Research Article

Association of Visceral Adipose Tissue Metabolic Activity with Spleen and Bone Marrow ^{18}F-FDG Uptake in Patients with Colonic Cancer

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Abstract

Background and Aim: Spleen and bone marrow uptake of ^{18}F-fluorodeoxyglucose (FDG) has been proposed as a marker of systemic inflammation. We examined whether these measures are associated with visceral adipose tissue (VAT) metabolic activity in colonic cancer. Patients and Methods: This prospective single-center study included 118 patients with pathologically proven colonic adenocarcinoma who underwent pretherapy FDG positron emission tomography/computed tomography; 79 also had post-therapy scans. Maximum standardized uptake values (SUVmax) were measured in VAT, subcutaneous adipose tissue (SAT), spleen and bone marrow. Associations were tested with Spearman correlation. Results: At baseline, spleen SUVmax was not correlated with VAT-SUVmax ($r = 0.108$, $p = 0.242$), SAT-SUVmax ($r = 0.001$, $p = 0.994$) or the VAT/SAT ratio ($r = 0.080$, $p = 0.386$). Bone marrow SUVmax was also not correlated with VAT-SUVmax ($r = 0.010$, $p = 0.917$), SAT-SUVmax ($r = -0.033$, $p = 0.726$) or the VAT/SAT ratio ($r = 0.037$, $p = 0.693$). On post-therapy scans, spleen SUVmax showed a weak correlation with VAT-SUVmax ($r = 0.231$, $p = 0.040$), which did not remain significant after correction for 12 comparisons. No other post-therapy correlation was significant. Conclusions: Spleen and bone marrow SUVmax were not associated with adipose tissue metabolic activity at baseline. The weak post-therapy association between spleen and VAT uptake is exploratory and needs confirmation alongside direct inflammatory markers.

Keywords: colonic neoplasms; ^{18}F-FDG PET/CT; visceral adipose tissue; spleen; bone marrow; inflammation

1. Introduction

Colorectal cancer (CRC) ranks third among the most frequently diagnosed malignancies globally and is the second most common cause of cancer-related mortality. Modifiable lifestyle factors, particularly obesity, are being actively studied for their contribution to colorectal carcinogenesis and to cancer outcomes. Growing evidence also implicates visceral adipose tissue (VAT) in CRC risk, through both chronic low-grade systemic inflammation and direct crosstalk with the tumor microenvironment. Moreover, obesity has been associated with poorer overall outcomes in CRC, including higher surgical morbidity and mortality.(1)

The precise molecular pathways behind this link are not yet fully understood. The main mechanisms identified so far are insulin resistance, higher oestrogen production, and abnormal signalling factors released by dysfunctional adipose tissue (AT). This dysfunction arises from the chronic hypoxia, inflammation and extracellular matrix (ECM) remodelling that accompany obesity. Notably, hypoxia and inflammation are themselves recognised hallmarks of cancer development. (2)

In obesity, chronic inflammation driven by dysfunctional adipose tissue (AT) plays a central role in the pathogenesis of colon cancer (CC). It creates a preneoplastic microenvironment that supports tumour growth and invasion. Injured AT in obesity develops hypoxia, cell death and immune cell infiltration, which switch on several inflammatory pathways and their pro-inflammatory mediators. During this process, adipocytes release damage-associated molecular patterns (DAMPs). These activate toll-like receptors and inflammasomes, which sustains a cytokine-mediated pro-inflammatory response.(3)

Visceral adipose tissue (VAT) is more hormonally and metabolically active than subcutaneous adipose tissue (SAT). Factors released by visceral adipocytes have been reported to mediate tumorigenesis in obesity-related cancers, including colon cancer. These factors include insulin-like growth factor, the inflammatory adipokines interleukin-6 and tumor necrosis factor-α. (4)

Inflammation raises glucose uptake by immune cells, particularly macrophages. 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) relies on this increased glucose metabolism to measure how inflamed a tissue is. Metabolically active visceral adipose tissue (VAT) also contains more macrophages, so we hypothesized that 18F-FDG PET/CT could show the inflammatory activity of metabolically active VAT. (5)

Inflammation may actively drive hematopoietic proliferation. 18F-FDG PET/CT can detect activation of hematopoietic tissue as increased uptake in the spleen and bone marrow (BM). Uptake reflects tissue glycolysis, so it rises in tissues made up of rapidly dividing, highly metabolic cells. (6)
FDG uptake estimates in the bone marrow, and spleen may be useful imaging-derived biomarkers of systemic inflammation, supporting CRC prognostication.(7)

However, the significance of PET-derived inflammatory markers, such as 18F-FDG uptake in the BM and spleen, is still unclear in patients with colorectal cancer (CRC), and few studies have looked at its prognostic value. This study therefore aimed to examine the relationship between BM and splenic 18F-FDG uptake and visceral adipose tissue (VAT) activity in patients with CRC. (7)

2. Patients and Methods

2.1 Study design

This prospective observational cohort study was performed at the Nuclear Medicine Unit, Cairo University, between September 2023 and June 2025. The Faculty of Medicine, Cairo University, approved the protocol (MD-240-2023) on September 20, 2023. All patients gave written informed consent.

2.2 Patients

We included 118 adults with pathologically confirmed colonic adenocarcinoma and a pretherapy FDG PET/CT scan. We excluded patients with prior chemotherapy, radiotherapy or surgery before scanning, double primary cancers, claustrophobia or pregnancy. Seventy-nine patients had a post-therapy scan after surgery, chemotherapy, radiotherapy and/or targeted therapy of approxemately 6 month to 1 year after baseline.

2.3 Image acquisition

Patients fasted for 4–6 hours, and blood glucose had to be below 11.1 mmol/L. FDG (3.7–7.4 MBq/kg) was injected 45–60 minutes before imaging. Scans from vertex to mid-thigh were acquired on a Philips Ingenuity TF 64 PET/CT system, using time-of-flight list-mode acquisition and iterative reconstruction. Follow-up scans used the same protocol.

2.4 Image analysis

Fat was identified on CT using a range of -70 to -110 Hounsfield units. Three regions of interest (ROIs) of 7–15 mm were placed on consecutive slices in VAT at LEVEL: L3, above or below the kidneys, at least 2 cm from tumor, vessels, muscle and bowel and SAT measured by the same way in gluteal regions,. The average SUVmax was calculated for each compartment, and the VAT/SAT ratio was derived. Spleen SUVmax was measured with an ROI on the spleen, and bone marrow SUVmax with an ROI on the L3 vertebra.

2.5 Statistical analysis

Data are presented as mean ± standard deviation (SD), median and range, or as number and percentage. Correlations were assessed with Spearman coefficients, separately for baseline and post-therapy scans. Each of the 12 tests used a two-sided significance level of 0.05; a Bonferroni-corrected threshold of 0.0042 was also applied. Analyses used SPSS.

3. Results

Baseline characteristics and uptake values are shown in Table 1. Spleen and bone marrow SUVmax were not significantly correlated with VAT-SUVmax, SAT-SUVmax or the VAT/SAT ratio at baseline (Table 2).
On post-therapy scans in 79 patients, spleen SUVmax showed a weak positive correlation with VAT-SUVmax ($r = 0.231$, $p = 0.040$). This did not meet the corrected threshold. Its correlation with the VAT/SAT ratio did not reach significance ($r = 0.205$, $p = 0.069$), and bone marrow SUVmax was not significantly correlated with any adipose tissue measure (Table 2).

Table 1. Baseline characteristics and pretherapy uptake values (N = 118)

Variable	Mean ± SD or n (%)	Range
Age (years)	57.88 ± 12.59	20–88
BMI (kg/m²)	29.28 ± 5.98	17.85–51.94
Male sex	77 (65.3)	
Female sex	41 (34.7)	
Spleen SUVmax	2.92 ± 0.72	1.30–5.10
Bone marrow SUVmax	3.17 ± 1.00	1.00–6.70

BMI body mass index, SD standard deviation, SUVmax maximum standardized uptake value, VAT visceral adipose tissue.

Table 2. Spearman correlations of spleen and bone marrow SUVmax with adipose tissue measures

Scan	Organ	VAT-SUVmax: r (p)	SAT-SUVmax: r (p)	VAT/SAT ratio: r (p)
Baseline (n = 118)	Spleen	0.108 (0.242)	0.001 (0.994)	0.080 (0.386)
Baseline (n = 118)	Bone marrow	0.010 (0.917)	-0.033 (0.726)	0.037 (0.693)
Post-therapy (n = 79)	Spleen	0.231 (0.040)	0.007 (0.951)	0.205 (0.069)
Post-therapy (n = 79)	Bone marrow	0.039 (0.731)	-0.105 (0.357)	0.118 (0.302)

SAT subcutaneous adipose tissue, SUVmax maximum standardized uptake value, VAT visceral adipose tissue.

4. Discussion

In this prospective cohort of patients with colonic adenocarcinoma, we found no significant association between 18F-FDG uptake in the spleen or BM and the metabolic activity of VAT, SAT or the VAT/SAT ratio on pretherapy PET/CT. On post-therapy scans, splenic SUVmax showed a weak positive correlation with VAT-SUVmax, but this did not remain significant after correction for multiple testing, and BM uptake was unrelated to any adipose tissue measure. Taken together, these results suggest that, in the setting of colon cancer, splenic and marrow FDG uptake are largely independent of VAT metabolic activity.

Our hypothesis was based on the concept that inflamed VAT and the hematopoietic organs form part of a single systemic inflammatory network. Inflamed adipose tissue releases cytokines that can stimulate myelopoiesis in the BM and spleen, and these organs in turn supply monocytes that infiltrate adipose tissue. Imaging data support this link outside oncology. Pahk et al. showed that VAT SUVmax correlated with high-sensitivity C-reactive protein and with the SUVmax of the spleen and BM in patients with metabolic syndrome (8). Similarly, Emami et al. showed that splenic FDG uptake rises with systemic inflammation, is accompanied by pro-inflammatory changes in circulating leukocytes, and independently predicts cardiovascular events, supporting a cardiosplenic axis in humans (9). The absence of a comparable association in our cohort therefore needs explanation.

The most likely explanation is that, in patients with an untreated colon tumor, hematopoietic tissue activity is driven mainly by the tumor rather than by adipose tissue. Tumors release cytokines and growth factors that stimulate myelopoiesis, and FDG uptake in the BM and spleen in CRC has been linked to serum inflammatory markers such as the neutrophil-to-lymphocyte ratio (7) and to inflammatory changes within the tumor itself, including infiltration by CD163-positive macrophages and interleukin-6 expression (10). A strong tumor-derived signal may outweigh the smaller contribution of VAT inflammation and hide any relationship between the two compartments at baseline. In addition, VAT has low absolute FDG uptake and a narrow range of values, which limits the ability of a correlation analysis to detect a modest association.

The weak correlation between splenic and VAT uptake after treatment, although not significant after Bonferroni

correction, is consistent with this explanation. Once the primary tumor has been removed or treated, the tumor-related stimulus to the hematopoietic organs falls, and a smaller contribution from adipose tissue inflammation may become easier to detect. However, this finding should be regarded as hypothesis-generating. Post-therapy spleen and BM uptake are also affected by chemotherapy, recovery of the marrow after myelosuppression and the use of granulocyte colony-stimulating factor, which can markedly increase FDG uptake in both organs (14). These effects probably explain why BM uptake showed no association with adipose tissue activity after treatment, as marrow uptake is more directly influenced by cytotoxic therapy than splenic uptake.

Previous studies have shown that VAT metabolic activity and hematopoietic organ uptake each carry prognostic information in CRC. A higher VAT/SAT SUVmax ratio has been associated with regional lymph node and distant metastasis (11), VAT glucose uptake has been linked to overall survival, particularly in women (12), and VAT activity has been reported to predict later metastases (13). Separately, BM and splenic uptake normalized to the liver have been associated with overall survival (7), and the spleen-to-liver uptake ratio has been reported as an independent predictor of recurrence-free survival (10). Our finding that these measures are largely unrelated suggests that they reflect different aspects of the host response to cancer: VAT activity may represent obesity-related local inflammation, whereas spleen and BM uptake may represent tumor-driven systemic inflammation. If so, the two types of measurement may provide complementary rather than overlapping information, and combining them in prognostic models is worth investigating.

This study has several strengths. It was prospective, all scans were acquired on the same PET/CT system with a standardized protocol, and the same measurement method was applied at baseline and after treatment, allowing both time points to be assessed in the same patients. Several limitations should also be acknowledged. First, the sample size, particularly at follow-up (n = 79), was modest, and the study may have been underpowered to detect weak correlations. Second, uptake was measured as SUVmax in small regions of interest, and spleen and BM values were not normalized to liver or blood-pool activity; SUVmax is sensitive to image noise, and normalized ratios such as those used in earlier studies (7, 10) might have been more robust. Third, BM activity was sampled only at the L3 vertebra, which may not represent the whole marrow. Fourth, serum inflammatory markers were not included in the analysis, so we could not confirm whether imaging findings reflected systemic inflammation. Fifth, the type and timing of treatment between the baseline and follow-up scans varied, and the possible effects of chemotherapy and growth-factor support on post-therapy uptake could not be fully accounted for. Finally, this analysis did not examine clinical outcomes, so the prognostic value of combining these measures remains to be determined.

In conclusion, splenic and BM 18F-FDG uptake were not associated with VAT metabolic activity in patients with colon cancer before treatment, and only a weak, non-significant association between splenic and VAT uptake was seen after treatment. These findings suggest that hematopoietic organ activity and VAT activity on 18F-FDG PET/CT reflect largely separate inflammatory processes in colon cancer. Larger studies using normalized uptake measures, serum inflammatory markers and survival outcomes are needed to determine whether these imaging markers offer complementary prognostic information.

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