Journal of Nuclear Medicine, published on February 5, 2021 as doi:10.2967/jnumed.120.254482

# Prognostic value of bone marrow metabolism on pretreatment $^{18}$F-FDG PET/CT in patients with metastatic melanoma treated with anti-PD-1 therapy

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Running title: $^{18}$F-FDG PET in melanoma before anti-PD-1

Total word count: 2477 words

**ABSTRACT**

**Purpose:** To investigate the prognostic value of $^{18}$F-FDG PET/CT parameters in melanoma patients before beginning anti-PD-1 therapy.

**Methods:** Imaging parameters including SUVmax, metabolic tumor volume (MTV), and bone marrow to liver SUVmean ratio (BLR) were measured from baseline PET/CT in 92 patients before the start of anti-PD-1 therapy. Association with survival and imaging parameters combined with clinical factors was evaluated. Clinical and laboratory data between high (> median) and low (≤ median) BLR groups were compared.

**Results:** Multivariate analyses demonstrated that BLR was an independent prognostic factor for PFS and OS ($P = 0.017$, $P = 0.011$, respectively). The high BLR group had higher levels of white blood cell count/neutrophil count and C-Reactive Protein than the low BLR group ($P < 0.05$).

**Conclusion:** Patients with high BLR were associated with poor PFS and OS, potentially explained by evidence of systemic inflammation known to be associated with immunosuppression.

**Key words**: $^{18}$F-FDG, PET/CT, bone marrow uptake, immunotherapy, melanoma

## INTRODUCTION

Metabolic tumor volume (MTV) and glucose metabolism of normal tissues associated with immunity on $^{18}$F-FDG PET/CT before and during immune checkpoint inhibitor (ICI) therapy have been explored as predictors of therapeutic efficacy (*1-4*). The link between $^{18}$F-FDG uptake by immune-mediating tissues, such as the bone marrow (BM) and spleen, and poor cancer outcomes is hypothesized to be explained by generalized (*5,6*).

We hypothesized that imaging parameters, including physiologic uptake in hematopoietic tissues on baseline PET/CT, combined with known clinical prognostic factors for melanoma, may more accurately predict the therapeutic efficacy and prognosis of melanoma patients treated with antibodies to the programed cell death 1 receptor (anti-PD-1) than clinical factors alone.

## MATERIALS AND METHODS

### Patients

Ninety-two melanoma patients who received anti-PD-1 antibody (pembrolizumab or nivolumab) as first line immunotherapy between April 2012 and June 2019 were enrolled in this retrospective study. The Institutional Review Board approved this study and waived the requirement for obtaining written informed consent.

### $^{18}$F-FDG PET/CT protocol and data analysis

Approximately 1 h after intravenous injection of $^{18}$F-FDG, PET/CT images from the vertex to the toes were acquired per standard of care protocol at our institution using the Discovery 600, 690, 710, or MI scanners (General Electric, Milwaukee WI)**.** Maximum standardized uptake value

(SUVmax), mean standardized uptake value (SUVmean), MTV and TLG with SUV ≥ 2.5 were measured for all $^{18}$F-FDG-avid lesions.

Liver and spleen SUVmean were measured by drawing a spherical volume of interest (VOI) in the center of an area of non-diseased right hepatic lobe (3cm) (Fig.1A) and spleen (2cm) (Fig.1C), respectively. For the BM, spherical 1.5cm VOIs were placed within the center of nondiseased L1 to L4 (lumbar) vertebral bodies (Fig.1B), and an average SUVmean of the lumbar vertebral bodies was calculated. Then, the BM to Liver Ratio (BLR) and Spleen to Liver Ratio (SLR) were calculated, by dividing the BM SUVmean by the liver SUVmean and the spleen SUVmean by the liver SUVmean, respectively (*1,7,8*).

**Comparison of the clinical characteristics and imaging parameters of patients with high and low BLR**

To clarify the clinical characteristics of patients with increased BM uptake, patients were classified into the high BLR (> median) group and low BLR (≤ median) group, respectively, and physical and laboratory data as well as imaging parameters were compared between the two groups.

**Statistical Analysis**

Values between groups were compared using the Mann-Whitney U test. Progression free survival (PFS) was assessed from the start date of immunotherapy to disease progression based on irRECIST (*9*). Overall survival (OS) was assessed from the start date of immunotherapy to death or last follow-up. Cutoff values of age and imaging parameters were set on median values. The patients' cohort was divided into separate groups based on the following parameters: age, gender, primary site, BRAF mutation status, presence of brain metastasis, serum lactate dehydrogenase (LDH) level, and imaging parameters. Factors identified as being significant in the log-rank test ($P < 0.05$) were entered into a multivariate Cox proportional hazards model. Kaplan–Meier curves were generated for subgroups. The

method of Holm was used to adjust the *P* values for multiple comparisons. Spearman's rank correlation coefficients were calculated to assess the relationships between continuous variables. *P* values < 0.05 were considered statistically significant.

## RESULTS

### Relationship of $^{18}$F-FDG PET Parameters with PFS and OS

Patient characteristics are summarized in Table 1. After the median follow-up of 18.2 months, 53 patients had disease progression, and 32 of them expired. Median PFS and OS were 11.6 months (95% CI 7.1 – 28.3 months) and more than 60 months, respectively. Multivariate analysis based on the results of univariate analysis (Supplemental Table 1) demonstrated that BLR and BRAF mutation were independent prognostic factors for PFS (*P* = 0.017 and 0.018, respectively), and BLR, BRAF mutation, and LDH elevation were independent prognostic factors for OS (*P* = 0.011, 0.0078, and 0.013, respectively) (Table 2). Figure 2 shows Kaplan–Meier curves generated for subgroups divided with variables significant in multivariate analysis for PFS and OS. The median PFS of the high BLR (> 0.78) group was 8.6 months (95% CI 3.0 to 42.5 months), significantly shorter than that of the low BLR group (28.3 months, 95% CI 7.7 to 54.9 months) (*P* = 0.027). Similarly, the median OS of the high BLR group was 28.0 months (95% CI 17.2 to 28.7 months), significantly shorter than that of the low BLR group (more than 60 months) (*P* = 0.019).

### Combining BLR and clinical factors

Combining BLR and independent clinical factors (BRAF mutation and LDH elevation) provided further patient stratification. The population was stratified in three risk categories: 1) low risk (low BLR and favorable clinical risk factors); (2) intermediate risk (low BLR and unfavorable clinical risk factors or high BLR and favorable clinical risk factors); and (3) high risk (high BLR and unfavorable clinical risk factors). OS of the high-risk group was significantly worse than that of any other risk group (Fig.3), and this combined approach to risk stratification differentiated patients

according to survival better than BLR or the set of clinical parameters alone. The median OS of patients with high BLR was 28.0 months, while in patients with high BLR together with BRAF mutation or LDH elevation, OS was 16.9 and 1.0 months, respectively.

**Comparison of the clinical characteristics and imaging parameters of patients with high and low BLR**

The high BLR group had higher counts of white blood cells, neutrophils, red blood cells, higher CRP level, and higher MTV; and lower levels of hemoglobin and albumin than the low BLR group ($P < 0.05$) (Supplemental Table 2). Neutrophil count had the strongest correlation with BLR ($\rho = 0.40$, $P = 0.0002$) among laboratory data, and MTV was weakly correlated with BLR ($\rho = 0.34$, $P = 0.0011$) (Supplemental Table 3).

## DISCUSSION

BLR on baseline $^{18}$F-FDG PET was significantly correlated inversely with PFS and OS in melanoma patients treated with anti-PD-1 therapy. Like previously published studies showing a relationship between laboratory markers of inflammation and BM metabolism (*7,10*), we found a significantly positive correlation between $^{18}$F-FDG uptake in the BM and neutrophil count ($\rho = 0.40$) (*11*) This correlation could potentially be explained by the predominance of neutrophils in the BM, high rates of granulopoiesis required to maintain the neutrophil population, and the preference of neutrophils to utilize glycolysis for energy production (*11,12*). A weak positive correlation between BLR and tumor burden (MTV, $\rho = 0.34$) was also found. Accumulation of inflammatory factors leads to immunosuppression which is associated with cancer progression and poor outcomes (*5*). In melanoma, bone marrow-derived cells play a key role in tumor progression, neo-vascularization and priming of metastasis (*13,14*), potentially explaining the negative relationship between BM hypermetabolism and clinical outcomes observed in our study.

By combining information on BRAF and LDH elevation with BLR, we could extract a very poorly prognostic high risk group with the median OS of 16.9 and 1.0 months, respectively. We believe that this combination of predictive factors could allow the identification of high risk patients who are not expected to benefit from anti-PD-1 therapy prior to treatment, allowing rapid selection of a potentially more efficacious treatment, such as novel therapies targeting cancer-related inflammation (*15*).

A recent retrospective study of 55 melanoma patients prior to treatment with anti-PD-1 has reported the utility of BLR for predicting outcomes (*3*). The difference between the current study and the previous one is that we analyzed a larger number of patients ($n$ = 92) and included patients with brain metastasis. Brain metastasis is not less frequent in patients with advanced melanoma who receive immunotherapy (*16*); in fact, 28.6% of our patients had brain metastasis before immunotherapy. Therefore, we determined that patients with brain metastasis should be included in the search for imaging biomarkers useful for predicting treatment response and prognosis of immunotherapy based on real-world clinical scenarios. While, there was a recent report that contradicting our results that melanoma patients who responded to immunotherapy had significantly higher $^{18}$F-FDG uptake in BM (BM SUVmean normalized by blood pool activity) than non-responders (*17*).

Our study has several limitations. First, it was retrospective in design. In addition, the use of different PET scanners could have resulted in variability in SUV measurements of MTV. However, the estimation of BM metabolism was assessed by standardizing values with liver background, allowing for the harmonization of PET features and potential generalizability of our model.

## CONCLUSION

Patients with increased metabolism in the bone marrow were associated with poor PFS and OS, potentially explained by evidence of systemic inflammation known to be associated with immunosuppression.

## DISCLOSURE

No potential conflicts of interest relevant to this article exist.

## KEY POINTS

QUESTION: Is pretreatment $^{18}$F-FDG uptake in the bone marrow useful in the prognostic evaluation of advanced melanoma patients treated with anti-PD-1 therapy?

PERTINENT FINDINGS: Univariate and multivariate analyses revealed that bone marrow to liver SUVmean ratio (BLR) was an independent prognostic factor for PFS and OS ($P = 0.017$, $P = 0.011$, respectively). Patients with high BLR uptake (> median) had a tendency to have systemic inflammation known to be associated with immunosuppression.

IMPLICATIONS FOR PATIENT CARE: BLR may be a helpful imaging biomarker to select patients with advanced melanoma for immune-modulating therapies

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## FIGURE LEGENDS

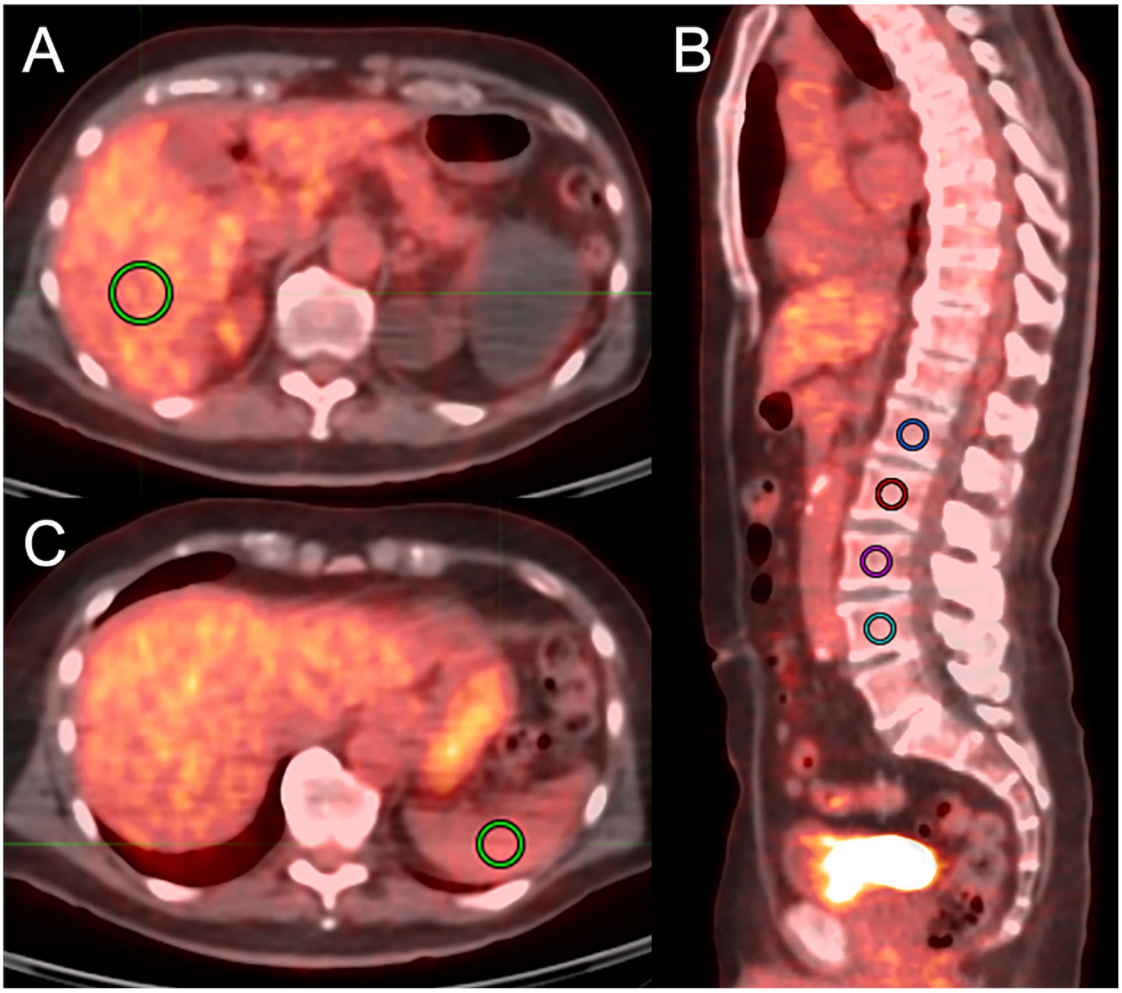



**FIGURE 1** Illustration of the placement of volume of interest (VOI) in the liver (A), the L1 to L4 (lumbar) vertebral bodies (B), and spleen (C).

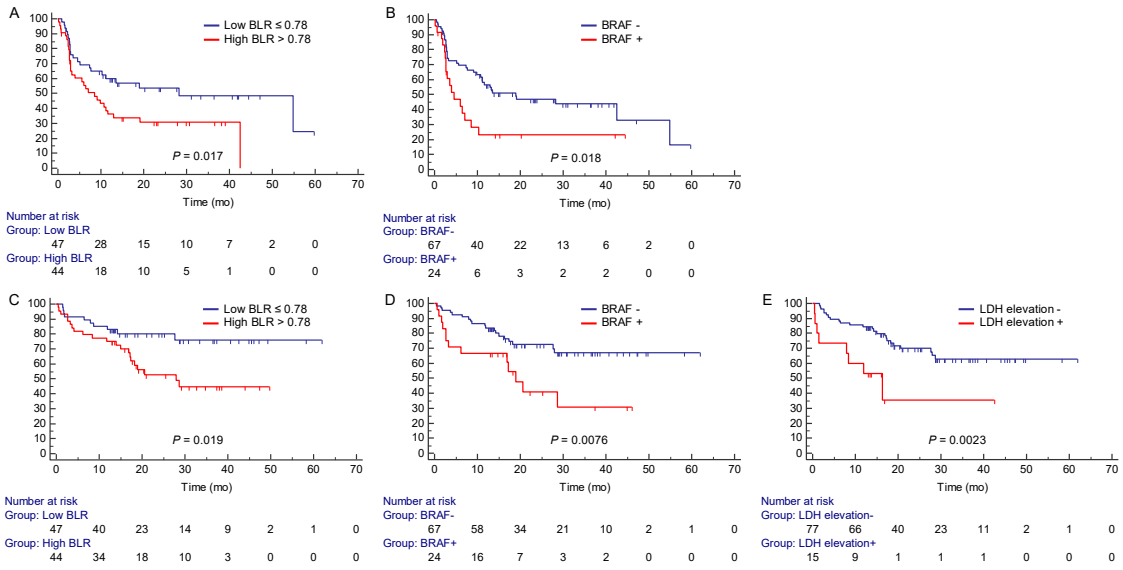



**FIGURE 2** Kaplan-Meier curves for progression free survival (A, B) and overall survival (C - E) divided into the two groups based on the factors identified as being significant in the multivariate analysis.

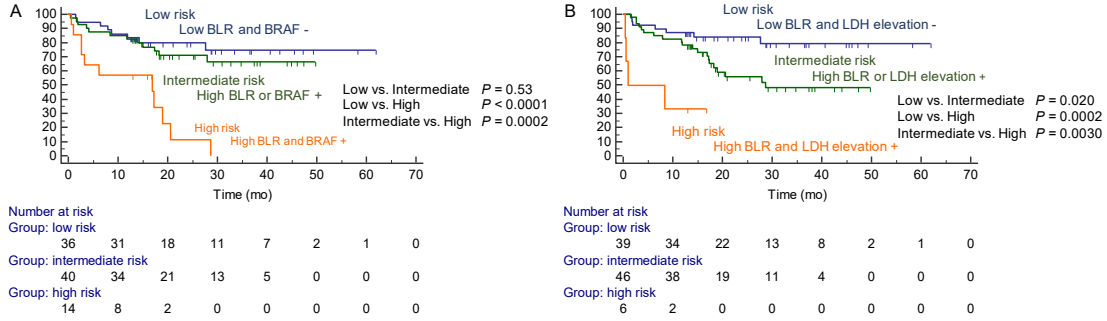



**FIGURE 3** Kaplan–Meier curves for overall survival in three risk groups stratified according to BLR combined with BRAF mutation (A) or LDH elevation (B).

**TABLE 1** Patient characteristics

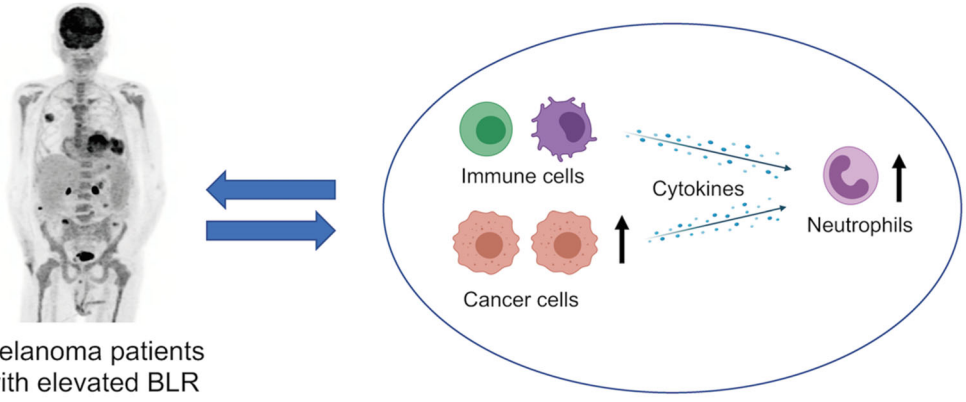
| | |
|---|---|
| Patients | *n* = 92 |
| White, n (%) | 79 (85.9%) |
| Hispanic, n (%) | 8 (8.7%) |
| Asian, n (%) | 3 (3.3%) |
| Other, n (%) | 2 (2.2%) |
| Age (years), median (interquartile range) | 69 (55 – 76) |
| Male, n (%) | 55 (59.8%) |
| Primary site, n (%) | |
| Skin | 74 (80.4%) |
| Other or unknown | 18 (19.6%) |
| BRAF V600 mutation, n (%) | 24/91 (26.4%) |
| Brain metastasis, n (%) | 26/91 (28.6%) |
| LDH level > normal, n (%) | 15/92 (16.3%) |
| Immune checkpoint inhibitors | |
| Pembrolizumab (anti-PD-1 antibody) | 72 |
| Nivolumab (anti-PD-1 antibody) | 9 |
| Nivolumab and ipilimumab (anti-CTLA-4 antibody) | 10 |
| Nivolumab and relatlimab (anti-LAG-3 antibody) | 1 |
| Intervals (days), median (interquartile range) | |
| Baseline PET to therapy initiation | 33.5 days (18 - 50) |
| Baseline PET and laboratory test | 22 days (9 – 34.3) |

**TABLE 2** Results of multivariate analyses for predicting progression free survival and overall survival

| Variable | Progression free survival | | | Overall survival | | |
|---|---|---|---|---|---|---|
| | Hazard ratio | 95% confidence interval | *P* | Hazard ratio | 95% confidence interval | *P* |
| High BLR (> 0.78) | 2.07 | 1.14 to 3.77 | 0.017 | 2.85 | 1.28 to 6.39 | 0.011 |
| BRAF mutation | 2.06 | 1.13 to 3.75 | 0.018 | 2.71 | 1.30 to 5.65 | 0.0078 |
| Brain metastasis | 1.85 | 0.99 to 3.45 | 0.053 | 2.09 | 0.99 to 4.43 | 0.054 |
| Elevated LDH | 2.00 | 0.90 to 4.42 | 0.085 | 3.31 | 1.29 to 8.46 | 0.013 |

LDH, lactate dehydrogenase; BLR, bone marrow to liver ratio

**Graphical abstract**

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**SUPPLEMENTAL TABLE 1** Results of univariate analyses for predicting progression free survival and overall survival

| Variable | | Median PFS (months) | | | P | Median OS (months) | | | P |
|---|---|---|---|---|---|---|---|---|---|
| | | Median | 95% confidence interval | | | Median | 95% confidence interval | | |
| | | | Lower limit | Upper limit | | | Lower limit | Upper limit | |
| Age | > 69 (43) | 28.3 | 9.1 | 54.9 | 0.12 | n/a | n/a | n/a | 0.25 |
| | ≤ 69 (49) | 8.6 | 3.3 | 13.3 | | n/a | n/a | n/a | |
| Gender | Male (55) | 19 | 7.3 | 54.9 | 0.25 | n/a | n/a | n/a | 0.39 |
| | Female (37) | 10.3 | 3.0 | 19.1 | | n/a | n/a | n/a | |
| Primary site | Other (18) | 12.9 | 2.4 | 13.3 | 1.00 | n/a | n/a | n/a | 0.17 |
| | Skin (74) | 11.2 | 6.5 | 42.5 | | n/a | n/a | n/a | |
| BRAF mutation | Presence (24) | 4.5 | 2.6 | 8.6 | 0.013 | 18.9 | 3.3 | 28.7 | 0.0076 |
| | Absence (67) | 19 | 10.8 | 54.9 | | n/a | n/a | n/a | |
| Brain metastasis | Presence (26) | 3.5 | 2.6 | 11.6 | 0.0080 | 18.2 | 3.7 | 28.7 | 0.0022 |
| | Absence (65) | 19.1 | 9.1 | 54.9 | | n/a | n/a | n/a | |
| Elevated LDH | Yes (15) | 6.5 | 0.6 | 13.3 | 0.030 | 16.3 | 1 | 16.3 | 0.0023 |
| | No (77) | 13.5 | 7.7 | 54.9 | | n/a | n/a | n/a | |
| SUVmax | > 14.27 (46) | 9.1 | 3.5 | 42.5 | 0.30 | n/a | n/a | n/a | 0.15 |
| | ≤ 14.27 (46) | 19 | 7.3 | 54.9 | | n/a | n/a | n/a | |
| SUVmean | > 5.20 (46) | 13.3 | 5.6 | 42.5 | 0.44 | n/a | n/a | n/a | 0.63 |
| | ≤ 5.20 (46) | 10.8 | 4.5 | 54.9 | | n/a | n/a | n/a | |
| MTV | > 25.62 (46) | 10.8 | 3.3 | 19.1 | 0.36 | n/a | n/a | n/a | 0.61 |
| | ≤ 25.62 (46) | 19.0 | 5.1 | 54.9 | | n/a | n/a | n/a | |
| TLG | > 126.84 (46) | 10.8 | 3.0 | 19.1 | 0.32 | n/a | n/a | n/a | 0.55 |
| | ≤ 126.84 (46) | 19.0 | 5.6 | 54.9 | | n/a | n/a | n/a | |
| BLR | > 0.78 (44) | 8.6 | 3.0 | 42.5 | 0.027 | 28.0 | 17.2 | 28.7 | 0.019 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ≤ 0.78 (47) | 28.3 | 7.7 | 54.9 | | n/a | n/a | n/a | |
| SLR | > 0.82 (45) | 8.6 | 3.3 | 54.9 | 0.16 | 28 | 17.2 | 28.7 | 0.0475 |
| | ≤ 0.82 (46) | 12.9 | 7.7 | 19.0 | | n/a | n/a | n/a | |

LDH, lactate dehydrogenase; MTV, metabolic tumor volume; TLG, total lesion glycolysis; BLR, bone marrow to liver ratio; SLR, spleen to liver ratio

**SUPPLEMENTAL TABLE 2** Comparison of physical and laboratory data between the high BLR and low BLR group

| | | High BLR (> 0.78) | Low BLR (≤ 0.78) | *P* |
|---|---|---|---|---|
| Age (years) | | 60.5 (49 - 75) | 72 (63.8 - 79) | 0.0008 |
| Height (cm) | Male | 178 (172.8 - 183) | 178 (173 - 183) | 0.68 |
| | Female | 160 (152.3 – 167.8) | 162 (157 - 168) | 0.61 |
| Body weight (kg) | Male | 82.6 (76.0 - 99.4) | 84.4 (79.5 – 98.4) | 0.60 |
| | Female | 69.1 (58.2 – 76.1) | 63.2 (57.3 – 71.2) | 0.47 |
| Lean body mass (kg) | Male | 61.1 (57.8 – 70.6) | 63.8 (60.1 – 68.5) | 0.38 |
| | Female | 46.7 (40.3 – 49.6) | 44.6 (42.3 – 47.1) | 0.92 |
| White blood cell count ($\times 10^3/\mu L$) | | 7.80 (6.10 - 9.60) | 6.00 (5.00 - 7.30) | 0.0014 |
| Neutrophil count ($\times 10^3/\mu L$) | | 5.02 (3.98 - 6.78) | 3.65 (2.78 - 4.42) | 0.0006 |
| Red blood cell count ($\times 10^6/\mu L$) | | 4.63 (4.33 - 5.12) | 4.45 (4.19 - 4.73) | 0.043 |
| Hemoglobin (g/dL) | | 13.1 (11.2 - 14.1) | 13.9 (13.3 - 14.7) | 0.030 |
| Hematocrit (%) | | 39.8 (35.6 – 43.0) | 41.3 (39.3 – 44.2) | 0.085 |
| Platelet count ($\times 10^3/\mu L$) | | 240 (194.8 - 311.3) | 208 (183.8 - 270.8) | 0.099 |
| Lactate dehydrogenase (U/L) | | 191 (166 - 238) | 194 (175.5 - 243) | 0.67 |
| Total protein (g/dL) | | 7.3 (7.0 - 7.7) | 7.25 (6.9 - 7.6) | 0.56 |
| Albumin (g/dL) | | 3.6 (3.4 - 4.0) | 3.95 (3.5 - 4.3) | 0.042 |
| C-Reactive Protein (mg/dL) | | 0.5 (0.2 - 1.9) | 0.2 (0.2 - 0.8) | 0.0046 |
| SUVmax | | 17.8 (11.3 – 29.8) | 12.7 (8.1 – 17.3) | 0.0053 |
| SUVmean | | 5.4 (4.1 – 6.6) | 4.6 (3.6 – 5.7) | 0.045 |
| Metabolic tumor volume (ml) | | 41.4 (11.2 – 164.2) | 7.6 (2.6 – 59.0) | 0.0018 |
| Total lesion glycolysis (g) | | 269.2 (58.5 – 892.4) | 37.6 (11.1 – 287.8) | 0.0007 |
| Spleen to liver SUVmean ratio | | 0.93 (0.81 – 1.04) | 0.78 (0.71 – 0.84) | < 0.0001 |

Continuous variables are presented as median (interquartile range).
BLR, bone marrow to liver ratio

**SUPPLEMENTAL TABLE 3** Correlogram between imaging parameters, physical data, and laboratory data


| | TLG | MTV | LBM | Neut | WBC | Ht | SUVmax | BW | Hgb | Height | RBC | Platelet | SUVmean | BLR | Cre | BUN | SLR | TP | CRP | LDH | Alb | Age |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **TLG** | | 0.983 | -0.064 | 0.342 | 0.268 | -0.146 | 0.612 | -0.065 | -0.197 | -0.046 | 0.059 | 0.434 | 0.465 | 0.349 | -0.066 | -0.066 | 0.053 | 0.079 | 0.345 | 0.311 | -0.189 | -0.186 |
| **MTV** | 0.983 | | -0.059 | 0.34 | 0.263 | -0.148 | 0.529 | -0.075 | -0.192 | -0.033 | 0.05 | 0.424 | 0.33 | 0.336 | -0.031 | -0.085 | 0.068 | 0.083 | 0.388 | 0.332 | -0.191 | -0.191 |
| **LBM** | -0.064 | -0.059 | | 0.177 | 0.132 | 0.252 | -0.036 | 0.88 | 0.301 | 0.857 | 0.226 | -0.203 | -0.091 | -0.106 | 0.464 | 0.23 | -0.185 | -0.145 | 0.005 | -0.127 | -0.044 | -0.03 |
| **Neut** | 0.342 | 0.34 | 0.177 | | 0.919 | -0.031 | 0.276 | 0.161 | -0.028 | 0.044 | 0.054 | 0.434 | 0.176 | 0.402 | 0.059 | 0.016 | 0.213 | 0.059 | 0.334 | -0.068 | -0.201 | -0.137 |
| **WBC** | 0.268 | 0.263 | 0.132 | 0.919 | | 0.025 | 0.266 | 0.158 | 0 | -0.005 | 0.145 | 0.473 | 0.195 | 0.389 | 0.027 | -0.013 | 0.205 | 0.168 | 0.332 | -0.065 | -0.097 | -0.166 |
| **Ht** | -0.146 | -0.148 | 0.252 | -0.031 | 0.025 | | -0.159 | 0.19 | 0.971 | 0.223 | 0.72 | -0.218 | -0.092 | -0.142 | 0.068 | -0.054 | -0.221 | 0.211 | -0.338 | -0.103 | 0.5 | -0.06 |
| **SUVmax** | 0.612 | 0.529 | -0.036 | 0.276 | 0.266 | -0.159 | | 0.006 | -0.195 | -0.056 | -0.015 | 0.332 | 0.775 | 0.263 | -0.115 | 0.022 | 0.141 | 0.155 | 0.132 | 0.089 | -0.121 | -0.048 |
| **BW** | -0.065 | -0.075 | 0.88 | 0.161 | 0.158 | 0.19 | 0.006 | | 0.223 | 0.603 | 0.219 | -0.145 | -0.053 | -0.08 | 0.465 | 0.2 | -0.211 | -0.108 | 0.026 | -0.121 | -0.048 | -0.073 |
| **Hgb** | -0.197 | -0.192 | 0.301 | -0.028 | 0 | 0.971 | -0.195 | 0.223 | | 0.263 | 0.669 | -0.256 | -0.126 | -0.216 | 0.065 | -0.062 | -0.284 | 0.17 | -0.369 | -0.174 | 0.474 | -0.061 |
| **Height** | -0.046 | -0.033 | 0.857 | 0.044 | -0.005 | 0.223 | -0.056 | 0.603 | 0.263 | | 0.18 | -0.226 | -0.076 | -0.099 | 0.407 | 0.21 | -0.105 | -0.185 | 0.009 | -0.082 | -0.037 | -0.016 |
| **RBC** | 0.059 | 0.05 | 0.226 | 0.054 | 0.145 | 0.72 | -0.015 | 0.219 | 0.669 | 0.18 | | -0.025 | 0.015 | 0.206 | -0.007 | -0.156 | 0.002 | 0.32 | -0.097 | -0.049 | 0.306 | -0.294 |
| **Platelet** | 0.434 | 0.424 | -0.203 | 0.434 | 0.473 | -0.218 | 0.332 | -0.145 | -0.256 | -0.226 | -0.025 | | 0.27 | 0.268 | -0.074 | -0.049 | 0.295 | 0.28 | 0.338 | 0.193 | -0.094 | -0.136 |
| **SUVmean** | 0.465 | 0.33 | -0.091 | 0.176 | 0.195 | -0.092 | 0.775 | -0.053 | -0.126 | -0.076 | 0.015 | 0.27 | | 0.207 | -0.15 | 0.021 | 0.035 | 0.072 | 0.001 | 0.063 | -0.056 | -0.017 |
| **BLR** | 0.349 | 0.336 | -0.106 | 0.402 | 0.389 | -0.142 | 0.263 | -0.08 | -0.216 | -0.099 | 0.206 | 0.268 | 0.207 | | -0.203 | -0.192 | 0.535 | 0.109 | 0.335 | 0.034 | -0.196 | -0.232 |
| **Cre** | -0.066 | -0.031 | 0.464 | 0.059 | 0.027 | 0.068 | -0.115 | 0.465 | 0.065 | 0.407 | -0.007 | -0.074 | -0.15 | -0.203 | | 0.51 | -0.014 | -0.093 | 0.092 | 0.168 | -0.119 | 0.301 |
| **BUN** | -0.066 | -0.085 | 0.23 | 0.016 | -0.013 | -0.054 | 0.022 | 0.2 | -0.062 | 0.21 | -0.156 | -0.049 | 0.021 | -0.192 | 0.51 | | -0.116 | -0.136 | -0.105 | 0.197 | -0.04 | 0.529 |
| **SLR** | 0.053 | 0.068 | -0.185 | 0.213 | 0.205 | -0.221 | 0.141 | -0.211 | -0.284 | -0.105 | 0.002 | 0.295 | 0.035 | 0.535 | -0.014 | -0.116 | | 0.213 | 0.354 | 0.135 | -0.185 | -0.045 |
| **TP** | 0.079 | 0.083 | -0.145 | 0.059 | 0.168 | 0.211 | 0.155 | -0.108 | 0.17 | -0.185 | 0.32 | 0.28 | 0.072 | 0.109 | -0.093 | -0.136 | 0.213 | | -0.064 | 0.024 | 0.381 | -0.224 |
| **CRP** | 0.345 | 0.388 | 0.005 | 0.334 | 0.332 | -0.338 | 0.132 | 0.026 | -0.369 | 0.009 | -0.097 | 0.338 | 0.001 | 0.335 | 0.092 | -0.105 | 0.354 | -0.064 | | 0.127 | -0.571 | 0.017 |
| **LDH** | 0.311 | 0.332 | -0.127 | -0.068 | -0.065 | -0.103 | 0.089 | -0.121 | -0.174 | -0.082 | -0.049 | 0.193 | 0.063 | 0.034 | 0.168 | 0.197 | 0.135 | 0.024 | 0.127 | | 0.058 | 0.055 |
| **Alb** | -0.189 | -0.191 | -0.044 | -0.201 | -0.097 | 0.5 | -0.121 | -0.048 | 0.474 | -0.037 | 0.306 | -0.094 | -0.056 | -0.196 | -0.119 | -0.04 | -0.185 | 0.381 | -0.571 | 0.058 | | -0.139 |
| **Age** | -0.186 | -0.191 | -0.03 | -0.137 | -0.166 | -0.06 | -0.048 | -0.073 | -0.061 | -0.016 | -0.294 | -0.136 | -0.017 | -0.232 | 0.301 | 0.529 | -0.045 | -0.224 | 0.017 | 0.055 | -0.139 | |

Values indicate Spearman rank correlation coefficient.

TLG, total lesion glycolysis; MTV, metabolic tumor volume; LBM, lean body mass; Neut, neutrophil; WBC, white blood cell; Ht, hematocrit; BW, body weight; Hgb, hemoglobin; RBC, red blood cell; BLR, bone marrow to liver ratio; Cre, creatinine; BUN, blood urea nitrogen; SLR, spleen to liver ratio; TP, total protein; CRP, C-reactive protein; LDH, lactate dehydrogenase; Alb, albumin