

# Exploring $^{18}\text{F}$ -FDG uptake patterns in liver, spleen, and bone marrow: Implications for inflammatory and infectious conditions

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## Abstract

**Objective:** This study aimed to explore the relationship between fluorine-18-fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) uptake in the liver, spleen, and bone marrow and inflammatory markers such as c-reactive protein (CRP), albumin, and erythrocyte sedimentation rate (ESR) in patients undergoing positron emission tomography/computed tomography (PET/CT) imaging for cancer diagnosis. **Subjects and Methods:** This retrospective cross-sectional study included a total of 708 patients with a diagnosis of malignancy. Fluorine-18-FDG PET/CT images acquired between January 2021 and December 2022. Exclusion criteria comprised prior chemotherapy, radiotherapy, hematological malignancies, or liver/spleen tumors. Statistical analysis included correlation analysis, univariate, and multivariate regression analysis. **Results:** C-reactive protein levels demonstrated a significant positive correlation with  $^{18}\text{F}$ -FDG uptake in the spleen ( $r=0.104$ ,  $P=0.006$ ) and bone marrow ( $r=0.112$ ,  $P=0.003$ ). Albumin showed a negative correlation with liver  $^{18}\text{F}$ -FDG uptake ( $r=-0.220$ ,  $P<0.001$ ). Regression analysis revealed ESR's impact on spleen-to-liver ( $P=0.023$ ) and bone marrow-to-liver ( $P=0.012$ )  $^{18}\text{F}$ -FDG uptake. **Conclusion:** This study demonstrates the association between inflammatory markers and  $^{18}\text{F}$ -FDG uptake in liver, spleen and bone marrow. C-reactive protein and ESR showing significant correlations with spleen and bone marrow  $^{18}\text{F}$ -FDG uptake, and albumin correlated with liver  $^{18}\text{F}$ -FDG uptake negatively. Erythrocyte sedimentation rate had significant impact on spleen and bone marrow  $^{18}\text{F}$ -FDG uptakes. These findings suggest the potential of  $^{18}\text{F}$ -FDG PET/CT in diagnosing inflammatory conditions, warranting further investigation into its clinical implications.

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## Introduction

Computed tomography (CT) integrated positron emission tomography (PET) employing the glucose analogue; fluorine-18-fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) PET/CT, represents a dynamic advancement in hybrid imaging technology. Its use in the assessment of infection and aseptic inflammation facilitates the diagnosis of a diverse spectrum of pathological conditions. Positron emission tomography/CT is increasingly evident that beyond its established efficiency in oncological imaging, it holds significant clinical promise in the diagnosis and treatment of infection and inflammation. This novel technique not only enables the prompt identification of infection or inflammation, but also can facilitate precise mapping of disease extent and severity, pinpointing sites amenable to tissue sampling, and evaluating therapeutic responses [1, 2].

The  $^{18}\text{F}$ -FDG molecule accumulates at various rates in different cell types and organs. However, the altered structure of the  $^{18}\text{F}$ -FDG molecule prevents further metabolism in the cell. This essentially traps  $^{18}\text{F}$ -FDG within cells and  $^{18}\text{F}$ -FDG accumulates in most tissues at a rate proportional to glycolysis [3]. The liver, spleen and bone marrow demonstrate homogenous low-grade  $^{18}\text{F}$ -FDG uptake and bone marrow and spleen exhibit less intense uptake compared to the liver [4]. Moreover, the reports also indicate there is some variability in the normal physiologic uptake of  $^{18}\text{F}$ -FDG across subjects [5, 6].

In this study, we aimed to investigate the  $^{18}\text{F}$ -FDG PET/CT accumulation patterns of liver, spleen and bone marrow in patients with acute or/and chronic inflammatory status that presented with high c-reactive protein (CRP), neutrophile-to-lymphocyte ratio, serum albumin, and erythrocyte sedimentation rate (ESR) levels.

## Subjects and Methods

This single-center retrospective cross-sectional study was conducted at Dicle University, School of Medicine, Department of Nuclear Medicine. The study ethics approval was obtained from the local clinical research ethics committee of our hospital (IRB no:41/ Date:17.01.2024). This study was conducted in agreement with the Declaration of Helsinki-Ethical principle for medical research involving human subjects.

### Case selection

Patients who applied to the nuclear medicine department for cancer diagnosis and staging and underwent whole-body PET/CT imaging between January 1, 2021, and December 30, 2022, were assessed. We included patients who had not received any chemotherapy or radiotherapy protocol, had not undergone surgery, had no diagnosis of hematological malignancy, and whose laboratory data had been studied within 1 week before or after the PET/CT imaging.

### Exclusion criteria

Patients undergoing PET/CT imaging for restaging, evaluating treatment response, and investigating recurrence-metastasis, along with those exhibiting metastases and primary tumors in the liver or spleen on PET/CT imaging, were excluded from the study. Additionally, patients diagnosed with hematological malignancies and those with chronic inflammatory diseases such as rheumatoid arthritis were also excluded.

### <sup>18</sup>F-FDG PET/CT scan

To obtain <sup>18</sup>F-FDG PET/CT images, patients were required to fast for more than 6 hours and maintain a blood glucose level below 140mg/dL. Intravenous injection of <sup>18</sup>F-FDG at a dose of 0.1mCi/kg was administered to the patients. Following the injection, patients were housed in a specially lead-coated room for 1 hour to allow for the medication to be distributed throughout the body. Subsequently, a total-body CT scan (from vertex to knees) was performed. This was followed by whole-body emission scanning using PET. The imaging was conducted utilizing a Siemens Horizon PET/CT device from the 2016 model, equipped with 3D-TOF technology. The device had a slice thickness of 3mm, and images were generated using PET iterative and CT bp-LOR reconstruction processing methods. The low-dose CT device, utilized for anatomical detail and attenuation correction, was set to 80mA and 120 kV (Siemens Healthcare, GmbH, Henkestrasse 127, 91052 Erlangen, Germany). The metabolic activity of the liver, spleen, and bone marrow was evaluated using maximum standardized uptake value (SUVmax) and SUVmean obtained from <sup>18</sup>F-FDG PET/CT scans.

### Laboratory assessment

Serum CRP, albumin, ESR, and hemogram derived neutrophil-to-lymphocyte ratio were studied. Those parameters were assessed for the potential association or correlation with SUVmax vs SUVmean of liver, spleen and bone marrow. Albumin <3.5gr/dL was labeled as hypoalbuminemia, while CRP >0.5mg/dL was assigned high.

### Statistical analysis

SPSS 15.0 for Windows statistical package program was employed in data analysis. The distributions of continuous variables were determined by Kolmogorov-Smirnov test. Parametric variables were given as mean±standard deviation and median (minimum and maximum). Categorical variables were presented as numbers and percentages. Correlation analysis was used to examine the relationships between variables, particularly Pearson correlation coefficients to assess the strength and direction of linear relationships between continuous variables. Regression analysis was employed to investigate the impact of predictor variables (such as CRP, albumin, and ESR) on outcome variables (SUVmax and SUVmean of liver, spleen, and bone marrow). Both univariate and multivariate regression analyses were conducted. P<0.05 was assumed as significant.

## Results

A total of 708 participants were evaluated. The mean age of the patients was 58.93±16.21 and 56.8% of those were female (Table 1). The most frequently diagnosed cancer was lung cancer and breast, colorectal, stomach and pancreas followed it. The mean <sup>18</sup>F-FDG PET/CT image acquisition duration was 75 minutes. Hypoalbuminemia was observed in 61% of the patients and high CRP values were observed in 74.5%.

Maximum SUV and SUVmean of spleen-to-liver ratio (SLR) and bone marrow-to-liver ratio (BLR) indices were calculated and presented in Table 2. Fluorine-18-FDG liver uptake was low in the cases of high CRP compared to those with normal CRP levels, while spleen and bone marrow exhibited a higher <sup>18</sup>F-FDG uptake in higher CRP levels (P<0.05) (Table 3). Additionally, in hypoalbuminemic cases <sup>18</sup>F-FDG liver uptake was lower and this effect of hypoalbuminemia did not observe in the spleen and bone marrow (Table 3).

C-reactive protein, albumin, and ESR showed an impact on SUVmax of SLR and BLR (P<0.05) in univariate analysis (Table 4 and Table 5). However, after employing a multivariate model including all these factors, the impact of these factors disappeared (P>0.05) except for ESR, which had an impact on <sup>18</sup>F-FDG uptakes of SLR. Serum glucose levels showed no correlation with overall <sup>18</sup>F-FDG uptake (SUVmax and SUVmean) (P>0.05).

## Correlation analysis

### Liver

Maximum SUV of liver had no correlation with CRP (P=0.246) and ESR (P=0.230), however, exhibited a negative correlation with albumin (P<0.001). In contrast, SUVmean exhibited a negative correlation with CRP (P=0.002) and albumin (P<0.001) (Table 6).

### Spleen

Maximum SUV of spleen had positive correlation with CRP (P=0.006) but not with albumin and ESR (P>0.05). Mean SUV had a positive correlation with CRP and ESR (P=0.002 and

**Table 1.** Clinical and laboratory features of the participants, SUVmax and SUVmean of the liver, spleen and bone marrow and the prevalent cancer types.

Variable	Mean, median and %	Organ	SUVmax	SUVmean
Age, year	58.93±16.21	Liver	3.22±0.67	1.95±0.43
Gender, male/female, n (%)	402 (56.8%)/306 (43.2%)	Spleen	2.70±0.59	1.74±0.37
CRP, mg/dl	1.60(0.03-153)	Bone marrow	2.71±0.69	1.80 (0.90-14.00)
ESR	26 (2-84)	Top 5 Cancer Diagnosis (n)		
Albumin, gr/dl	3.49 (0.73-4.71)	Lung		182
Hgb, gr/dl	12.44±2.43	Breast		68
Glucose before PET	108 (67-140)	Colo-rectal		61
		Stomach		26
		Pancreas		42
		Unknown Primary		147

CRP; c-reactive protein, ESR; erythrocyte sedimentation rate, Hgb; hemoglobin, SUV; standardized uptake values, PET; positron emission tomography

**Table 2.** The median SUVmax and SUVmean of BLR and SLR is given in the table.

	SUVmax	SUVmean
Bone marrow-to-liver	0.77 (0.08-2.92)	0.85 (0.07-8.75)
Spleen-to-liver	0.78 (0.30-9.09)	0.85 (0.09-6.43)

**Table 3.** The association between <sup>18</sup>F-FDG uptake (SUVmax and SUVmean) of liver, spleen, and bone marrow and CRP and albumin.

<sup>18</sup> F-FDG uptake	CRP≤0.5 mg/dl, n=177	CRP>0.5 mg/dl, n=517	P value	Alb≤3.5 mg/dl, n=429	Alb>3.5 mg/dl, n=276	P value
SUVmax of Liver	3.87±2.88	3.55±0.81	0.024	3.51±0.81	3.83±2.35	0.014
SUVmean of Liver	2.32±1.69	2.04±0.48	0.004	2.20±0.47	2.26±1.32	0.003
SUVmax of Spleen	2.85±2.01	3.09±1.04	0.777	2.85±1.08	2.92±1.57	0.463
SUVmean of Spleen	1.91±1.54	2.09±0.47	0.241	1.82±0.57	1.88±1.08	0.375
SUVmax of bone marrow	2.76±0.79	2.92±0.89	0.031	2.87±0.86	2.89±0.88	0.398
SUVmean of bone marrow	1.75±0.53	1.87±0.77	0.026	1.86±0.81	1.81±0.55	0.360
SUVmax of SLR	0.75±0.11	0.83±0.40	<0.001	0.83±0.43	0.77±0.14	0.020

(Continued)

<b>SUVmean of SLR</b>	0.85±0.43	0.90±0.18	0.020	0.91±0.32	0.84±0.16	0.001
<b>SUVmax of BLR</b>	0.77±0.21	0.84±0.27	0.001	0.83±0.27	0.80±0.24	0.106
<b>SUVmean of BLR</b>	0.84±0.26	0.96±0.49	<0.001	0.96±0.42	0.86±0.29	0.002

Alb; albumin, SLR; spleen-to-liver ratio, BLR; bone marrow-to-liver ratio

**Table 4.** The impact of CRP, albumin, and ESR on SUVmax and SUVmean of BLR.

<sup>18</sup> F-FDG uptake		Univariate		Multivariate	
		P value	CI 95.0%	P value	CI 95.0%
CRP	SUVmax	0.004	0.000 – 0.002	0.881	0.001 – 0.008
	SUVmean	0.001	0.002 – 0.003	0.757	-0.065 – 0.088
Albumin	SUVmax	0.009	-0.098 – 0.140	0.549	-0.070 – 0.131
	SUVmean	0.004	-0.170 – 0.033	0.193	-0.657 – 0.135
ESR	SUVmax	<0.001	0.001 – 0.004	0.103	-0.001 – 0.009
	SUVmean	0.191	-0.001 – 0.007	0.357	-0.005 – 0.002

**Table 5.** The impact of CRP, albumin, and ESR on SUVmax and SUVmean of SLR.

<sup>18</sup> F-FDG uptake		Univariate		Multivariate	
		P value	CI 95.0%	P value	CI 95.0%
CRP	SUVmax	0.100	0.000 – 0.002	0.620	-0.056 – 0.085
	SUVmean	<0.001	0.001 – 0.002	0.757	-0.065 – 0.088
Albumin	SUVmax	0.009	-0.098 – 0.140	0.061	-0.002 – 0.095
	SUVmean	<0.001	-0.092 – -0.047	0.679	-0.049 – 0.076
ESR	SUVmax	<0.001	0.001 – 0.003	0.001	0.001 – 0.004
	SUVmean	<0.001	0.002 – 0.004	0.003	0.001 – 0.005

P=0.001, respectively), however, not with albumin (P>0.05).

### Bone marrow

Maximum SUV of bone marrow demonstrated a positive correlation with CRP (P=0.003) and ESR (P<0.05) not with albumin (P>0.05). Mean SUV had a positive correlation with CRP and ESR (P<0.001, P=0.05, and P=0.015, respectively).

Albumin had no correlation with SUVmean of spleen (P>0.05).

Regression analysis of SUVmax and SUVmean of liver, spleen, and bone marrow demonstrated that albumin had an impact on liver <sup>18</sup>F-FDG uptake, while CRP and ESR had no impact on spleen <sup>18</sup>F-FDG uptake, and ESR had an impact on spleen and bone marrow <sup>18</sup>F-FDG uptake (Table 7).

**Table 6.** The correlation analysis of SUVmax and SUVmean of liver, spleen and bone marrow with CRP, albumin, and ESR.

	<sup>18</sup> F-FDG uptake	CRP	Albumin	ESR
<b>Liver</b>	SUVmax	0.246 (r=-0.046)	<0.001 (r=-0.220)	0.230 (r=-0.088)
	SUVmean	0.002 (r=-0.115)	<0.001 (r=-0.181)	0.511 (r=-0.048)
<b>Spleen</b>	SUVmax	0.006 (r=0.104)	0.679 (r=0.020)	0.052 (r=0.143)
	SUVmean	0.002 (r=0.116)	0.182 (r=-0.064)	0.001 (r=0.239)
<b>Bone marrow</b>	SUVmax	0.003 (r=0.112)	0.498 (r=0.032)	0.043 (r=0.136)
	SUVmean	<0.001 (r=0.136)	0.674 (r=-0.020)	0.015 (r=0.177)

**Table 7.** Univariate analysis of SUVmax and SUVmean of liver and spleen with CRP, albumin, and ESR.

<sup>18</sup> F-FDG uptake		Univariate (Liver)		Univariate (Spleen)		Univariate (Bone Marrow)	
		P value	CI 95.0%	P value	CI 95.0%	P value	CI 95.0%
<b>CRP</b>	SUVmax	0.363	-0.002 – 0.006	0.594	-0.002 – 0.004	0.594	-0.002 – 0.004
	SUVmean	0.161	-0.001 – 0.005	0.656	-0.002 – 0.003	0.656	-0.002 – 0.003
<b>Albumin</b>	SUVmax	0.011	-0.728 – 0.600	0.316	-0.107 – 0.331	0.316	-0.107 – 0.311
	SUVmean	0.018	-0.046 – 0.394	0.531	-0.097 – 0.188	0.531	-0.097 – 0.188
<b>ESR</b>	SUVmax	0.183	0.002 – 0.008	0.023	0.001 – 0.008	0.012	0.001 – 0.011
	SUVmean	0.363	0.002 – 0.004	0.002	0.001 – 0.006	0.337	-0.003 – 0.010

## Discussion

The standardized uptake value (SUVmax or SUVmean) of organs typically falls within a narrow range, and significant changes in their values may indicate various clinical conditions such as infection and inflammation. This study aimed to investigate the characteristics of <sup>18</sup>F-FDG involvement in the spleen, liver and bone marrow during active or chronic inflammation or infection (as indicated by high CRP and ESR levels, and low albumin). It demonstrated that higher CRP levels and lower plasma albumin are associated with reduced <sup>18</sup>F-FDG uptake in the liver. However, albumin had no impact on <sup>18</sup>F-FDG uptake in the spleen and bone marrow.

In recent years, PET has risen as a crucial functional diagnostic tool across various medical conditions. Predominantly, PET/CT imaging has been extensively employed for di-

agnosing, staging and monitoring malignancies [1, 2, 7]. Besides, it has been suggested that PET/CT can be used for the early diagnosis of infections and inflammatory diseases and in monitoring the response of their treatments [8, 9]. White blood cells and other inflammatory cells exhibit extensive glucose metabolism when they activate at sites of infection. Moreover, inflammatory mediators prompt a localized enhancement of glucose transporters, leading to elevated cellular <sup>18</sup>F-FDG uptake in the inflammation sites. Consequently, infection sites are frequently discernible on <sup>18</sup>F-FDG PET/CT scans before crucial structural changes like abscess formation [10].

For a better understanding of the <sup>18</sup>F-FDG acquisition in the liver, spleen and bone marrow during active infection or inflammation, their physiological acts should be considered. Under normal circumstances, the spleen is the largest lymphoid organ in the body and typically exhibits lower



$^{18}\text{F}$ -FDG uptake compared to the liver, resulting in an expected SLR of around 0.9, which does not change significantly with age [11]. Both tumors and inflammatory and infective processes exhibit increased  $^{18}\text{F}$ -FDG uptake in the spleen, bone marrow and liver. Rini et al. (2002) reported that high spleen  $^{18}\text{F}$ -FDG uptake is predictive of splenic involvement of lymphoma with a sensitivity, specificity, and accuracy of 92%, 100%, and 97%, respectively [12].

Rao et al. (2016) presented compelling evidence, indicating that the SUVmax ratio between the spleen and liver averaged  $1.69 \pm 1.02$  in lymphoma patients and  $1.44 \pm 0.48$  in those with inflammation. Despite these variations, the SUVmax ratio between the spleen and liver did not demonstrate a statistically significant difference between the two groups. This observation prompted them to propose that the diffuse and heightened  $^{18}\text{F}$ -FDG uptake in the spleen and liver might be a shared characteristic across various inflammatory conditions, possibly due to immune system activation within these organs [13]. In contrast, in this study, SUV levels of the liver were lower with higher CRP and hypoalbuminemia compared to normal CRP and albumin levels, but SUV levels of the spleen did not change. Multivariate analysis showed CRP, albumin and ESR have no impact on SUV levels of liver, spleen, and bone marrow.

Fluorine-18-FDG uptake is dependent on time; the interval between  $^{18}\text{F}$ -FDG administration and PET scan significantly influences SUV, which escalates with prolonged time to imaging after  $^{18}\text{F}$ -FDG injection. So, the SUV values presented in this study may differ from previous studies, since the mean duration for the assessment of  $^{18}\text{F}$ -FDG uptake was 75 minutes, which is relatively longer compared to previous studies [14]. We prefer to utilize the late-phase images based on the rationale that tumor  $^{18}\text{F}$ -FDG uptake tends to increase over time while background uptake decreases. This timing ensures optimal contrast between the tumor and surrounding tissues, enhancing the accuracy of our assessments.

C-reactive protein demonstrated a positive correlation with SUVmax and SUVmean of SLR and BLR, suggesting that inflammation and infection may heighten  $^{18}\text{F}$ -FDG acquisition in the spleen and bone marrow. Pijl et al. (2021) reported that high spleen  $^{18}\text{F}$ -FDG uptake is associated with a higher inflammatory response, especially in cases of cardiovascular located infection foci [15].

High plasma glucose levels have been found to be associated with less  $^{18}\text{F}$ -FDG uptake in previous studies [15, 16]. However,  $^{18}\text{F}$ -FDG accumulation of malignant lesions may remain sufficiently high for reliable qualitative clinical diagnosis in chronic and acute hyperglycemic states [16, 17]. In this study, plasma glucose levels were kept in a narrow range (67-140mg/dL) to minimize the glucose effects on  $^{18}\text{F}$ -FDG acquisition in the organs.

Balink et al. (2015) reported that in patients with unknown origin fever or inflammation, compared with elevated ESR levels, elevated CRP levels more often indicate a true positive  $^{18}\text{F}$ -FDG PET/CT outcome [18]. Similarly, Tseng et al. (2013) demonstrated that  $^{18}\text{F}$ -FDG PET/CT may be clinically useful for the detection of occult foci of infection in patients with sepsis of unknown origin [19]. C-reactive protein, albumin, and ESR had an impact on  $^{18}\text{F}$ -FDG uptake at various

degrees in the spleen, liver, and bone marrow. These results represent the complexity of the association between  $^{18}\text{F}$ -FDG uptake and immune pathways. However, we believe that  $^{18}\text{F}$ -FDG PET/CT may have a clinical impact on diagnostic and treatment management of hospitalized patients in order to source identification in the setting of unknown infection or fever [20, 21]. Elshalakani et al. (2022) examined the utility of PET/CT in discerning the underlying causes of fever of unknown origin in a cohort of 40 patients. Their findings underscored the pivotal role of  $^{18}\text{F}$ -FDG PET/CT in providing precise diagnoses, with malignancy detected in 20 patients (50%), infectious origins identified in 7 patients (17.5%), and non-infectious inflammatory conditions diagnosed in 6 patients (15%) [21].

Previous studies suggested that  $^{18}\text{F}$ -FDG PET/CT is a more effective tool for identifying cancer of unknown primary (CUP) than CT alone and may offer some survival benefits [22, 23]. Rimer et al. (2023) reported, a significantly higher detection rate (DR) of the primary tumor in patients with CUP who received a  $^{18}\text{F}$ -FDG PET/CT scan (36.5%) compared to those who only received a CT scan (17.6%) [23]. In this study, after lung cancer (25.7%), the second most frequently diagnosed malignancy was cancer of unknown primary, with an incidence of 20.8%. This study has once again provided robust evidence supporting the efficacy of  $^{18}\text{F}$ -FDG PET/CT in detecting cancers of unknown primary origin.

The impact of hypoalbuminemia on  $^{18}\text{F}$ -FDG uptake is unknown. A previous study indicated hypoalbuminemia ( $<3.5$  g/dL) is associated with less  $^{18}\text{F}$ -FDG uptake in the liver in individuals with malnutrition [24]. Galvez et al. (2023) found that a decrease in brain SUVpeak was only observed with weight losses of 10% or more, corresponding to severe malnutrition [25]. Our study demonstrated hypoalbuminemia is associated with lower liver  $^{18}\text{F}$ -FDG SUVmax and SUVmean and increased SLR and BLR. This finding indicates in hypoalbuminemic patients' liver may not be a good reference for the  $^{18}\text{F}$ -FDG uptake comparisons [24, 25].

Positron emission tomography/CT may have diagnostic importance for patients presenting with non-specific complaints and an elevated ESR by revealing abnormal  $^{18}\text{F}$ -FDG uptake indicative of various conditions such as infection, malignancy, or auto-inflammatory diseases like sarcoidosis or large-vessel vasculitis [26]. Lensen et al. (2013) conducted two complementary studies in patients with elevated ESR and nonspecific symptoms, one retrospective and one prospective, to provide a comprehensive analysis of their research question [23]. In the retrospective study, PET/CT scans suggested malignancy in 8 patients, auto-inflammatory disease in 8 patients (including 5 with large-vessel vasculitis), and infection in 3 patients. Two scans showed non-specific abnormalities, and 9 scans were normal. In the prospective study, 25 PET/CT scans exhibited suspected auto-inflammatory disease, particularly large-vessel vasculitis in 14 cases. Infection and malignancy were suspected in 5 and 3 cases, respectively. Seven scans demonstrated non-specific abnormalities, and 20 were normal. Among the 40 abnormal PET/CT results, 22 diagnoses were confirmed, and 3 alternative diagnoses were established. In this study, ESR had a weak positive correlation with SUV values of the spleen and bone marrow but not the liver, and in univariate ana-

lysis, the only factor had an impact on SUV values of spleen and bone marrow. These results suggest that abnormal ESR levels have potential in the diagnosis of malignancy, unknown infection, or other inflammatory conditions due to their good correlation with  $^{18}\text{F}$ -FDG uptake [24]. However, to avoid false positives and negatives in  $^{18}\text{F}$ -FDG uptake, it is recommended to use high cut-off values for ESR [18, 26, 27].

### Limitations of the study

Data collection relies on past medical records and cannot describe the severity/stages of the accompanying diseases. The causes of infection and inflammatory conditions other than presence of malignancy are not clear. The retrospective nature of the study may limit the ability to control for confounding variables adequately. Moreover, the single measurements of ESR, CRP and albumin may not reflect the precise links between them and  $^{18}\text{F}$ -FDG uptakes. Study is single center and, it may limit the diversity of patient demographics and clinical presentations, thus affecting the generalizability of the findings to other healthcare settings. Variability in  $^{18}\text{F}$ -FDG uptake measurements or interpretations between different observers or scanners could introduce measurement bias. Standardization protocols may have been implemented to minimize this bias, but it cannot be entirely ruled out. The study did not include a comprehensive evaluation of clinical outcomes such as disease progression, response to treatment, or long-term follow-up. This limits the ability to draw conclusions about the clinical significance of the observed  $^{18}\text{F}$ -FDG uptake patterns with ESR, albumin, and CRP changes.

In conclusion, this study revealed significant associations between CRP levels, hypoalbuminemia, and  $^{18}\text{F}$ -FDG uptake in the liver, spleen and bone marrow, highlighting the potential of PET/CT as a diagnostic tool for identifying  $^{18}\text{F}$ -FDG PET/CT abnormalities in patients with inflammatory or infectious states or malignancies. However, the association between CRP, ESR, and albumin and  $^{18}\text{F}$ -FDG uptake in various organs is not uniform and considerably variable. The severity of inflammation and infection, stages of tumors and some local and systemic factors may have unpredictable influences of these parameters on  $^{18}\text{F}$ -FDG activity of liver, spleen and bone marrow. However, the observed correlations between ESR levels and  $^{18}\text{F}$ -FDG uptake in the spleen and bone marrow provide additional evidence may have provide considering the utility of PET/CT in detecting and monitoring inflammatory processes.

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