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Concordance and Discordance Between PET/CT and CEA/CA19-9 Dynamics and Their Predictive Value for Clinical Prognosis in Colorectal Cancer

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ABSTRACT

Aim: The study aimed to evaluate the concordance between treatment-related changes in fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) -derived metabolic parameters and serum tumor markers [carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9)] and to investigate the clinical significance of concordant and discordant response patterns in colorectal cancer.

Methods: This retrospective study included 81 patients with histologically confirmed colorectal cancer who underwent FDG PET/CT before and after systemic chemotherapy. Metabolic response was defined as a ≥30% maximum standardized uptake value reduction, and ≥20% decrease in CEA or CA19-9 levels defined as tumor marker response. Patients were categorized into concordant-good-response, concordant-poor-response, and discordant-response groups based on PET and CEA responses. Survival was analyzed using Kaplan-Meier and Cox regression methods.

Results: Following systemic chemotherapy, treatment responses were evaluated using changes in FDG PET/CT metabolic parameters and serum tumor markers. Significant reductions were observed in all PET-derived metabolic parameters ($p<0.001$) and in CEA levels ($p=0.008$) after treatment, whereas CA19-9 did not show a significant change ($p=0.751$). No significant association was found between PET response and CEA response ($p=0.492$) or between PET response and CA19-9 response ($p=0.807$); however, a significant association was observed between CEA and CA19-9 responses ($p<0.001$). Concordance groups were significantly associated with mortality ($p=0.036$), and overall survival (OS) differed among groups (log-rank $p=0.043$). The concordant good-response group had the longest survival, whereas the concordant poor-response group had the shortest. The discordant response group exhibited intermediate survival outcomes.

Conclusion: The combined assessment of PET-derived metabolic response and CEA response is associated with OS in colorectal cancer. Concordance patterns may provide clinically meaningful information, while discordant responses likely reflect heterogeneous tumor biology.

Keywords: Colorectal cancer, FDG PET/CT, CEA blood test, treatment, prognosis

Introduction

Colorectal cancer continues to rank as the third most frequently diagnosed malignancy worldwide, with rising incidence in developing regions despite a decline in high-income countries [1]. Current global estimates indicate substantial regional and population-based variation in the burden of colorectal cancer, which is anticipated to increase in the years ahead [2]. Current treatment strategies for colorectal cancer include surgical resection for localized disease and multimodal approaches for advanced stages, primarily involving chemotherapy, with radiotherapy and immunotherapy used in selected cases. Biomarkers such as

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carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) are primarily used in clinical practice for monitoring disease progression [3].

In contrast, functional imaging modalities, particularly fluorine-18-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT), enable the evaluation of tumor metabolism and may provide a more comprehensive assessment of treatment response. In the setting of serial CEA elevation, ^{18}F-FDG PET/CT is recommended as a problem-solving tool in accordance with National Comprehensive Cancer Network guidelines [4].

However, the relationship between metabolic imaging findings and serum tumor markers is not always consistent, and discordant results are frequently encountered in clinical practice. The clinical implications of such discordance remain unclear.

Therefore, this study aimed to evaluate the concordance between treatment-related changes in ^{18}F-FDG PET/CT findings and in serum tumor markers and to investigate the clinical significance of discordant results in relation to patient outcomes.

Methods

This retrospective analysis comprised 81 patients with histologically confirmed colorectal cancer who underwent FDG PET/CT examinations both before and after systemic chemotherapy. Clinical, imaging, and laboratory data were obtained from institutional records. Ethical approval has been obtained from the University of Health Sciences Türkiye, Ankara Etlik City Hospital No. 1 Scientific Research Ethics Committee (approval no: AEŞH-BADEKI-2025-735, date: 24.12.2025). The requirement for informed consent has been removed.

All patients received systemic chemotherapy between pre-treatment and post-treatment PET/CT examinations, and treatment response was evaluated based on changes in PET-derived parameters and serum tumor markers.

Patients who underwent surgical resection between the two PET/CT examinations were excluded.

Demographic data (age, sex), tumor location (colon or rectum), serum tumor markers (CEA and CA19-9), and primary tumor PET parameters were recorded from both the pre- and post-treatment PET/CT scans. PET parameters included the maximum standardized uptake value (SUV_{max}) derived from the primary tumor, as well as metabolic tumor volume (MTV) and total lesion glycolysis (TLG), which were both calculated using the same volume of interest. Serum tumor markers were measured within one month of the PET/CT to ensure temporal consistency.

Metabolic response was defined based on changes in SUV_{max}. A reduction of ≥30% was considered a metabolic response, based on thresholds inspired by PET response criteria in solid tumors (PERCIST) criteria, although SUV_{max} rather than peak SUV_{max} normalized to lean body mass was used [4]. Tumor marker response was defined as a ≥20% decrease in CEA or CA19-9; additionally, a ≥50% reduction in CEA was explored for sensitivity analysis [5]. Patients with complete metabolic response (CMR), defined as the absence of FDG-avid lesions, were classified as responders.

Based on PET (SUV_{max}) and CEA responses, patients were categorized into three groups: concordant good response (both responses present), concordant poor response (no response in either parameter), and discordant response (mismatch between PET and CEA responses).

Percentage changes were calculated as (post-pre)/pre×100. However, analyses were primarily based on directional changes (increases vs. decreases). For volumetric parameters (MTV and TLG), only patients with measurable values at both time points were included.

Statistical Analysis

Statistical evaluation was performed using IBM SPSS Statistics for Mac (version 27.0; IBM Corp., Armonk, NY, USA).

Shapiro-Wilk test was used to evaluate the distribution of continuous variables and results were expressed accordingly as either mean ± standard deviation or median with interquartile range. Changes between pre- and post-treatment measurements were examined with the Wilcoxon signed-rank test, whereas categorical data were compared using the chi-square or Fisher's exact tests, where applicable.

The association between PET-derived metrics and tumor markers was explored using Spearman correlation analysis. Overall survival (OS) was calculated from the date of baseline PET/CT to death or the last known follow-up. Survival probabilities were estimated using Kaplan-Meier curves and differences between groups were assessed with the log-rank test. To further investigate the effects of the variables on OS, Cox proportional hazards models were applied. Statistical significance was defined as a two-sided p value below 0.05.

AI-assisted language tools were used for English editing of the manuscript.

Results

A total of 81 patients who underwent systemic chemotherapy were included, and their treatment responses were evaluated by changes in FDG PET/CT metabolic parameters and serum tumor markers. The mean age was 64.1±11.3 years (range: 25-90), and 47 (58.0%) were male and 34 (42.0%) were female. 50 patients (61.7%) had colon cancer and 31 (38.3%) had rectal cancer. The mean follow-up duration was 20.6±10.1 months (range: 6-70). According to the PET-CEA concordance classification, 22.2% of patients had a concordant good response, 18.5% had a concordant poor response, and 59.3% had a discordant response. No significant association was observed between PET-CEA concordance groups and metastatic disease status (χ^2=0.457, p=0.796). The baseline demographic and clinical characteristics of the study population are summarized in Table 1.

Comparison of pre- and post-treatment values demonstrated a significant reduction in CEA levels (median, 7.30 vs. 4.80; p=0.008), whereas the decrease in CA19-9 levels was not statistically significant (median, 22.80 vs. 18.20; p=0.751).

Table 1. Baseline demographic and clinical characteristics of the study population (n=81)	
Variable	**Value**
Age (years), mean ± SD	64.1±11.3
Age (range)	25-90
Sex, n (%)	
Male	47 (58.0%)
Female	34 (42.0%)
Diagnosis, n (%)	
Colon cancer	50 (61.7%)
Rectal cancer	31 (38.3%)
Follow-up duration, mean ± SD	20.6±10.1
Follow-up duration, range	6-70
PET-CEA concordance groups, n (%)	
Concordant good	18 (22.2%)
Concordant poor	15 (18.5%)
Discordant	48 (59.3%)
SD: Standard deviation	

All PET-derived metabolic parameters, including SUV_{max}, MTV, TLG, and mean SUV (SUV_{mean}), showed significant reductions after treatment (all p<0.001) (Table 2).

No significant association was observed between PET response and CEA response (χ^2=0.472, p=0.492) or between PET response and CA19-9 response (χ^2=0.060, p=0.807). In contrast, a significant association was found between CEA and CA19-9 responses (χ^2=19.147, p<0.001).

A significant association was observed between concordance groups and mortality (χ^2=6.65, p=0.036). Mortality rates were 33.3% in the concordant good response group, 40.0% in the concordant poor response group, and 12.5% in the discordant response group (Table 3).

Among discordant cases, a significant difference in mortality was observed between the PET-discordant group (PET-responsive/CEA-non-responsive) and the CEA-discordant group (CEA-responsive / PET-non-responsive) (2/38 vs. 4/10, p=0.013, Fisher's exact test).

Correlation analysis based on directional changes (increase vs. decrease) demonstrated a moderate positive association of CEA with both SUV_{max} (r=0.405, p=0.002) and SUV_{mean} (r=0.463, p<0.001), and a weaker but significant correlation with TLG (r=0.336, p=0.013). No significant correlation was observed between CEA and MTV (p=0.421) or between CA19-9 and PET parameters (p>0.05).

Kaplan-Meier analysis demonstrated a statistically significant difference in OS among concordance groups (log-rank p=0.043). Patients in the concordant good response group had the longest survival (mean: 49.1 months), while those in the concordant poor response group had the shortest survival (mean: 26.9 months). The discordant group showed survival outcomes comparable to those of the concordant good response group (Figure 1).

In univariate Cox regression analysis, both age (hazard ratio: 1.059, p=0.019) and concordance status (p=0.045) were significantly associated with OS. However, in multivariable analysis that included both variables, concordance status was no longer statistically significant (p=0.221), and age also lost statistical significance (p=0.101).

CMR was observed in 16 patients. There was no significant difference in OS between patients with and without CMR (log-rank p=0.409).

No significant association was observed between tumor location (colon vs. rectum) and PET-CEA concordance groups (χ^2=0.679, p=0.878), indicating similar distributions of concordance patterns across tumor sites.

Table 2. Changes in tumor markers and PET-derived metabolic parameters before and after treatment			
Variable	**Pre-treatment median (IQR)**	**Post-treatment median (IQR)**	**p value***
CEA	7.30 (3.27-44.70)	4.80 (2.17-19.00)	0.008
CA19-9	22.80 (8.50-75.70)	18.20 (10.60-55.70)	0.751
SUV_{max}	15.15 (8.48-20.28)	7.25 (4.53-14.30)	<0.001
MTV	13.40 (7.43-30.25)	7.50 (4.78-14.10)	<0.001
TLG	102.00 (53.23-230.05)	37.55 (17.08-91.28)	<0.001
SUV_{mean}	8.20 (5.20-10.65)	4.60 (3.05-8.00)	<0.001

*: Wilcoxon signed-rank test
IQR: İnterquartile range, PET: Positron emission tomography, CEA: Carcinoembryonic antigen, CA19-9: Carbohydrate antigen 19-9, SUVmax: Maximum standardized uptake value, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, SUVmean: Mean standardized uptake value

Table 3. Mortality according to response groups			
Response group	**Total (n)**	**Deaths (n)**	**Mortality (%)**
Concordant good	18	6	33.3%
Concordant poor	15	6	40.0%
Discordant	48	6	12.5%
Total	81	18	22.2%

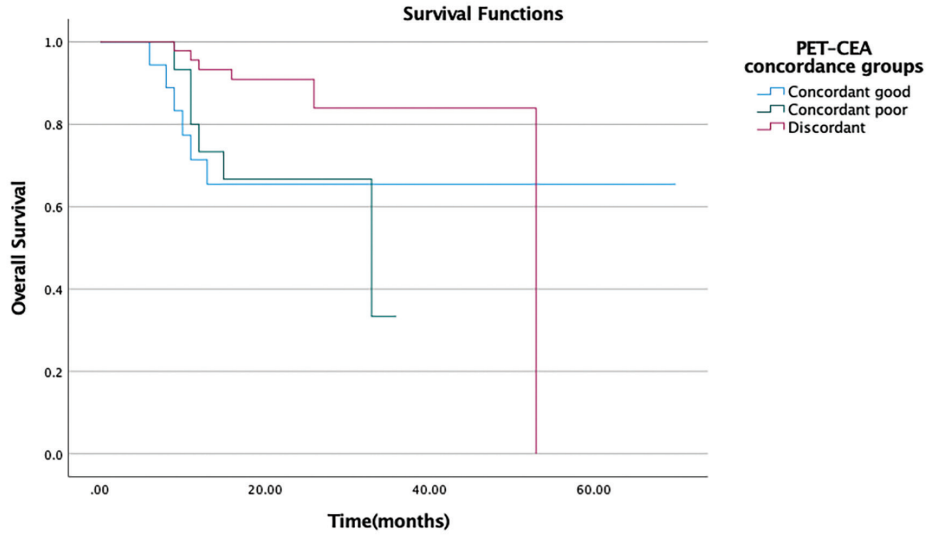

Figure 1. Kaplan-Meier survival curves according to PET-CEA concordance groups (concordant good response, concordant poor response, and discordant response). Patients in the concordant good response group demonstrated the longest overall survival, whereas those in the concordant poor response group had the shortest overall survival. The discordant response group showed survival outcomes comparable to those of the concordant good-response group. Differences between groups were statistically significant (log-rank test, p=0.043). Censoring marks are omitted for clarity

PET: Positron emission tomography, CEA: Carcinoembryonic antigen

Discussion

Colorectal cancer prognosis is influenced by multiple clinicopathological and molecular factors, reflecting the multifactorial nature of disease outcomes [5]. Within this framework, reliance on a single biomarker is unlikely to fully represent disease dynamics. Consequently, discordance between different assessment modalities may occur in clinical practice. Accordingly, in the present study, treatment response was evaluated using both FDG PET- derived parameters and serum tumor markers.

In the present study, a significant association was observed between PET-CEA concordance groups and mortality. Within the discordant response group, mortality differed significantly by discordance type, with higher mortality in the CEA-discordant subgroup (CEA responders with no PET response). Previous studies have reported only a moderate correlation between FDG PET- derived metabolic parameters and serum tumor markers, suggesting that these modalities reflect different aspects of tumor biology rather than interchangeable measures of disease burden [6]. Taken together, these findings support the concept that PET- derived parameters and serum tumor markers provide complementary information in the assessment of treatment response.

FDG PET/CT has an established role in evaluating treatment response in colorectal cancer, particularly because it can detect metabolic changes earlier than conventional morphological imaging. Previous studies have demonstrated that therapy-induced alterations in tumor glucose metabolism are significantly associated with both OS and progression-free survival [7]. In addition, metabolic response assessment using simplified parameters, such as SUV, has been shown to be clinically reliable, supporting the use of semiquantitative approaches in routine practice. These findings are consistent with our results, in which metabolic response, defined by changes in SUV_{max}, was associated with survival outcomes.

In the present study, no significant association was observed between concordance groups and metastatic disease status. This finding suggests that the observed discordance between PET and serum tumor markers cannot be solely attributed to differences in tumor burden. Although PET-derived parameters were obtained from the primary tumor rather than whole-body disease, both PET metabolic parameters and serum tumor markers demonstrated significant reductions following treatment. Therefore, the discordance observed in this study may reflect differences in the biological information captured by these modalities rather than merely differences in the extent of disease.

No significant association was observed between tumor location (colon vs. rectum) and PET-CEA concordance groups, suggesting that concordance patterns are not influenced by primary tumor site. This finding further supports the notion that concordance reflects underlying tumor biology rather than anatomical or site-related factors.

Despite improvements in treatment and early detection, colorectal cancer remains a major cause of cancer-related mortality worldwide, although survival rates have improved over time [8]. Prognosis in colorectal cancer is influenced by multiple clinical and biological factors, including performance status, tumor burden, and systemic inflammatory markers [9]. Previous studies have demonstrated that elevated preoperative CEA and CA19-9 levels are associated with poorer survival outcomes, with the worst prognosis observed when both markers are increased, suggesting their potential

prognostic value [10]. Treatment response in colorectal cancer is commonly assessed using standardized criteria such as Response Evaluation Criteria in Solid Tumors, which incorporate both radiologic tumor burden and normalization of tumor marker levels; in this context, serum markers such as CEA are frequently used as adjuncts in response evaluation rather than standalone indicators [11].

In our study, the combined assessment of tumor marker response (CEA) and metabolic response, defined as a ≥30% reduction in SUVmax inspired by PERCIST-based criteria, was significantly associated with OS. Patients with a concordant good response (i.e., a decrease in both PET and CEA) demonstrated more favorable survival outcomes, whereas those with a concordant poor response exhibited the worst survival outcomes. Discordant patterns were associated with intermediate outcomes. Although discordant patterns were associated with intermediate survival outcomes, this group exhibited the lowest mortality rate. This apparent discrepancy may be explained by the heterogeneous biological behavior underlying discordant responses. Previous studies have demonstrated that prognosis in colorectal cancer is influenced by multiple clinical and biological factors, including performance status, tumor burden, and laboratory parameters. However, in our study, no significant difference was observed between metastatic and non-metastatic patients. This finding may be explained by the characteristics of our study population: all patients received systemic chemotherapy and did not undergo upfront surgical resection. Therefore, even patients classified as non-metastatic may belong to a more advanced, biologically aggressive subgroup that is not suitable for surgery, and this may have attenuated the expected prognostic differences between metastatic and non-metastatic disease.

The prognostic role of age in colorectal cancer has been widely investigated; however, its independent impact on survival remains controversial. Some studies suggest that survival differences become more evident in patients older than 60 years, whereas younger age groups show comparable outcomes [12]. Consistent with previous reports, chronological age alone does not appear to be an independent determinant of survival outcomes in colorectal cancer, suggesting that other factors such as tumor biology and treatment-related variables may play a more prominent role [13]. Previous studies have indicated that, although older age is associated with increased morbidity and mortality, its independent effect on survival becomes less clear when patients with similar disease stages and treatments are compared, which further supports this concept. In our study, age was significantly associated with OS in univariate analysis; however, this association was not maintained in multivariate analysis. The apparent prognostic impact of age in colorectal cancer may be explained by its association with comorbidities and differences in treatment patterns, as older patients are more likely to receive less aggressive therapy and have reduced tolerance to treatment [13]. These findings support the notion that age may act as a surrogate marker rather than an independent determinant of prognosis.

In our study, the combined assessment of PET and CEA response was significantly associated with OS in univariate analysis; however, this association did not remain significant in multivariate models. Nevertheless, the observed survival patterns across concordance groups suggest that the integration of metabolic and tumor marker responses may still provide clinically meaningful information. This may be explained by the fact that PET-derived parameters and serum tumor markers reflect complementary aspects of tumor biology, including metabolic activity and systemic tumor burden. While the prognostic impact of age may largely be influenced by comorbidity burden and treatment selection, response-based parameters may offer a more direct reflection of tumor behavior and treatment-related disease dynamics.

CA19-9 is a well-established tumor marker primarily used in pancreatic cancer, where it has demonstrated prognostic value and utility in monitoring treatment response [14]. However, its role in colorectal cancer is less consistent compared to CEA [15]. In our study, CA19-9 showed an association with CEA but did not demonstrate a significant relationship with treatment response. This finding may reflect its more limited applicability to colorectal cancer and its lower sensitivity in capturing treatment-related disease dynamics compared to CEA.

MTV is defined as the volume of tumor tissue with increased FDG uptake and represents the sum of voxels with SUV values above a predefined threshold. This volume can be measured semiquantitatively using contouring methods on attenuation-corrected PET/CT images. TLG is a parameter that combines tumor volume and metabolic activity, and is calculated as the sum of the products of SUV_{mean} and MTV [16]. In our study, all PET-derived metabolic parameters and CEA levels showed significant reductions following treatment, whereas CA19-9 did not demonstrate a significant change. In addition, only a weak correlation was observed between TLG and CEA, suggesting that these parameters may reflect different aspects of tumor biology. While TLG integrates metabolically active tumor burden by combining lesion volume and uptake, CEA may better represent systemic disease dynamics. This is consistent with our finding of no significant association between PET and CEA responses, which further supports the conclusion that PET-derived metrics and serum tumor markers provide complementary rather than overlapping information in the assessment of treatment response.

Study Limitations

This study has several limitations. First, its retrospective design and relatively small sample size may limit the generalizability of the findings. Second, PET-derived parameters were obtained from the primary tumor rather than from whole-body tumor burden, which may have affected the assessment of the extent of metabolic disease. Finally, the heterogeneity of treatment regimens may have influenced survival outcomes and response patterns.

Overall, these findings highlight that integrating PET-derived metabolic parameters with serum tumor markers may offer a more comprehensive and clinically meaningful approach for evaluating treatment response in colorectal cancer.

Conclusion

The combined assessment of FDG PET/CT- derived metabolic response and serum tumor marker (CEA) response was associated with OS in patients with colorectal cancer. Concordance patterns, particularly concordant good and concordant poor responses, demonstrated distinct survival outcomes, while discordant patterns reflected heterogeneous disease behavior. Although these associations were not maintained in multivariate analysis, the observed trends suggest that integrating metabolic and tumor marker responses may provide clinically meaningful insights into treatment response. Further studies with larger cohorts and assessment of whole-body tumor burden are warranted to validate these findings.

Ethics

Ethics Committee Approval: Ethical approval has been obtained from the University of Health Sciences Türkiye, Ankara Etlik City Hospital No. 1 Scientific Research Ethics Committee (approval no: AEŞH-BADEKI-2025-735, date: 24.12.2025).

Informed Consent: Informed consent was obtained from all participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.D.Ş., A.E.K., E.Y., Ö.A.İ., D.M.K., Ö.Ö., Concept: S.D.Ş., D.M.K., Design: S.D.Ş., D.M.K., Data Collection or Processing: S.D.Ş., A.E.K., E.Y., Analysis or Interpretation: S.D.Ş., Literature Search: S.D.Ş., A.E.K., Writing: S.D.Ş., Ö.Ö.

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