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A B S T R A C T

Introduction/Justification: ^{18}F-FDG PET/CT is widely used in the management of multiple myeloma (MM), a disease that often presents with extensive bone involvement. Radiolabeled prostate-specific membrane antigen (PSMA), primarily a marker for prostate cancer, is also associated with tumor neoangiogenesis, and studies have demonstrated its uptake in MM lesions. Hybrid PET/CT imaging with both FDG and PSMA tracers allows for several quantitative metrics, enabling objective comparisons beyond visual analysis. **Objectives:** This study aims to compare ^{18}F-FDG and ^{68}Ga-PSMA PET/CT quantitative metrics in the skeletal system of patients with MM. **Materials and Methods:** The study included ^{18}F-FDG and ^{68}Ga-PSMA PET/CT images acquired within a 1- to 8-day interval from 15 patients (53% male, mean age 66.7 ± 10.7 years) with symptomatic, biopsy-proven MM. CT was used to segment the entire skeleton in PET images, with the skull excluded in ^{18}F-FDG images due to artifacts from brain uptake coregistration. SUV quantification was performed using in-house software developed in MATLAB. Descriptive statistics and individual percentage deviations between the radiotracers were used to evaluate bone mean and maximum Standardized Uptake Values (SUVmean and SUVmax). Correlation analysis between the radiotracers was conducted using Spearman's rank correlation coefficient (r) with a significance level of $p < 0.05$. **Results:** For bone SUVmean, values were higher for ^{18}F-FDG compared to ^{68}Ga-PSMA, with an average of 0.9 ± 0.1 vs. 0.5 ± 0.1, corresponding to a -40% ± 9% difference (range: -25% to -57%). Conversely, for bone SUVmax, values were lower for ^{18}F-FDG compared to ^{68}Ga-PSMA, with an average of 8 ± 3 vs. 19 ± 14, corresponding to a 154% ± 2% difference (range: -21% to 762%). A moderate correlation was found for bone SUVmean between ^{18}F-FDG and ^{68}Ga-PSMA ($r = 0.55$, $p = 0.03$), while no significant correlation was observed for bone SUVmax ($r = 0.17$, $p = 0.55$). **Conclusion:** This study reveals distinct quantitative uptake patterns between ^{18}F-FDG and ^{68}Ga-PSMA PET/CT in the skeletal system of MM patients. ^{18}F-FDG exhibited significantly higher SUVmean than ^{68}Ga-PSMA, likely due to physiological ^{18}F-FDG uptake in bone marrow. A moderate correlation was observed for SUVmean between the two tracers. The higher SUVmax values for ^{68}Ga-PSMA, with no correlation with ^{18}F-FDG SUVmax, may reflect the different biological targeting mechanisms of each tracer. This suggests that some regions of increased PSMA uptake (possibly indicating neoangiogenesis) may not correspond to areas of increased glycolysis, highlighting the potential complementary role of these radiotracers in MM evaluation.

Keywords: Multiple Myeloma, PET/CT, SUV Quantification, ^{18}F-FDG, ^{68}Ga-PSMA.

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MIR-4421 AS A POSSIBLE MODULATOR OF MAPK/AKT PATHWAY THROUGH ERP29 IN PHARYNGEAL CANCER

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A B S T R A C T

Introduction/Justification: ERP29 gene encodes a chaperone protein essential for protein folding and secretion. Our previous study linked ERP29 inhibition to an increased risk of pharyngeal cancer (PC) and reduced patient survival, possibly due to the binding affinity between microRNA miR-4421 and ERP29 messenger RNA (mRNA). This interaction leads to ERP29 silencing, which may influence PC progression especially by decreasing necrosis and increasing cell migration. However, the precise mechanism underlying this process remains unknown, particularly its impact on well-established signaling pathways such as MAPK/Akt, which are frequently dysregulated in PC and play a critical role in tumor progression, cell survival, and metastasis. **Objectives:** This study aims to explore the role of miR-4421 and ERP29 in PC survival and progression. **Materials and Methods:** We first evaluated ERP29 and miR-4421 prognostic value in head and neck cancer patients assessing the Kaplan–Meier Plotter (kmplot.com/analysis/). We used PC FaDu cell line (ATCC) in two different scenarios: FaDu cisplatin (CDDP)-sensitive and FaDu CDDP-resistant (FaDu-R). ERP29 expression was silenced using a specific siRNA. We identified and validated genes modulated by ERP29 in FaDu and FaDu-R cells by TaqMan plate array and quantitative PCR (qPCR), respectively. We tested if miR-4421 inhibitor could reverse ERP29 silencing effect, with gene expression analyzed by qPCR in FaDu and FaDu-R cells. Statistical analysis was performed by t-test using SPSS 21.0 software (SPSS Incorporation, USA). **Results:** Lower ERP29 ($p = 0.03$) and higher miR-4421 ($p < 0.01$) expressions were associated with poor overall survival in head and neck cancer patients. In FaDu cells, ERP29 silencing increased MAPK1 (FC: 2.4, $p = 0.03$), AKT1 (FC: 17.5, $p < 0.01$), and JUN (FC: 29.0,

p = 0.01) expression when compared to cells expressing ERP29. In contrast, the transfection of miR-4421 inhibitor reverted those effects, decreasing the expression of MAPK1 (FC: 0.6, p = 0.03), AKT1 (FC: 0.1, p = 0.02), and JUN (FC: 0.1, p = 0.02) compared to the negative control. In FaDu-R cells, ERP29 silencing increased SOS1 (FC: 2.2, p < 0.01), MAPK1 (FC: 2.1, p < 0.01), and AKT1 (FC: 2.2, p = 0.04) expression when compared to cells expressing ERP29. Conversely, miR-4421 inhibitor decreased the expression of SOS1 (FC: 0.2, p = 0.03), MAPK1 (FC: 0.4, p = 0.01), and AKT1 (FC: 0.2, p = 0.04) compared to the negative control. **Conclusion:** Inhibition of ERP29 expression may impact MAPK/Akt pathway, contributing to PC patients' poor survival. However, these effects could be reversed by inhibiting the binding of miR-4421 to ERP29. Our study enhances the understanding of PC progression and CDDP resistance, and we hope that our findings will aid in the development of targeted therapy for PC patients by ensuring ERP29 expression. **Acknowledgements:** The study was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq grant numbers 140019/2020-0, 307944/2022-0, and 408177/2023-3) and Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP grant number 2023/12810-9) - Cancer Theranostics Innovation Center, (CancerThera) (CEPID FAPESP grant number 2021/10265-8).

Keywords: ERP29, MAPK/Akt pathway, miR-4421, Pharyngeal cancer.

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PAPEL DO PET/CT COM 18F- FDG NA AVALIAÇÃO DO COLANGIOCARCINOMA: UM ESTUDO RETROSPECTIVO

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R E S U M O

Introdução/Justificativa: O colangiocarcinoma é uma neoplasia maligna do trato biliar com prognóstico geralmente desfavorável. O diagnóstico precoce e o estadiamento preciso são cruciais para o manejo adequado desses pacientes. A tomografia por emissão de pósitrons/tomografia computadorizada (PET/CT) com 18F-fluordesoxiglicose (FDG) tem se mostrado uma ferramenta promissora na avaliação dessa doença, porém seu papel ainda não está completamente estabelecido. **Objetivos:** Este estudo visa avaliar o impacto do PET/CT com 18F- FDG no estadiamento do colangiocarcinoma, com foco na detecção de envolvimento linfonodal regional e doença metastática à distância. **Materiais e Métodos:** Realizamos um estudo retrospectivo utilizando um programa de busca de expressões no laudo RIS, com as palavras-chave "CID 10 C22" e "colangiocarcinoma", no período de 01/01/2019 a 01/01/2023. Inicialmente, 176 exames foram identificados, resultando em 71 exames após remoção de duplicidades. Excluímos ainda 5 exames que utilizaram outros traçadores, além de 2 pacientes por apresentarem colangiocarcinoma como tumor sincrônico durante avaliação de outro câncer primário, totalizando 64 exames elegíveis. Os exames foram classificados de acordo com suas indicações: • Estadiamento: 27 exames • Reavaliação: 31 exames • Diagnóstico diferencial de lesão hepática: 4 exames • Outros tumores hepáticos: 2 exames Focamos nossa análise nos 27 exames realizados para estadiamento, avaliando o impacto do PET/CT na detecção de envolvimento linfonodal e metastático. **Resultados:** Avaliação Linfonodal Regional: • Exames positivos: 11 pacientes (40,7%) • Exames negativos: 16 pacientes (59,3%) Os sítios de linfonodos regionais que apareceram nos estudos foram: ducto hilar, cístico, ducto biliar comum, artéria hepática, pancreaticoduodenal posterior e linfonodos da veia porta. Avaliação Metastática: • Exames positivos: 14 pacientes (51,9%) • Exames negativos: 13 pacientes (48,1%) Distribuição dos Sítios Metastáticos: 1. Pulmão: 5 pacientes (35,7%) 2. Osso: 5 pacientes (35,7%) 3. Linfonodos abdominais: 8 pacientes (57,1%) 4. Carcinomatose peritoneal: 2 pacientes (14,3%) 5. Linfonodos torácicos: 1 paciente (7,1%) 6. Adrenal: 1 paciente (7,1%). **Conclusão:** O PET/CT com 18F-FDG demonstrou ser uma ferramenta valiosa no estadiamento do colangiocarcinoma, detectando envolvimento linfonodal regional em 40,7% dos casos e doença metastática em 51,9% dos pacientes. A técnica foi particularmente útil na identificação de metástases em diversos sítios, com destaque para linfonodos abdominais, pulmão e ossos. Esses achados sugerem que o PET/CT com 18F-FDG pode ter um impacto significativo no manejo clínico desses pacientes, potencialmente alterando a estratégia terapêutica em casos onde a doença metastática não era previamente suspeitada.

Palavras-chave: 18F-FDG PET/CT, Colangiocarcinoma, MEDICINA NUCLEAR, Oncologia, PET/CT.

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COMPARATIVE RADIOLABELING OF THE CYCLIC PEPTIDE CTHRSSVVC WITH [68GA] GALLIUM AND [18F]FLUORINE. A POTENTIAL PROBE FOR MOLECULAR IMAGING OF CD163^{+} MACROPHAGES

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