Clinical Imaging 39 (2015) 592–596

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: http://www.clinicalimaging.org

Simplified protocol of cardiac 18F-fluorodeoxyglucose positron emission tomography viability study in normoglycemic patients with known coronary artery disease☆

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ARTICLE INFO

Article history:
Received 21 November 2014
Received in revised form 4 February 2015
Accepted 6 February 2015

Keywords:
FDG-PET/CT
Myocardial viability
Glucose load protocol
Coronary artery disease
Myocardial perfusion

ABSTRACT

Purpose: The purpose was to evaluate quality of 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) myocardial scans and its correlation with background glucose (BG) after simplified 5% intravenous glucose load protocol.
Methods: An intravenous glucose load protocol was applied in 69 normoglycemic patients with confirmed coronary artery disease. The blood glucose level was measured every 15 min.
Results: Eighty-four percent of images were optimal, 8.7% suboptimal, and 7.3% uninterpretable. The quality of 18F-FDG-PET was BG independent and body mass index dependent ($P = .0007$).
Conclusions: Simplified glucose load protocol is a safe and efficient method of preparation for FDG cardiac viability study in patients with normoglycemia.

1. Introduction

Fluorodeoxyglucose positron emission tomography (FDG-PET) cardiac imaging is one of the most sensitive procedures for myocardial viability assessment. The quality of PET scans is mandatory for reliable image interpretation. Glucose serum level is a well-known factor influencing quality of FDG-PET scans. Since glucose is one of many substrates for energy production in myocardial cells, the patient's metabolic preparation plays a key role in cardiac FDG-PET imaging. FDG is an 18F-labeled glucose analog that accumulates in the myocardium proportionally to normal glucose using the same transport system. The myocardial uptake of FDG depends on several metabolic variables. In general, low plasma levels of free fatty acids (FFAs) and high plasma levels of insulin result in optimal cardiac glucose and 18F-FDG uptake. This metabolic state is achieved by administration of the glucose to stimulate the endogenous insulin or by the administration of exogenous insulin and glucose. Unfortunately, there is no standardization in patient preparation for FDG cardiac imaging; therefore, many various glucose load protocols (oral and intravenous) are used. Since there is no consensus as to which one is superior over the other, each nuclear medicine department team performing the cardiac FDG viability studies has to make its own choice of the protocol. In general, intravenous protocols are supposed to be more complicated, and that limits their application in daily routine. An oral glucose load protocol on the contrary is easy to perform, but in many cases, it is of suboptimal or even uninterpretable quality. The hyperinsulinemic euglycemic clamp and the oral glucose load protocol are the best described methods in the current literature, whereas less information is available about intravenous insulin and glucose injection. To our knowledge, there is no literature describing the quality of scans acquired after 5% intravenous glucose with insulin injection. In our opinion, this method of glucose and insulin delivery will allow for better standardization of the amount of ingested glucose and lead to better quality of scans than the oral load protocol. On the other hand, the proposed protocol is less time consuming and less demanding than the hyperinsulinemic euglycemic clamp. In our study, we sought to evaluate the correlation between background glucose (BG) levels after intravenous glucose load protocol with the quality of the obtained images.

The aim of the study was to assess the quality of myocardial PET scans after 5% intravenous glucose load protocol in the group of 69 non-diabetic patients with known coronary artery disease (CAD). The qualitative visual assessment of PET scans was performed. The quality of the

☆ Conflicts of interest: The authors declare that they have no conflict of interest.

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http://dx.doi.org/10.1016/j.clinimag.2015.02.009
0899-7071/

scans was further analyzed in the potential relation to BG and body mass index (BMI). The study outcomes were compared with the available published reports.

2. Materials and methods

2.1. Patients selection

Sixty-nine nondiabetic patients with CAD confirmed during routine coronarography were subjected to cardiac 18F-FDG-PET for left ventricle viability evaluation before the decision of cardiovascular revascularization. Exclusion criteria for the study were a history of impaired glucose intolerance/impaired fasting glucose, diabetes mellitus, hypoglycemic treatment, and any known inflammatory condition such as renal insufficiency or neoplasmatic disease. Patients with fasting blood glucose level exceeding 120 mg/dl were also excluded from the study due to the potential glucose intolerance. After signing the informed consent, all patients underwent the rest of single photon emission computed tomography (SPECT) perfusion 99mTc-MIBI study within 3 months [range −8 to +90 days, mean 15.93 days, standard deviation (S.D.)= 24.96] from PET examination. The intravenous glucose load protocol was applied to all the patients. Each patient received the intravenous glucose–insulin injection following the presented protocol after overnight fasting.

2.2. Patient preparation—glucose load protocol

Two hundred fifty milligrams of 5% glucose with 8 IU of regular, soluble insulin was infused for 60 min, corresponding to a 1.8–2-mU/kg/min insulin and 3-mg/kg/min glucose infusion. The serum glucose level was assessed at the beginning of infusion and every 15 min after. The range of serum glucose 70–150 mg/d was considered as "normal response" to the infusion. If the blood sugar did not exceed 150 mg/dl during the time of 1 h insulin–glucose infusion, the 18F-FDG was injected. When the blood sugar level exceeded 150 mg/dl, the patient received Ringer's solution (as the source of K ions) and soluble insulin at a rate of 1 IU for each 10 mg of glucose per deciliter over the level of 150 mg/dl. The serum glucose levels were checked every 15 min. While the measurements stayed within the normal range (less than 150 mg/dl), the 18F-FDG was injected.

Images were acquired at 30–60 min after FDG injection with a Biograph 64 PET/CT scanner (Siemens Medical Solutions, Inc.) operating with the Somaris/5 SyngoCT 2006 software. The CT data (11 eff mA, 120 kV, slice thickness 3 mm, 1.5 mm pitch) were used both for attenuation correction of PET data as well as for anatomic structure recognition for precise localization of 18F-FDG uptake. Emission images of the heart were acquired with the zoom 2 for 10 min. Acquired images were reconstructed using the filtered backprojection method. The data were reconstructed over a 128×128 matrix with 5.25-mm pixel size and 2-mm slice thickness.

The acquired data were reconstructed and analyzed using the Syngo MI application software. The evaluation of myocardial images and qualitative evaluation of PET data were performed using Cedars Sinai commercial software package (Cedars QPS; Cedars-Sinai Medical Center).

2.3. Image analysis

A visual analysis of acquired images was performed. A 3-point scale was used for scan quality assessment. The image was assessed as "optimal" if the myocardial FDG distribution was homogenous and background activity was low. It was assessed as "suboptimal but acceptable" if the background activity was moderate and/or the 18F-FDG myocardial distribution was inhomogeneous but there were no technical problems with automatic endocardial and epicardial borders recognition during transformation of the data to create the Polar Map. Both "optimal" and "suboptimal but acceptable" scans were adequate for further semiquantitative evaluation and clinical interpretation. The image was "uninterpretable" if it was inadequate for visual interpretation because of absent or low myocardial FDG uptake and high background activity. An additional "reverse mismatch" pattern was related to a subgroup of patients with high glucose accumulation which was restricted only to the myocardial area of abnormal SPECT perfusion.

For statistical analysis, patients were divided into two subgroups: group 1—a group that included all patients with "optimal" image quality and group 2—a group which covered all but optimal FDG accumulation patterns: suboptimal, reverse mismatch, and uninterpretable.

All human have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

2.4. Statistical analysis

Statistica 10 software was used for statistical analysis. Kolmogorov–Smirnov test was used to check normal distribution of continuous variables, which were further presented as mean±S.D. or median depending on distribution. Comparisons between groups of variables were conducted with analysis of variance or nonparametric Mann–Whitney *U* test.

Relationships between scan quality and BG, time to FDG infusion, and BMI were determined by Spearman's rank-correlation test and were expressed as Spearman's rank-correlation coefficient. *P* values lower than .05 were considered as statistically significant.

3. Results

The clinical characteristics of the patients included in the study are presented in the Table 1.

3.1. Glucose load protocol

Mean BG was 98.0 mg/dl (min 52, max 120, S.D. 14.1) at the beginning of infusion and 120.9 (min 71, max 159, S.D. 20.6) at the time of FDG infusion. There was no drop of BG below the normal range. There was no intolerance of the glucose/insulin infusion in the group of patients included in the study. The maximal BG during the glucose/insulin infusion was 201 mg/dl. Detailed measurements of BG at certain time points of the infusion in the two investigated groups of patients, as well as the relationships with BMI, are presented in Table 2.

The statistical comparison between group 1 (optimal myocardial FDG accumulation) and group 2 (all other perfusion patterns) showed no significant differences between the glucose serum levels. The mean time of the insulin–glucose infusion for both groups of patients was 60.7 min (50–90 min) and depended on the BG level. During infusion, BG increased to 150 mg/dl in 23/69 patients (33%) (mean 175.3± 12.7 mg/dl). Those patients received the Ringer's infusion and additional insulin. Mean 2.4 IU of soluble insulin (min 1, max 6 IU) was applied.

Out of 23 patients with an increase in BG >150 mg/dl, 5 received 1 IU, 10 patients received 2 IU, 4 patients received 3 IU, 3 patients

Table 1
Clinical characteristics

Age, y (mean±S.D.)	62.2±11
Male, %	76.8
BMI, kg/m^2 (mean±S.D.)	27.2±4.3
Clinical risk factors of CAD, %	
Hypertension	78.7
Diabetes	0
IFG/IGT	0
Dyslipidemia	58.6
Smoking	66.8
Family history	44.5
FSG, mg/dl	97.6±11.6

IFG/IGT, impaired fasting glycemia/impaired glucose tolerance; FSG, fasting serum glucose on the day of PET.