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#### A B S T R A C T

**Introduction/Justification:** Lung cancer remains a leading cause of mortality worldwide. PET/CT with  $^{18}\text{F}$ -FDG is widely used for detecting, staging, and monitoring lung cancer by assessing increased glycolytic metabolism in tumor cells. Prostate-specific membrane antigen (PSMA), although primarily a marker for prostate cancer, is also associated with tumor neoangiogenesis and has shown uptake in various malignancies, including lung cancer, suggesting potential theranostic applications. **Objectives:** This study aims to compare the uptake of  $^{18}\text{F}$ -FDG and  $^{18}\text{F}$ -PSMA in primary and metastatic lung cancer lesions, analyzing differences between adenocarcinoma and squamous cell carcinoma (SCC) subtypes. **Materials and Methods:** Fourteen patients (9 men and 5 women), aged 55–82 years and diagnosed with lung cancer (10 adenocarcinoma, 4 SCC), underwent PET/CT scans on two separate days: 60 minutes after intravenous administration of 0.1 mCi/kg of  $^{18}\text{F}$ -FDG and 90 minutes after intravenous administration of 0.1 mCi/kg of  $^{18}\text{F}$ -PSMA. Images were assessed by two nuclear medicine physicians and one radiologist. The maximum standardized uptake value (SUVmax) was measured for both tracers in primary tumors, regional lymph nodes, and distant metastatic lesions. The lesions were defined in both tracers by an SUVmax uptake above the background and visual analysis. **Results:** A total of 288 lesions were analyzed (247 adenocarcinoma, 41 SCC). In adenocarcinoma,  $^{18}\text{F}$ -PSMA identified 215 lesions, compared to 237 detected by  $^{18}\text{F}$ -FDG. Nine lesions were exclusive to  $^{18}\text{F}$ -PSMA, while 32 were detected only by  $^{18}\text{F}$ -FDG. Forty-five lesions showed higher  $^{18}\text{F}$ -PSMA uptake, while 174 exhibited predominant  $^{18}\text{F}$ -FDG uptake. The median SUVmax for  $^{18}\text{F}$ -FDG was 6.5 (range: 1.8–24.5), compared to 4.0 (range: 0.7–24.8) for  $^{18}\text{F}$ -PSMA. In SCC,  $^{18}\text{F}$ -PSMA identified 36 lesions, while  $^{18}\text{F}$ -FDG detected 41. No lesions showed predominant  $^{18}\text{F}$ -PSMA uptake, and SUVmax values were higher for  $^{18}\text{F}$ -FDG (median: 8.8; range: 1.3–36.6) compared to  $^{18}\text{F}$ -PSMA (median: 2.5; range: 0.9–10.4). We found that SUV values for  $^{18}\text{F}$ -PSMA are statistically different between SCC and adenocarcinoma subtypes in the lesions that showed uptake of both radiotracers (Mann-Whitney U test,  $p$ -value < 0.0001). Also, a positive correlation was observed for  $^{18}\text{F}$ -FDG and  $^{18}\text{F}$ -PSMA SUVs in both histological subtypes, being strong for SCC ( $r = 0.0,8140$ ,  $p$ -value < 0.0001) and moderate for adenocarcinoma ( $r = 0.4278$ ,  $p$ -value < 0.0001). **Conclusion:** These findings highlight distinct uptake patterns between adenocarcinoma and SCC using  $^{18}\text{F}$ -FDG and  $^{18}\text{F}$ -PSMA PET/CT. SCC demonstrated markedly higher  $^{18}\text{F}$ -FDG uptake with minimal  $^{18}\text{F}$ -PSMA uptake, indicating limited utility of  $^{18}\text{F}$ -PSMA in this subtype. In contrast, adenocarcinoma showed higher  $^{18}\text{F}$ -FDG uptake in most lesions, but a subset exhibited significant  $^{18}\text{F}$ -PSMA uptake, suggesting a potential link between neoangiogenesis and glycolytic metabolism. These results support a complementary role for  $^{18}\text{F}$ -PSMA in adenocarcinoma evaluation,

particularly in cases with high PSMA expression. Further studies are needed to determine its clinical impact on personalized treatment strategies and theranostic applications.

**Keywords:** Lung cancer, PET/CT, Tumor Metabolism,  $^{18}\text{F}$ -FDG,  $^{18}\text{F}$ -PSMA.

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#### ADIPOSE TISSUE METABOLISM IN RECTAL CANCER PATIENTS WITH CACHEXIA

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#### A B S T R A C T

**Introduction/Justification:** Adipose tissue (AT) glucose uptake, assessed by Fludeoxyglucose F-18 (FDG) positron emission tomography/computed tomography (PET/CT), reflects tissue metabolic activity and may be linked to both glucose metabolism by adipocytes and inflammatory cell activity. Additionally, adipose tissue radiodensity, measured by computed tomography (CT), has emerged as a promising metabolic biomarker. Increased AT radiodensity may indicate inflammation or the presence of brown adipose tissue (BAT), providing insights into pathophysiological processes underlying cancer cachexia. **Objectives:** The purpose of this study was to evaluate adipose tissue metabolism, assessed by the visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) glucose uptake through  $^{18}\text{F}$ -FDG PET/CT analysis and VAT and SAT radiodensity assessed by CT in cachexia (C) and non-cachexia (NC) rectal cancer patients. **Materials and Methods:** This is a cross-sectional study involving patients diagnosed with rectal cancer. Cachexia was categorized according to

Fearon's criteria, being defined as weight loss greater than 5%, or weight loss greater than 2% in individuals already showing depletion according to current bodyweight and height (body-mass index [BMI] < 20 kg/m<sup>2</sup>) or low skeletal muscle mass (defined according to Martin's criteria). Body composition and tissue radiodensity was analyzed using computed tomography (CT) images processed with the SliceOmatic software based on the difference in tissue measurements by Hounsfield Units (HU). The segmentation and data collection of PET/CT images are performed in FIJI and the Beth Israel Plugin for FIJI. In the segmented areas (VAT and SAT), glucose uptake values (<sup>18</sup>F-FDG) are collected, represented by the Standard Uptake Value (SUV) variable. M-value was determined using euglycemic hyperinsulinemic clamp. Demographics characteristics, disease-related data, and biochemical test results were collected from medical records. Statistical analyses were performed using Jamovi<sup>®</sup> version 2.3. This study protocol was approved by the Institutional Review Board (CAAE: 91217418.2.0000.5404). **Results:** A total of 36 patients were included in the analysis. Cachexia was diagnosed in 25 patients (69.4%). The median age was 64 years (range: 43-74) in the C group and 62 years (range: 47-72) in the NC group. Weight loss greater than 5% occurred in all C patients, and low muscularity in 36.4% of this group. Cachexia patients had a higher VAT SUV mean (0.815 ± 0.184) compared to NC (0.644 ± 0.148), p=0.005. VAT glucose uptake was correlated with VAT radiodensity (rho=0.678, p < 0.001) and weight loss (rho=0.434, p=0.015) while it was negatively correlated with VAT area (rho=-0.412, p=0.021). Additionally, VAT radiodensity showed a negative correlation with VAT area (rho=-0.452, p=0.008), SAT area (rho=-0.465, p=0.006), and BMI (rho=-0.695, p=0.015). Positive correlations were observed between VAT radiodensity and SAT radiodensity (rho=0.633, p < 0.001) and SAT SUV mean (rho=0.532, p=0.002). No significant correlation was found between VAT SUV mean and M-value; however, M-value-TBW correlated with VAT radiodensity (rho=0.369, p=0.03). **Conclusion:** These findings suggest that VAT metabolism may serve as a potential biomarker in cachexia and underscore the need to expand investigations into the metabolic alterations that influence the pathophysiology of cachexia.

**Keywords:** Adipose tissue radiodensity, Cancer cachexia, Flu-deoxyglucose F-18 (<sup>18</sup>F-FDG) PET/CT, Weight loss.

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#### FATORES ASSOCIADOS À PIOR QUALIDADE DE VIDA DE PACIENTES COM CÂNCER DE CABEÇA E PESCOÇO TRATADOS COM RADIOTERAPIA E QUIMIOTERAPIA NA UNICAMP

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#### R E S U M O

**Introdução/Justificativa:** A radioterapia (RT) e a quimioterapia (QT) são essenciais no tratamento do câncer de cabeça e pescoço (CCP), mas seus efeitos adversos comprometem a qualidade de vida (QdV) dos pacientes. Sintomas como xerostomia, mucosite e disfagia afetam a funcionalidade, enquanto alterações na aparência e dificuldades na comunicação impactam o bem-estar emocional e social. Embora esses efeitos sejam reconhecidos, ainda há uma necessidade de melhor compreensão dos fatores sociodemográficos e clínicos associados à QdV desses pacientes. **Objetivos:** Este estudo teve como objetivo avaliar se as características sociodemográficas, os aspectos clínicos e as características do tumor influenciam a percepção da QdV de pacientes com CCP tratados com RT e QT. **Materiais e Métodos:** Foram avaliados 32 pacientes com CCP atendidos no Hospital de Clínicas da UNICAMP durante o tratamento com RT e/ou QT exclusiva. As informações sociodemográficas (idade, sexo, cor da pele, grau de instrução, tabagismo e etilismo), aspectos clínicos (dor, escala de performance ECOG, marcadores hematológicos, índice de inflamação imune sistêmica e de resposta à inflamação sistêmica) e as características do tumor (localização, grau de diferenciação e estágio TNM) foram coletadas dos prontuários dos pacientes e por questionário específico. A QdV dos pacientes foi avaliada pelo instrumento FACT-H&N que possui 39 questões distribuídas nos domínios de bem-estar físico, social, emocional, funcional e preocupações adicionais específicas para CCP. A análise dos dados foi realizada por meio do cálculo das médias dos escores de cada domínio e do escore total, sendo que menores escores indicam pior QdV. A análise estatística foi realizada utilizando o teste t para comparação entre grupos, o valor de p < 0,05 foi considerado significativo. **Resultados:** Observamos que pacientes negros apresentaram menor bem-estar emocional (19,0 vs. 23,5; p=0,002), enquanto tabagistas apresentaram escores mais baixos de bem-estar físico (20,0 vs. 25,5; p=0,03) e bem-estar específico (19,0 vs. 29,0; p=0,02). Dor moderada ou intensa foi associada a pior bem-estar físico (20,5 vs. 26,5; p=0,002), emocional (18,0 vs. 22,0; p=0,01) e global (101,0 vs. 122,0; p=0,02). Pacientes com status funcional ECOG ≥ 1 apresentaram piores escores de bem-estar funcional (19,0 vs. 23,0; p=0,001) e total (101,5 vs. 123,5; p=0,04). A presença de anemia foi associada a menor bem-estar específico (21,5 vs. 30,0; p=0,002) e total (99,0 vs. 120,5; p=0,009). Pacientes com índice de resposta à inflamação sistêmica elevado apresentaram menor bem-estar físico (20,5 vs. 25,0; p=0,04), funcional (16,5 vs. 22,0; p=0,01), específico (21,0 vs. 28,0; p=0,03) e total (99,0 vs. 116,0; p=0,03). Além disso, pacientes com tumores na faringe relataram pior bem-estar físico (20,0 vs. 26,5; p=0,01), enquanto aqueles com tumores pouco diferenciados apresentaram menor bem-estar