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Lower maximum standardized uptake value of fluorine-18 fluorodeoxyglucose positron emission tomography coupled with computed tomography imaging in pancreatic ductal adenocarcinoma patients with diabetes

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Standardized uptake value

Abstract

BACKGROUND: The effects of diabetes mellitus (DM) on sensitivity of fluorine-18 fluorodeoxyglucose positron emission tomography coupled with computed tomography (^{18}F-FDG PET/CT) for diagnosing pancreatic ductal adenocarcinomas (PDACs) is not well known. This study was aimed to evaluate the effects of DM on the validity of ^{18}F-FDG PET/CT in PDAC.

METHODS: A total of 173 patients with PDACs who underwent ^{18}F-FDG PET/CT were enrolled (75 in the DM group and 98 in the non-DM group). The maximum standardized uptake values ($SUVs_{max}$) were compared.

RESULTS: The mean SUV_{max} was significantly lower in the DM group than in the non-DM group (4.403 vs 5.998, $P = .001$). The sensitivity of SUV_{max} (cut-off value 4.0) was significantly lower in the DM group than in the non-DM group (49.3% vs 75.5%, $P < .001$) and also lower in normoglycemic DM patients (n = 24) than in non-DM patients (54.2% vs 75.5%, $P = .038$).

The authors declare no conflicts of interest.

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CONCLUSION: DM contributes to a lower SUV_{max} of ^{18}F-FDG PET/CT in patients with PDACs.

Pancreatic ductal adenocarcinoma (PDAC) accounts for 7% of cancer deaths worldwide and 8.2% in Korea, with nearly equal numbers of new cases and deaths reported annually.[1,2] The location of the pancreas in the retroperitoneal space masks early symptoms, and pancreatic cancer is frequently undetected until prominent clinical signs seem to appear abruptly. The overall 5-year survival in all stages of pancreatic cancer has not improved and remains at approximately 6% in the United States. Over the past 20 years, improvements in surgical techniques and perioperative and postoperative management have decreased surgical mortality, and long-term survival rates after surgery at high-volume pancreas surgery medical centers have improved from 12% to 40% at some instances.[3–5] Additionally, fluorine-18 fluorodeoxyglucose positron emission tomography coupled with computed tomography (^{18}F-FDG PET/CT) has become an important diagnostic modality in pancreatic cancer management, including differential diagnosis of pancreatic lesions, evaluation of cancer stage, evaluation of treatment response, and assessment of tumor recurrence.[6–8] Furthermore, the maximum standardized uptake value (SUV_{max}) of ^{18}F-FDG PET/CT is correlated with the overall survival of pancreatic cancer patients.[9,10]

^{18}F-FDG PET/CT is a noninvasive imaging technique that can scan the entire body in 1 session and is a well-accepted imaging modality used for diagnosis, staging, and evaluation of treatment response in several different types of malignancy.[11–13] ^{18}F-FDG imaging of cancer relies on a molecular shift in glucose transporters in malignant cells, resulting in increased uptake of glucose within the tumor. ^{18}F-FDG is transported into cells in a manner similar to glucose; therefore, the relatively high metabolic activity and increased uptake of glucose in malignant cells enable differentiation of cancer tissue from normal tissue. ^{18}F-FDG PET/CT can be used to measure the amount of ^{18}F-FDG uptake in malignant tissue, and the maximum amount of ^{18}F-FDG uptake is calculated as SUV_{max}.[14] However, some issues have to be considered. The biodistribution of ^{18}F-FDG may be affected by various conditions that alter normal tissue metabolism, such as hyper/hypoglycemia, local inflammation or infection, diabetes mellitus (DM), and administration of insulin or oral hypoglycemic agents.[15–17] Several in vitro and in vivo studies have reported that the uptake of ^{18}F-FDG in cancer cells declines with increase in glucose level in the medium or blood and that insulin loading decreases the ^{18}F-FDG uptake into the tumor cells in an animal model.[18–21] Clinical studies have shown that compared with normoglycemia, hyperglycemia is associated with a higher false negative rate of ^{18}F-FDG PET/CT in the evaluation of malignancy and decreased sensitivity in detecting pancreatic cancer.[22] However, most of the human data need to be analyzed to determine whether hyperglycemia or DM can influence the detection of malignancy, especially in pancreatic cancer, because up to 80% of pancreatic cancer patients have hyperglycemia or DM, even in the presymptomatic phase.[23]

The aim of this study was to investigate whether DM can affect the functional role of ^{18}F-FDG PET/CT as a diagnostic tool in patients with PDACs.

Patients and Methods

Patients

Patients who had pathologically confirmed PDACs and underwent ^{18}F-FDG PET/CT as a diagnostic work-up were enrolled as study subjects between September 2005 and March 2012 at Seoul National University Bundang Hospital. Patient demographics, serum biochemistry, radiologic results including ^{18}F-FDG PET/CT and histologic findings were retrospectively reviewed. The exclusion criteria were as follows: subcentimeter-sized small cancer at CT scan, prior history of anticancer treatment (eg, surgical resection, systemic chemotherapy, or radiotherapy) before undergoing ^{18}F-FDG PET/CT, or presence of pancreatic cystic tumors or pancreatic neuroendocrine tumors.

DM was diagnosed from the patients' clinical histories and laboratory test results (hemoglobin A1c [HbA1c] $\geq$ 6.5%; fasting plasma glucose $\geq$ 126 mg/day; or 2-hour plasma glucose $\geq$ 200 mg/dL in repeated testing, following the Standards of Medical Care in Diabetes of the American Diabetes Association).[24] The study was approved by the Institutional Review Board of Seoul National University Bundang Hospital and conformed to the ethical guidelines of the Declaration of Helsinki, 1964, as revised in 2004. The requirement for informed consent was waived.

Study design

The patients were divided into 2 groups (DM vs non-DM group), and the SUV_{max} was compared between the 2 groups. Other confounding factors that may influence glucose uptake of cancer tissue, such as plasma glucose level or cancer stage, were identified. Demographic and clinical data, including sex, age, body mass index (BMI), hypertension, smoking and alcohol consumption history, serum levels of carbohydrate antigen 19-9 (CA 19-9), location of the tumor (head, body, and tail), and the longest diameter of the tumor measured with CT scan, were obtained. The 7th edition of the tumor-node-metastasis system from the American Joint Committee on Cancer was used to determine the clinical stage of the study patients.[25]