4] Advanced modalities, including MRI, are effective in assessing local invasion, whereas contrast-enhanced CT scans are highly valuable for evaluating tumor size, location, and spread. Moreover, CT colonography offers three-dimensional visualization of the colon without invasive procedures.[5]

Contrast-enhanced abdominal CT scans allow precise measurement of tumor parameters such as area and thickness, which are critical for treatment planning [6]. An important area of investigation is their correlation with Carcinoembryonic Antigen (CEA) levels, a tumor marker frequently elevated as the disease progresses, particularly in metastatic cases.[7]

However, studies on the correlation between tumor size and CEA levels have produced inconsistent findings,[8] reported a significant association, while[9] found that elevated CEA did not always correspond with larger tumor size, particularly in early-stage disease. Halilovic et al.[10] observed stronger correlations in metastatic cases but not in localized tumors.

This study contributes new insights by providing radiologically quantified measurements of tumor area and thickness using contrast-enhanced abdominal CT scans, rather than relying on subjective or gross surgical size estimations used in many previous reports.[6] The finding that tumor area, but not thickness, correlates significantly with serum CEA levels helps clarify earlier inconsistencies in the literature, where studies often used heterogeneous definitions of tumor size.[8,12] By separating two distinct morphological parameters (area and thickness), this research demonstrates that overall tumor surface burden, rather than local wall invasion depth, more accurately reflects CEA production in colorectal adenocarcinoma.[13] These results therefore refine the understanding of the relationship between tumor morphology and biomarker expression, supporting the use of CT-based area measurement as a more reliable indicator of systemic tumor activity.[12]

These discrepancies suggest that the relationship between tumor size and CEA levels may be influenced by clinical factors such as disease stage and metastasis **[10,18].** However, these clinical parameters were not included in the present study, as the analysis was focused on radiological parameters (tumor area and thickness) and their direct relationship with CEA levels. Future studies incorporating disease stage and metastatic status are warranted to explore their combined influence on biomarker expression.[13] Further research is therefore needed to clarify this correlation across different stages of colorectal adenocarcinoma. Such studies may enhance the predictive value of CEA and provide clinicians with more accurate guidance for diagnosis and treatment planning.[14]

MATERIAL AND METHODS

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This research was an analytical observational study with a retrospective cross-sectional design, in which independent and dependent variables were examined simultaneously. The study aimed to evaluate the correlation between the area and thickness of colorectal adenocarcinoma measured by contrast-enhanced abdominal CT scans and carcinoembryonic antigen (CEA) levels. Data collection took place at the Medical Records Unit, Radiology Department, and Laboratory of RSUP Prof. Dr. dr. I.G.N.G Ngoerah, Denpasar, covering the period from January 2018 to July 2023. The study population consisted of inpatients diagnosed with colorectal adenocarcinoma confirmed histopathologically, who had undergone both contrast-enhanced abdominal CT scans and CEA testing. Subjects were selected using simple random sampling according to inclusion and exclusion criteria, with a **minimum required sample size of 38** calculated for correlation analysis. The sample size was determined through **a power analysis based on Cohen's formula (1992),** assuming a medium effect size ($r = 0.4$), $\alpha = 0.05$, and power $(1-\beta) = 0.80$.

Inclusion criteria:

1) Patients aged 18 years or older
2) Complete medical records available
3) Histopathologically confirmed colorectal adenocarcinoma
4) Contrast-enhanced abdominal CT scan and CEA results recorded in the hospital's electronic system

Exclusion criteria:

1) Incomplete medical records
2) Other types of colorectal tumors
3) Severe comorbidities influencing CEA levels (such as advanced liver disease or other malignancies)
4) Prior major abdominal surgery or procedures affecting imaging interpretation
5) Active smoking status

Tumor area and thickness were measured using PACS INFINITT software (INFINITT Healthcare, South Korea) with multiplanar reconstruction (MPR**)** in axial, coronal, and sagittal planes. The tumor area was obtained by manually tracing the outer tumor border on the axial slice showing the largest cross-sectional area using the *region of interest (ROI)* tool, and the value was automatically calculated by the software in square centimeters (cm^2). For patients with multiple lesions, the lesion with the largest area was selected for analysis. The tumor thickness was defined as the maximum perpendicular distance measured from the luminal surface of the bowel wall to the outermost tumor margin on the same axial slice used for area measurement. The use of MPR views in coronal and sagittal planes helped ensure measurement accuracy and consistency. All measurements were performed by a radiologist from the Radiology Department of RSUP Prof. Dr. I.G.N.G. Ngoerah, Denpasar, and verified under supervision to maintain measurement reliability.

Data were collected retrospectively from electronic medical records, including demographic characteristics, CT scan measurements, and CEA levels. Serum CEA levels (ng/mL) were obtained from the hospital's laboratory database. Measurements were performed using the electrochemiluminescence immunoassay **.** The normal reference range applied in this study was <5 ng/mL for non-smokers and <10 ng/mL for smokers, as used by the institution's clinical laboratory. To ensure temporal comparability between imaging and biomarker data, CEA levels were collected within 2–4 weeks before or after the CT scan**,** minimizing potential fluctuations that could affect correlation accuracy.

All patient data were anonymized, coded, and stored securely with restricted access to the research team. Statistical analysis was performed using SPSS version 25.0. Descriptive statistics were used to summarize subject characteristics, and normality testing determined the choice of correlation method (Pearson or Spearman). Correlation analysis examined the relationship between tumor

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parameters and CEA levels, while linear regression was applied to assess the combined effect of tumor area and thickness on CEA, with adjustment for potential confounders such as age and sex. Ethical approval for this study was obtained from the Research Ethics Committee of the Faculty of Medicine, Udayana University/RSUP Prof. Dr. I.G.N.G. Ngoerah, Denpasar, Indonesia**,** under approval number 1148/UN14.2.2.VII.14/LT/2023**.**
The study was conducted in accordance with the principles of respect, beneficence, non-maleficence, and justice.

RESULT

Table 1. Descriptive Statistics of Age, CEA Levels, Tumor Area, and Tumor Thickness in 40 Study Subjects

Variable	N	Minimum	Maximum	Mean	Standard Deviation
Age (years)	40	40	80	58.63	10.394
CEA level (ng/mL)	40	1.43	90.44	14.21	17.825
Tumor area (cm^2)	40	3.36	77.52	27.07	16.739
Tumor thickness (cm)	40	0.90	7.40	2.66	1.638

Based on the descriptive statistical analysis of 40 study subjects, the mean age was 58.63 years, ranging from 40 to 80 years, with a standard deviation of 10.394. The mean CEA level was 14.21 ng/mL, with values ranging from 1.43 to 90.44 ng/mL and a standard deviation of 17.825. The mean tumor area was 27.07 cm^2, with a minimum of 3.36 cm^2 and a maximum of 77.52 cm^2, and a standard deviation of 16.739. Meanwhile, the mean tumor thickness was 2.66 cm, ranging from 0.90 to 7.40 cm, with a standard deviation of 1.638.

Table 2. Distribution of Respondents by Sex and Histopathological Biopsy Types (N = 40)

Variable	Frequency (n)	Percentage (%)
Sex		
Male	22	55.0
Female	18	45.0
Histopathological Category		
Adenocarcinoma, Low Grade (well/moderately differentiated)	28	70.0
Adenocarcinoma, High Grade / Poorly Differentiated	3	7.5
Mucinous Adenocarcinoma, Low Grade	4	10.0
Intramucosal Adenocarcinoma	1	2.5
Adenocarcinoma NOS (Not Otherwise Specified)	2	5.0
Other Adenocarcinoma (site-specific: rectum, colon, etc.)	2	5.0

The majority of respondents in this study were male, accounting for 22 individuals (55%), while female respondents represented 18 individuals (45%). Regarding

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histopathological biopsy results, most cases (70%) were classified as low-grade adenocarcinoma (well or moderately differentiated), indicating preserved cellular differentiation and generally a better prognosis. Mucinous adenocarcinoma and high-grade adenocarcinoma were found in 10% and 7.5% of cases, respectively, reflecting smaller proportions of more aggressive forms. These findings suggest that most colorectal adenocarcinoma cases in this cohort were identified at stages with potentially favorable therapeutic responses.

Table 3. Shapiro–Wilk Normality Test Results for CEA Levels, Tumor Area, and Tumor Thickness

Variable	Shapiro–Wilk Statistic	df	Sig.
CEA level (ng/mL)	0.621	40	0.124
Tumor area (cm^2)	0.865	40	0.345
Tumor thickness (cm)	0.839	40	0.206

Normality testing was performed using the Shapiro–Wilk test, as the sample size was fewer than 50. Based on Table 5.4, all tested variables—CEA levels, tumor area, and tumor thickness—had significance values (p) greater than 0.05. This indicates that the data were statistically normally distributed. Therefore, subsequent statistical analyses were carried out using parametric methods, specifically Pearson correlation and linear regression, while controlling for potential confounders such as age and sex.

In this study, only age and sex were included as control variables in the multivariate analysis because these data were consistently available for all subjects. Other potentially relevant clinical factors such as disease stage, metastatic status, tumor differentiation, lymph node involvement, and specific genetic markers were not analyzed due to data limitations. This is recognized as a study limitation and may influence the relationship between tumor characteristics and CEA levels.

Table 4. Correlation between Colorectal Adenocarcinoma Area (Contrast-Enhanced Abdominal CT Scan) and CEA Levels

Variable	Correlation Coefficient (r)	p-value	N
Tumor Area (cm^2) vs CEA (ng/mL)	0.513**	0.001	40

The Pearson correlation test showed a positive and statistically significant association between CEA levels and tumor area (r = 0.513, p = 0.001). This indicates that larger tumor size tends to be associated with higher CEA levels in the blood. Since the p-value was less than 0.05, this relationship can be considered statistically significant, suggesting that CEA may serve as an indirect indicator of tumor size in patients with colorectal adenocarcinoma.

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Table 5. Relationship between Colorectal Adenocarcinoma Area (Contrast-Enhanced Abdominal CT Scan) and CEA Levels after Controlling for Age and Sex

Model	Variable	B Coefficient	95% CI	p-value
Model 1	(Constant)	-15.858	-51.623 – 19.907	0.374
	Age	0.222	-0.283 – 0.726	0.378
	Sex	1.687	-8.951 – 12.326	0.749
	Tumor Area (cm^2)	0.533	0.221 – 0.846	0.001
Model 2	(Constant)	-12.919	-43.095 – 17.257	0.391
	Age	0.209	-0.282 – 0.701	0.394
	Tumor Area (cm^2)	0.543	0.240 – 0.845	0.001
Model 3	(Constant)	-0.733	-10.258 – 8.792	0.877
	Tumor Area (cm^2)	0.547	0.246 – 0.848	0.001

As shown in Table 5.6, there was a statistically significant association between colorectal adenocarcinoma area measured on contrast-enhanced abdominal CT scans and CEA levels, both in the initial and simplified regression models. In Model 1, after adjusting for age and sex, tumor area remained a significant predictor of CEA (B = 0.533, 95% CI: 0.221–0.846, p = 0.001), while age (p = 0.378) and sex (p = 0.749) were not significant. In Model 2, after excluding sex from the model, tumor area still showed a significant relationship with CEA (B = 0.543, 95% CI: 0.240–0.845, p = 0.001), with age remaining non-significant (p = 0.394). In the Final Model (Model 3), tumor area alone was retained as the predictor, and the result was consistent: tumor area remained a significant predictor of CEA levels (B = 0.547, 95% CI: 0.246–0.848, p = 0.001). Overall, these findings indicate that tumor area is a strong and independent predictor of CEA levels. Each 1 cm^2 increase in tumor area was associated with an approximate 0.547 ng/mL increase in CEA, even after controlling for age and sex.

Table 6. Pearson Correlation Test between CEA Levels and Tumor Thickness

Variable	Correlation Coefficient (r)	p-value	N
Tumor Thickness vs CEA (ng/mL)	0.196	0.224	40

Based on Table 5.7, the correlation between CEA levels and tumor thickness showed a Pearson correlation coefficient of r = 0.196 with a p-value of 0.224. This indicates a very weak positive relationship that was not statistically significant (p > 0.05). Thus, CEA levels were not meaningfully associated with tumor thickness in this dataset.

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Table 7. Relationship between Colorectal Adenocarcinoma Thickness (Contrast-Enhanced Abdominal CT Scan) and CEA Levels after Controlling for Age and Sex

Model	Variable	B Coefficient	95% CI	p-value
Model 1	(Constant)	-14.030	-54.884 – 26.825	0.491
	Age	0.251	-0.311 – 0.813	0.372
	Sex	5.164	-6.483 – 16.811	0.375
	Tumor Thickness (cm)	2.279	-1.275 – 5.833	0.202
Model 2	(Constant)	-4.266	-38.557 – 30.024	0.802
	Age	0.219	-0.337 – 0.774	0.430
	Tumor Thickness (cm)	2.128	-1.397 – 5.653	0.229
Model 3	(Constant)	8.520	-2.391 – 19.431	0.122
	Tumor Thickness (cm)	2.139	-1.366 – 5.644	0.224

Tumor thickness did not show a statistically significant relationship with CEA levels across all three regression models. Although the regression coefficients were consistently positive, suggesting a tendency for higher CEA with increasing tumor thickness, the wide 95% confidence intervals crossing zero and p-values above 0.05 indicated that this relationship was not statistically meaningful. In Model 1, after controlling for age and sex, tumor thickness had a regression coefficient of 2.279 (95% CI: -1.275 to 5.833, p = 0.202), implying a non-significant increase of 2.279 ng/mL in CEA for every 1 cm increase in thickness. Neither age (p = 0.372) nor sex (p = 0.375) had significant effects. In Model 2 (age and thickness only) and the Final Model (Model 3) (thickness only), tumor thickness remained non-significant, with p-values of 0.229 and 0.224, respectively. Overall, tumor thickness was not a significant predictor of CEA levels, whether or not age and sex were controlled.

DISCUSSION

The respondents' characteristics in this study included age, sex, CEA levels, tumor area, and tumor thickness, assessed using contrast-enhanced abdominal CT scans. The mean age was 58.63 years (range: 40–80), indicating that most cases occurred in middle-aged to elderly individuals. This aligns with the literature, which identifies advanced age as a major risk factor for colorectal cancer due to accumulated genetic mutations and chronic mucosal inflammation over time.[11,12] The mean CEA level was 14.21 ng/ml, reflecting elevated biomarker values within the study population. Elevated CEA levels, as explained in Chapter II, are widely used in colorectal cancer monitoring and may suggest a larger tumor burden, local invasion, or even metastasis.[13,14]

Tumor size parameters also varied considerably, with the tumor area ranging from 3.36 cm^2 to 77.52 cm^2 (mean: 27.07 cm^2) and thickness ranging from 0.90 cm to 7.40 cm (mean: 2.66 cm). These radiological findings are important for assessing disease stage and progression, as larger and thicker tumors are associated with greater invasive potential and

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systemic involvement.[15,16] Regarding sex distribution, the majority of respondents were male (55%), which is consistent with epidemiological data indicating a higher prevalence of colorectal cancer in men compared to women. This discrepancy is often attributed to hormonal influences, lifestyle, and higher rates of smoking and alcohol consumption among men, factors that may also contribute to elevated CEA levels.[13,14]

Normality testing using the Shapiro–Wilk method, as shown in Table 5.3, revealed that all numerical variables (CEA levels, tumor area, and tumor thickness) had significance values greater than 0.05, confirming a normal statistical distribution. This supports the use of parametric methods such as Pearson correlation and linear regression for further analysis, allowing adjustment for confounding factors like age and sex, which can directly or indirectly affect CEA levels.[11,12] Overall, the clinical profile of the respondents is consistent with the literature on colorectal adenocarcinoma. The elevated mean CEA levels and relatively large tumor sizes underscore the role of CEA as a biomarker of tumor burden, reinforcing the value of contrast-enhanced CT scans and CEA measurements as diagnostic, evaluative, and prognostic tools in colorectal cancer management.

The findings of this study demonstrate a statistically significant relationship between the size of colorectal adenocarcinoma, as measured through contrast-enhanced abdominal CT scans, and serum CEA levels. Pearson's correlation analysis yielded r = 0.513 with p = 0.001, indicating a moderate-to-strong positive correlation. This suggests that the larger the tumor area identified radiologically, the higher the CEA levels detected in the patient's blood. These results imply that CEA levels may reflect the systemic tumor burden and serve as an indirect indicator of colorectal adenocarcinoma size.[13,14]

Biologically, this finding is consistent with the role of CEA as a glycoprotein produced by adenocarcinoma cells. As the number of malignant cells increases and tissue invasion expands, CEA production rises significantly. Previous studies have shown that CEA is an important biomarker in staging, monitoring therapeutic response, and early detection of recurrence in colorectal cancer.[17,18] The results of the stepwise linear regression further confirmed that tumor size was a significant independent predictor of CEA levels, while age and sex were not significant confounders.[16]

In contrast to tumor size, Pearson's correlation analysis between colorectal adenocarcinoma thickness and CEA levels yielded r = 0.196 with p = 0.224, indicating a very weak and statistically nonsignificant correlation. This suggests that an increase in tumor thickness is not consistently associated with elevated CEA levels. From a biological perspective, this difference can be explained by the fact that tumor thickness reflects the depth of local invasion, whereas CEA production is more strongly influenced by the overall tumor mass rather than depth of infiltration alone.[14,16]

From a radiological perspective, limitations of CT scans in accurately measuring tumor thickness may also influence the findings. Measurement reliability can be affected by image quality, bowel movement, or the presence of intraluminal gas or fluid, which may contribute to variability in interpretation. [21] This reinforces the notion that CEA levels are better indicators of tumor size and volume rather than depth. Consequently, tumor thickness alone cannot be regarded as a predictive marker for CEA levels. A more comprehensive assessment requires a multidimensional approach, combining radiological parameters such as tumor size and volume with serum biomarkers, to better characterize tumor burden and disease progression.[16]

CONCLUSION

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Based on the results and discussion, this study concludes that there is a statistically significant positive relationship between colorectal adenocarcinoma size, as measured by contrast-enhanced abdominal CT scan, and serum CEA levels, with Pearson's correlation ($r = 0.513$; $p = 0.001$) and final regression model analysis ($B = 0.547$; 95% CI: 0.246–0.848; $p = 0.001$) confirming tumor size as an independent predictor even after controlling for age and sex. In contrast, no significant association was found between tumor thickness and CEA levels ($r = 0.196$; $p = 0.224$), indicating that tumor thickness cannot be used as a predictor of CEA in this study. These findings highlight the clinical importance of prioritizing tumor size assessment via CT scan, supported by CEA measurement, in monitoring disease progression and determining prognosis in colorectal adenocarcinoma.

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DECLARATIONS

I, Dewa Putu Jaya Prasatya, as the principal investigator, hereby declare that this thesis was completed under the guidance and supervision of Ni Nyoman Margiani (Supervisor I), I Gusti Agung Gede Mahendra Wijaya (Supervisor II), and I Wayan Gede Artawan Eka Putra (Supervisor III), to whom I express my highest gratitude for their valuable direction and continuous support throughout the research and preparation of this work.

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