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Impact of Serum Albumin Levels on FDG Uptake in the Liver, Spleen, and Bone Marrow During Gastrointestinal Cancer Staging: A PET-CT Study

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Abstract

Background: Serum albumin is an essential biomarker in cancer patients, reflecting nutritional status and systemic inflammation. This study investigates the impact of serum albumin levels on FDG uptake in the liver, spleen, and bone marrow during the staging of gastrointestinal cancers using FDG PET-CT.

Methods: This retrospective study included 610 patients with various types of cancers. FDG PET-CT scans were used to measure FDG uptake in the liver, spleen, and bone marrow. Patients were grouped into hypoalbuminemia (< 3.5 g/dL) and normal albumin levels (≥ 3.5 g/dL). The study analyzed the correlation between serum albumin and SuVmax and SuVmean of the liver, spleen, and bone marrow.

Results: Patients with normal albumin levels exhibited significantly higher liver FDG uptake, with a mean Liver SuVmax of 3.73 ± 1.78 compared to 3.32 ± 0.75 in those with hypoalbuminemia ($p < 0.0001$). Similarly, Liver SuVmean was higher in the normal albumin group (2.17 ± 1.20) than in the hypoalbuminemia group (1.95 ± 0.48, $p = 0.0009$). No significant differences in FDG uptake were observed in the spleen and bone marrow between the two groups. The study found a weak positive correlation between albumin levels and liver FDG uptake, but no significant correlation with FDG uptake in the spleen and bone marrow.

Conclusion: Serum albumin levels are significantly associated with liver FDG uptake in patients with gastrointestinal cancers, suggesting that albumin may play a role in liver metabolism. However, albumin levels do not significantly impact FDG uptake in the spleen or bone marrow. These findings highlight the potential of albumin as a marker for liver metabolism in cancer patients but suggest that other factors influence the spleen and bone marrow.

Keywords: Albumin, FDG PET-CT, gastrointestinal cancers, liver metabolism, hypoalbuminemia

INTRODUCTION

Cancer continues to be a principal cause of morbidity and mortality globally, with patient outcomes being influenced by a multifactorial interplay of physiological and pathological variables. Among these variables, nutritional status, as assessed by biochemical markers such as serum albumin, has gained prominence as a critical factor in prognostication. Hypoalbuminemia, defined as a reduced concentration of serum albumin, is commonly observed in patients with malignancies and has been correlated with adverse clinical outcomes, including increased all-cause mortality (1-5).

Serum albumin is not merely a reflection of nutritional status in patients with cancer but also a marker of systemic inflammation and disease severity. Cancer patients frequently endure metabolic dysregulation, anorexia, and cachexia—conditions that impair protein synthesis and promote catabolic processes (3,4). Additionally, the systemic inflammatory response associated with malignancies can alter albumin metabolism, leading to decreased hepatic production and increased capillary permeability, which facilitates the extravasation of albumin into the interstitial space. Thus, hypoalbuminemia emerges not solely as a consequence of malnutrition but as a complex pathophysiological process intertwined with tumor biology and host response.

The integration of positron emission tomography/computed tomography (PET/CT) with 2-[18F]fluoro-

2-deoxy-D-glucose (FDG) leads a transformative advancement in clinical oncologic imaging (6). This approach provides a comprehensive acquisition of both glucose metabolism and anatomical imaging data, all within a single diagnostic session. FDG-PET/CT demonstrates its utility and versatility in enhancing patient care and management from initial staging to restaging, early treatment response assessment to metastatic disease evaluation, and even prognostication in intestinal cancer and diverse malignant tumors (6,7). Kitajima et al. claim that FDG-PET/CT results are excellent for evaluation of gastrointestinal cancers beyond local lymphadenopathy and metastatic disease, in their review (7).

The impact of serum albumin on liver, spleen and bone marrow FDG uptake in cancer patients is not clear. A previous study conducted by Otomi et al. revealed that FDG uptake in liver was lower in patients with malnutrition (8). In this regard, further studies are needed.

This study aims to investigate the albumin levels during the early stages of various types of cancers (gastric, pancreatic, lung, renal cell, etc.) and their impact on liver, spleen, and bone marrow FDG uptake.

METHODS

Study Design and Population

This retrospective cross-sectional study was conducted at Dicle University, School of Medicine, Department of Nuclear Medicine. The ethics approval was provided from the local clinical research ethics committee of Dicle University The Committee of Clinical Research (IRB no and date: 195/12.06.2024). This study was conducted according to the Declaration of Helsinki-Ethical principle for Human Researches. The data were obtained by investigating the hospital software system.

Case Selection and Exclusion

Case selection criteria encompassed patients referred to the nuclear medicine department for oncological evaluation, undergoing comprehensive whole-body PET-CT scans from January 1, 2021, to December 30, 2022. Inclusion criteria comprised individuals devoid of prior chemotherapy or radiotherapy, lacking surgical interventions, free from hematological malignancies, with laboratory analyses conducted within a week surrounding the PET/CT procedure. Patients undergoing PET-CT scans for restaging, treatment response assessment, or recurrence-metastasis investigation were excluded from the cohort. Furthermore, individuals presenting with hepatic or splenic metastases or primary tumors on PET-CT imaging were excluded. Additionally, patients with hematological malignancies or chronic inflammatory conditions like rheumatoid arthritis were not included in the study.

FDG PET-CT Scan

For FDG PET-CT imaging acquisition, patients were instructed to undergo a fast exceeding 6 hours, maintaining blood glucose levels below 140 mg/dL. Intravenous administration of FDG at a dosage of 0.1 mCi/kg was performed. Following injection, patients were confined to a specially lead-coated environment for 1 hour to facilitate tracer distribution. Subsequently, a total-body CT scan spanning from vertex to knees was conducted, succeeded by whole-body PET emission scanning. Imaging procedures were executed utilizing a Siemens Horizon PET/CT apparatus, model 2016, featuring 3D-TOF technology. The device boasted a 3 mm slice thickness, employing PET iterative and CT bp-LOR reconstruction methodologies for image generation. A low-dose CT device, utilized for anatomical delineation and attenuation correction, operated at 80 mA and 120 kV (Siemens Healthcare, GmbH, Henkestrasse 127, 91052 Erlangen, Germany). Evaluation of hepatic, splenic, and bone marrow metabolic activity was performed via SuVmax and SuVmean metrics extracted from FDG PET/CT scans.

Laboratory Assessment

Serum albumin and C-reactive protein (CRP) were noted. Those parameters were assessed for the potential association or correlation with SuVmax ve SuVmean of liver, spleen and bone marrow. Albumin <3.5 gr/dL was labeled as hypoalbuminemia.

STATISTICAL ANALYSIS

Data analysis was conducted using SPSS 15.0 for Windows statistical software. The distributions of continuous variables were assessed via the Kolmogorov-Smirnov test. Parametric variables were expressed as mean ± standard deviation and median (minimum and maximum), while categorical variables were presented as numbers and percentages. Correlation analysis, utilizing Pearson correlation coefficients, was employed to explore relationships between variables, evaluating the strength and direction of linear associations among continuous variables. Regression analysis was utilized to examine the influence of predictor variables (such as CRP, albumin, and ESR) on outcome variables (SuVmax and SuVmean of the liver, spleen, and bone marrow), encompassing both univariate and multivariate regression analyses. Statistical significance was set at $p<0.05$.

RESULTS

The mean age of the patients in this study was 58.7 ± 16.5 years. The gender distribution revealed that 55.3% of participants were male and 44.7% were female. A total of 610 cancer patients were assessed in this cohort, of which 24.43% had gastrointestinal cancers. Among the gastrointestinal cancers, pancreatic cancer was the most frequent, accounting for 29.53% of the cases

Table 1. The prevalence and features' of various types of cancers included in the study

Cancer Type	Age, years	Gender Male/female, n	Albumin, gr/dL	CRP, mg/dl
Gastrointestinal System Tumors				
Colon, n=39	60.28±13.47	22/17	3.52±0.81	2.3(0.09-127.17)
Rectum, n=23	52.22±13.77	10/13	3.81±0.59	5.39(0.08-47.76)
Stomach, n=26	61.23±11.85	13/13	3.26±0.97	1.21(0.04-137)
Pancreas, n=44	64.60±10.68	25/19	3.22±0.56	3.37(0.06-140.78)
Eosephagus, n=7	63.53±11.48	6/1	3.46±0.49	2.44(0.44-36.02)
Clatskin tumor, n=6	63.17±10.20	5/1	3.37±0.41	7.77(0.27-81.99)
GIST, n=4	59.00±15.85	3/1	3.69±0.28	0.49(0.13-3.54)
Extra-Gastrointestinal Tumors				
Lung, n=183	61.13±13.79	136/47	3.47±0.64	3.10(0.07-215.72)
Breast, n=67	51.66±13.22	1/66	4.16±0.41	0.43(0.04-61.97)
Mesothelioma, n=36	63.53±11.48	31/5	3.46±0.49	5.38(0.13-34.59)
Skin, squamous cell cancer, n=20	74.00±17.12	14/6	3.73±0.46	1.74(0.05-15.02)
Unknown Primary, n=147	60.77±17.10	74/73	3.37±0.67	2.60(0.02-245.23)
Nasophrayngeal, n=4	26.25±17.34	4/0	4.36±0.33	0.41(0.24-2.74)
Mediastinal mass, n=12	47.92±20.09	7/5	3.97±0.96	1.97(0.17-77.66)
Malign melanoma, n=7	59.00±25.89	4/3	3.74±0.57	0.35(0.08-3.01)
Laryngeal cancer, n=15	67.20±10.67	14/1	3.56±0.64	0.75(0.07-188.56)
Endometrium, over cancers, n=12	56.00±13.58	0/12	3.67±0.58	2.69(0.27-81.99)
Renal cell cancer, n=7	50.57±13.52	7/0	4.07±0.31	6.57(0.35-39.05)

(Table 1). The mean SuVmax and SuVmean values for FDG uptake in the liver, spleen, and bone marrow across different types of gastrointestinal cancers within this cohort are summarized in Table 2.

The Correlation Analysis (Albumin and SuVmax and SuVmean of Liver, Spleen and Bone Marrow)

The correlation coefficients for both Liver SuVmax (0.12) and SuVmean (0.11) with Albumin are relatively low, though they have statistically significant p-values (0.0112 and 0.0185, respectively) (Figure 1). This suggests a weak positive correlation between albumin levels and FDG uptake in the liver. Clinically, this might indicate that as albumin levels slightly increase, there is a modest increase in liver metabolic activity as measured by FDG uptake. However, the weak strength of this correlation implies that albumin is not a strong predictor of liver FDG uptake on its own and should be interpreted within the context of other clinical and metabolic factors.

The correlation between albumin and FDG uptake in the spleen (SuVmax= 0.05, SuVmean= 0.03) is very weak and not statistically significant (p-values of 0.3163 and 0.5312, respectively) (Figure 2). Clinically, this suggests that albumin levels do not have a meaningful impact on spleen FDG uptake. This lack of association might be expected, as spleen FDG uptake is often influenced by factors such as immune activation rather than albumin levels.

The correlations between albumin and bone marrow FDG uptake are negligible (SuVmax = 0.02, SuVmean = -0.05) and not statistically significant (p-values

Table 2. FDG Uptake in the Liver, Spleen, and Bone Marrow in different types of GIS cancers

Cancer Type	Liver, SuVmax and SuVmean	Spleen, SuVmax and SuVmean	Bone Marrow, SuVmax and SuVmean	SLR (Spleen-to-Liver Ratio)	BLR (Bone-to-Liver Ratio)
Colon, n=39	3.65±0.72 2.13±0.40	2.88±0.57 1.90±0.34	3.08±0.86 1.94±0.47	0.79±0.10 0.90±0.11	0.86±0.24 0.93±0.27
Rectum, n=23	3.55±0.77 1.96±0.46	2.80±0.57 1.77±0.36	3.20±0.88 2.00±0.53	0.79±0.09 0.91±0.13	0.92±0.29 1.05±0.32
Stomach, n=26	3.31±0.64 1.98±0.38	2.70±0.47 1.78±0.32	2.84±0.52 1.85±0.38	0.83±0.13 0.91±0.13	0.87±0.15 0.94±0.17
Pancreas, n=44	3.91±0.67 2.27±0.45	2.94±0.68 1.92±0.45	2.83±0.62 1.82±0.54	0.75±0.12 0.85±0.14	0.73±0.16 0.83±0.28
Eosephagus, n=7	3.55±0.63 2.11±0.34	3.20±0.71 1.95±0.47	3.11±0.69 1.85±0.48	0.90±0.14 0.92±0.14	0.87±0.28 0.87±0.14
Clatskin tumor, n=6	4.05±0.89 2.36±0.57	3.13±0.87 2.00±0.56	3.15±0.29 2.10±0.35	0.77±0.10 0.84±0.09	0.80±0.17 0.92±0.22
Gastrointestinal Stromal Tumor, n=4	3.57±0.60 2.22±0.55	3.55±1.31 2.12±075	3.17±1.45 2.00±0.86	0.97±0.23 0.94±0.17	0.86±0.28 0.88±0.23

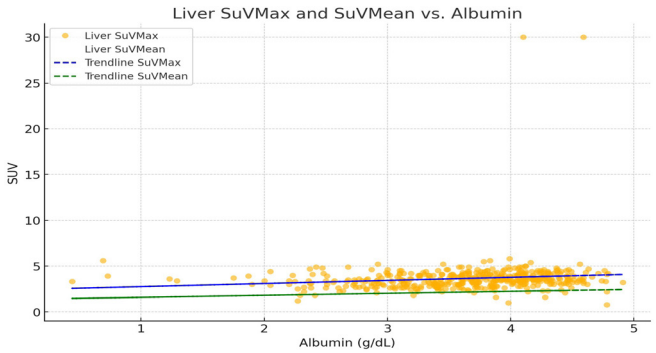

Figure 1. Scatter plot demonstrating the relationship between Albumin levels (g/dL) and FDG uptake in the liver, represented by SuVmax and SuVmean. The blue circles and green crosses depict individual data points for Liver SuVmax and SuVmean, respectively. Dashed lines indicate the trendlines for each parameter, illustrating a weak positive correlation between Albumin levels and FDG uptake in the liver.

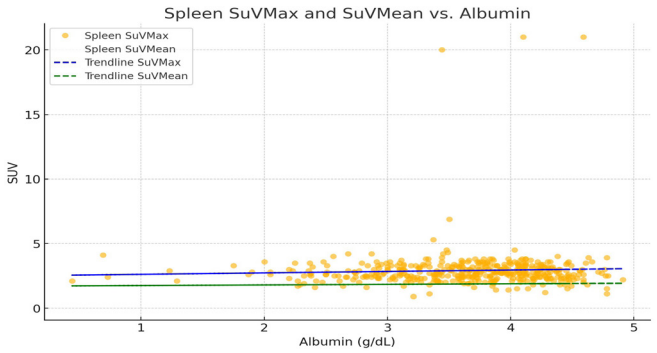

Figure 1. Scatter plot demonstrating the relationship between Albumin levels (g/dL) and FDG uptake in the spleen, represented by SuVmax and SuVmean. The blue circles and green crosses depict individual data points for Spleen SuVmax and SuVmean, respectively. Dashed lines indicate the trendlines for each parameter, illustrating the weak correlation between Albumin levels and FDG uptake in the spleen.

of 0.7294 and 0.2742, respectively) (**Figure 3**). This indicates no meaningful relationship between albumin levels and bone marrow metabolic activity. Clinically, bone marrow activity is more likely influenced by other factors such as hematopoietic activity, inflammation, or bone marrow pathology rather than by albumin levels.

Patients with normal albumin levels (≥3.5 g/dL) exhibited significantly higher liver FDG uptake, with a mean Liver SuVmax of 3.73 ± 1.78 compared to 3.32 ± 0.75 in those with hypoalbuminemia (p< 0.0001) (Table 3). Similarly, the Liver SuVmean was higher in the normal albumin group (2.17 ± 1.20) than in the hypoalbuminemia group (1.95 ± 0.48, p= 0.0009). However, there were no significant differences in spleen or bone marrow FDG uptake between the two groups. The Spleen SuVmax and SuVmean were similar in both groups (p= 0.8302 and p= 0.4283, respectively), as were the Bone Marrow SuVmax (p= 0.6784) and Bone Marrov SuVmean (p = 0.4420) (**Table 3**). These results suggest that albumin levels significantly impact liver metabolic activity but do not affect the spleen or bone marrow.

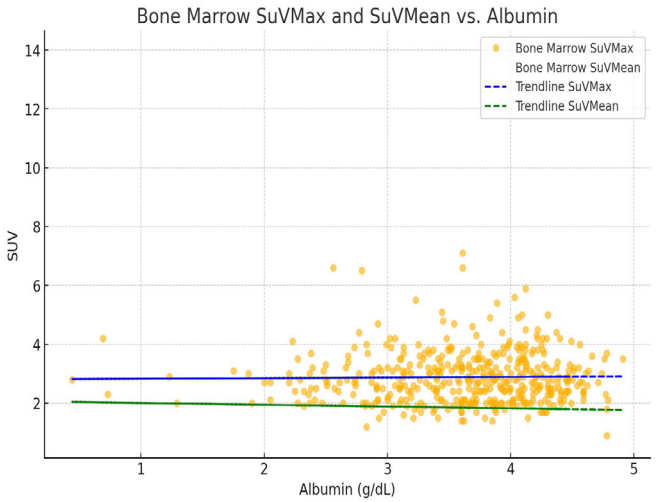

Figure 1. Scatter plot demonstrating the relationship between Albumin levels (g/dL) and FDG uptake in the bone marrow, represented by SuVmax and SuVmean. The blue circles and green crosses depict individual data points for Bone Marrow SuVmax and SuVmean, respectively. Dashed lines indicate the trendlines for each parameter, illustrating the lack of significant correlation between Albumin levels and FDG uptake in the bone marrow.

DISCUSSION

This study explored the relationship between serum albumin levels and FDG uptake in the liver, spleen, and bone marrow during the staging of gastrointestinal cancers using FDG PET-CT. The findings indicated a significant association between serum albumin levels and liver metabolic activity, with no significant impact on FDG uptake in the spleen or bone marrow. This highlights the potential of albumin as a marker for liver metabolism in cancer patients, emphasizing the importance of maintaining optimal nutritional and systemic conditions in this population.

Several studies have corroborated the findings regarding the influence of serum albumin on FDG uptake in gastrointestinal cancers. For instance, Song et al. examined the role of F-18 FDG PET/CT in predicting lymph node metastasis in gastric cancer and found that serum albumin levels, among other factors, were associated with FDG uptake in the liver, which further aligns with the current study's conclusion about

Table 3. Comparison of SUV parameters between hypoalbuminemia and normal albumin levels in the Liver, Spleen, and Bone Marrow in different types of GIS cancers

SUV Parameter	Hypoalbuminemia, n=89	Normal Albumin; n=60	p-value
Liver SuVmax	3.32 ± 0.75	3.73 ± 1.78	0.0000
Liver SuVmean	1.95 ± 0.48	2.17 ± 1.20	0.0009
Spleen SuVmax	2.86 ± 1.51	2.89 ± 1.30	0.8302
Spleen SuVmean	1.81 ± 0.43	1.86 ± 1.02	0.4283
Bone Marrow SuVmax	2.86 ± 0.87	2.89 ± 0.87	0.6784
Bone Marrov SuVmean	1.90 ± 1.10	1.83 ± 0.57	0.4420

albumin's role in liver metabolism. Elevated FDG uptake in the liver was often associated with better nutritional status, reflected by normal albumin levels (9).

Moreover, Lee et al. reported a clinical implication of FDG uptake in the bone marrow and liver on PET/CT in gastric cancer patients, noting a significant correlation between serum albumin levels and metabolic activity. This supports the idea that maintaining adequate albumin levels could play a role in optimizing liver function and potentially improving cancer outcomes (10).

On the contrary, some studies have not found a significant association between albumin and FDG uptake in organs like the spleen and bone marrow. Kim et al., in their study on diffuse splenic FDG uptake in rectal cancer patients, noted that albumin levels did not significantly correlate with FDG uptake in the spleen, suggesting that other factors such as immune regulation and systemic inflammation might play a more prominent role in influencing spleen metabolism (11). Additionally, Saito et al. examined FDG PET/CT imaging in gastrointestinal mantle cell lymphoma and observed no consistent pattern linking serum albumin with FDG uptake in the bone marrow, reinforcing the findings that albumin may not significantly impact the metabolic activity of bone marrow in these patients (12).

The collective evidence indicates that while serum albumin levels are associated with liver FDG uptake, they do not significantly affect FDG uptake in the spleen or bone marrow. The weak correlation observed in the current study, as well as in previous literature, suggests that liver metabolic activity is influenced by a complex interplay of factors, including but not limited to albumin levels. The differential impact on the spleen and bone marrow might be due to these organs' distinct physiological roles and regulatory mechanisms, such as cytokine activity and immune cell function, which are less dependent on albumin.

The findings demonstrate the potential of albumin as a marker for liver metabolism and the importance of maintaining adequate albumin levels in cancer patients. However, they also indicate that the metabolic activities in the spleen and bone marrow are regulated by other systemic and local factors. Future research should further explore these mechanisms and evaluate the prognostic implications of serum albumin in cancer metabolism and progression.

Limitations

The study has several limitations that should be acknowledged. First, its retrospective design inherently limits the ability to establish causality between albumin levels and FDG uptake in different organs. Retrospective studies are also prone to selection bias and confounding variables, which might have influenced the findings. Second, the sample size, although adequate for initial analysis, may not be sufficient to generalize the results to the broader population of patients with gastrointestinal cancers. The inclusion of various cancer types with potentially different metabolic behaviors further complicates the interpretation of albumin's impact across different organ systems.

Another limitation is the reliance on a single measurement of albumin and FDG uptake, which may not fully capture the dynamic changes in a patient's nutritional and metabolic status over time. Serum albumin levels can fluctuate due to various factors such as acute illness, inflammation, and therapeutic interventions, potentially confounding the results. Similarly, FDG uptake can be influenced by several factors including the tumor's metabolic activity, inflammatory response, and liver function, which were not controlled for in this study.

The study also did not account for other potential confounding factors that may influence FDG uptake, such as the presence of systemic inflammation, liver disease, or the use of medications that could alter metabolic activity. The absence of data on patient outcomes, such as survival rates, limits the ability to assess the prognostic significance of albumin in this context. Furthermore, the study's exclusion criteria, while necessary to reduce heterogeneity, may have resulted in the exclusion of patients with more advanced or complex disease, potentially biasing the findings toward a more favorable prognosis.

Lastly, the study did not explore the underlying mechanisms linking albumin to FDG uptake in the liver, spleen, and bone marrow. While the results suggest an association, they do not provide insight into the biological pathways involved. Future studies with a prospective design, larger sample sizes, and a more detailed examination of potential confounding variables are needed to validate these findings and elucidate the mechanisms by which albumin influences organ-specific metabolism in cancer patients.

CONCLUSION

This study demonstrates a significant association between serum albumin levels and FDG uptake in the liver during the staging of gastrointestinal cancers using FDG PET-CT. Patients with normal albumin levels showed higher liver FDG uptake, suggesting that albumin might play a role in modulating liver metabolic activity. In contrast, no significant association was found between serum albumin levels and FDG uptake in the spleen and bone marrow, indicating that these organs' metabolic activities are likely governed by different physiological and immunological factors.

DECLARATIONS

Ethics: The authors would like to thank the staff and patients at the Dicle University School of Medicine Department of Nuclear Medicine for their support and cooperation in this study. We also extend our gratitude to the hospital administration for providing access to the necessary data and facilities that made this research possible. Special thanks to the radiology and laboratory teams for their meticulous work in performing the PET-CT scans and laboratory assessments, which were integral to this study.

Ethical Issues: This study was conducted in accordance with the Declaration of Helsinki and was approved by the local clinical research ethics committee of Dicle University (IRB no: 195 and date= 12.06.2024). Informed consent was obtained from all participants involved in this study. As this research involved a retrospective review of existing data, it posed minimal risk to participants, and no additional interventions were performed. There were no ethical issues encountered during the conduct of this study.

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AI: This study has benefited from the language revision and graphic processing provided by the latest Chat GPT-4.0; however, all final decisions have been made by the authors.

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