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Original

Assessment of the myocardial FDG-PET image quality with the use of maximal Standardized Uptake Value myocardial to background index. Application of the results in regard to semiquantitative assessment of myocardial viability with cardiac dedicated software

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Abstract

BACKGROUND: The objective of this study was to semiquantitatively assess the degree of myocardial fluorodeoxyglucose (FDG) uptake in glucose-loaded myocardial viability positron emission tomography/computed tomography (PET/CT) scans, to calculate the myocardial to background index, and correlate the index with image quality assessed on the basis of visual qualitative assessment.

MATERIAL AND METHODS: The myocardial FDG-PET/CT study was carried out in 69 non-diabetic patients, who had known coronary artery disease, by intravenous injection of 250 ± 70 MBq (range: 180–320 MBq) FDG. Images were interpreted visually and patients were divided into three groups according to the grade of myocardial uptake: optimal, suboptimal, and uninterpretable. Semiquantitative analysis was performed by calculating the standardized uptake value (SUVmax) for myocardium and background (blood pool) activity and expressed as the myocardial to background (M/B) activity ratio.

RESULTS: On the basis of visual (qualitative) analysis, 60/69 (86.96%) patients showed optimal quality of FDG cardiac uptake, 3/69 (4.35%) were suboptimal, and uninterpretable FDG PET scan results were found in 6/69 (8.70%) patients. The M/B index was found to be significantly higher in images of optimal vs. suboptimal quality (6.87 ± 3.99 vs. 1.65 ± 0.78 respectively; $p < 0.0001$).

CONCLUSIONS: The index ratio of 2.2, which is consistent with the upper borderline value for visually uninterpretable images, was considered the cut-off value for scans of optimal and non-optimal quality.

KEY words: fluorodeoxyglucose-positron emission tomography, SUVmax, myocardial to background ratio, myocardial uptake, myocardial viability

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Background

FDG-positron emission tomography (FDG-PET) cardiac imaging is one of the most clinically applicable and sensitive procedures for myocardial viability assessment. However, normal myocardial metabolism is diverse which often results in heterogeneous accumulation of radiopharmaceutical. If the background activity is too high, the activity of the blood inside the left ventricle increase the number of counts due to the limitations of reconstruction algorithms. Since the myocardial images are always displayed normalized to the pixel of highest activity and the scale of visual presentation is linear, the images of not optimal quality might overestimate the viability and underestimate the scar. Moreover, there is lack of standardized software for cardiac PET imaging processing on most PET imaging systems. The viability assessment can be performed qualitatively and quantitatively with the use of the software designed originally for SPECT perfusion studies. Using quantitative analysis, area of reduced FDG uptake is reported as a percentage of the left ventricle, similar to the SPECT perfusion defects, where 50% threshold for viability assessment is commonly used [1, 2]. Automatic recognition of the left ventricular borders using only PET slices in cases where cardiac 18F-FDG uptake is scarce or heterogeneous is especially difficult. In our clinical experience many myocardial scans with high background activity are not conclusive and the repeat acquisition is essential. Owing to the dynamic progress of hybrid imaging most PET systems are in fact PET/CT. The standard evaluation of cardiac PET/CT imaging includes always a quick check-up of the quality of the fused images performed with the general software and then the use of specific cardiac programs for further semiquantitative and qualitative PET analysis, which is conclusive only when the image is of good quality. It will therefore be desirable to find an easy test allowing to check the image quality to ensure the conclusive result of further semiquantitative assessment. FDG accumulation can be easily calculated with the use of regions of interest precisely placed with the help of CT morphologic data. More importantly, the use of PET/CT allows for the quantitative assessment with the use of the FDG standard uptake value (SUV).

The aim of this study was to obtain myocardial to background (blood pool) (M/B) SUVmax ratio in order to assess the cut-off value optimal for further application of cardiac specific software calculating the amount of viable myocardium to reduce the risk of inadequate viability assessment.

Material and methods

Patients

Cardiac FDG-PET/CT was performed for clinical purposes in a group of 69 non-diabetic patients with coronary artery disease confirmed using coronary angiography and fasting blood glucose below 120 mg/dL. The subjects included 56 men and 13 women with a mean age of 62 ± 11.1 years.

Imaging protocol

If informed consent was waived by the institutional review board (IRB) for a study, an intravenous glucose load protocol was applied to all the patients in accordance with a previously published description [3]. Each patient received an intravenous glucose-insulin injection after overnight fasting, which was well tolerated.

The injected activity was 250 ± 70 MBq (range, 180–320 MBq). The mean time from FDG administration to image acquisition was 58 min (range, 35–100 min; standard deviation [SD] = 19.2).

Acquisition parameters

Images were acquired with a Biograph 64 PET/CT scanner (Siemens Medical Solutions, Inc.) operating with Somaris/5 SyngoCT 2006 software, as described previously [4].

Technical parameters of PET and CT scans are listed below:

— For topogram: scan length 256 mm, slice 0,6 mm, scan time 0,2 s, mA 35; kV 120, tube position: top , position craniocaudal.
— For CT scan: Scan time 3,36 s, slice 3 mm, delay 4 s, no of images 111, Eff mAs-11, kV 120, FoV 700 mm, recon type axial.
— For PET scan: scan range match CT FoV, no of beds: 1, scan duration /bed 10 min, scan direction: craniocaudal. A pixel size was 2.57 × 2.57 × 2.46 mm, a 128 × 128 matrix, and 2 mm slice thickness, zoom 2 was used.

CT data were used both for attenuation correction of PET data and anatomic structure recognition for precise localization of 18F-FDG uptake.

Image reconstruction parameters

Acquired PET data were reconstructed qualitatively with the use of Syngo MI application software. Random and scatter correction was used as implemented by the manufacturer.

PET data reconstruction: a filtered backprojection method with 10 mm Gaussian filter was used.

CT reconstruction parameters: recon type was axial, kernel B18f very smooth, window: abdomen

The semiquantitative PET/CT analysis was performed using the Syngo TrueD software package. Processed PET/CT images were corrected for attenuation and reconstructed, then displayed in coronal, transverse, and sagittal planes.

Statistical analysis

The statistical analysis was performed using Statistica software and the non-parametric Mann-Whitney U test.

Image analysis

A qualitative PET and semiquantitative PET/CT assessments of the acquired data were performed in all patients. Semiquantitative and visual image analysis was performed by 2 independent investigators.

Qualitative PET data assessment

A visual analysis of acquired PET images was performed using the Syngo Software: TrueX and MI Syngo applications. The quality of the scans has been assessed visually by two independent observers. In the event of discordant findings, the final decision was made by consensus.

Visual analysis was based on a 3-point scale:

— An image was assessed as optimal if the myocardial FDG concentration was high, distribution was homogenous and background activity was visually low. The myocardial activity clearly exceeded the liver.
— An image was classified as suboptimal when the background activity was visually moderate, and/or the FDG myocardial distribution was inhomogeneous, accumulation comparable with

the liver but there were no technical problems with automatic endocardial and epicardial borders recognition in the QPS application software.

— An image was classified as uninterpretable if it is inadequate for assessing visually myocardial FDG uptake and had high background activity is present.

For statistical analysis, patients were divided into two subgroups: Group 1 — a group with optimal image quality and group 2 — a group including suboptimal and uninterpretable results.

Semiqualitative PET data assessment

A semiquantitative PET analysis was performed with the use of QPS (Cedars-Sinai Medical Center), a software package that offers a semiquantitative analysis, with automatic endocardial and epicardial borders recognition. A 17-segment polar map was used. A 50% threshold for viability assessment was used [1, 2].

Semiquantitative analysis of PET/CT image

Regions of interest (ROIs) were drawn on the transversal fused PET/CT images, and SUVmax was calculated. For the determination of cardiac FDG accumulation, the three-dimensional ROI was placed over the heart muscle to measure the SUVmax of the myocardium (SUVmaxMyo). For the determination of the background blood activity, an ROI of 0.5–1.0 cm^2 was placed in an area of the left ventricle, near the mitral valve. A two-dimensional ROI was chosen for the background calculation to avoid false results caused by high activity from the surrounding left ventricular muscle. Furthermore, owing to the above mentioned high left ventricular muscle activity possibly causing partial volume effect, the background activity was compared in two areas: Inside the left ventricle and in the descending aorta (SUVmax LV and SUVmax Ao, respectively). The image quality was expressed as the M/B activity ratio.

Ethical considerations

The knowledge about the specific cut off value will stress the problem of risk of inadequate viability assessment in case of heterogeneous, low FDG myocardial accumulation. Even if our calculation will be specific for particular reconstruction and acquisition parameters the knowledge will optimize and justify the necessity for repeated acquisition, which (if necessary) will be performed on the same day without additional tracer injection. Subjects have received a full disclosure of the nature of the study, the risks, benefits and alternatives, with an extended opportunity to ask questions. All data collected would be coded to protect identity and privacy.

The project has educational and scientific value. It is not involving the additional risk, only such, as is present during average standard PET/CT scan. The potential risk to the participant is justified by the benefit of the knowledge gained, because thanks to this calculation there will be no need for additional repeated future FDG injection due to not conclusive results.

The proposed study is ethical in terms, and respecting the participants' welfare and dignity and their right to privacy and confidentiality.

Results

There were no statistically significant differences in the background glucose uptake between group 1 and group 2 (98.85 ± 15.00 vs. 96.0 ± 10.54; p = 0.24, respectively, at the beginning of FDG loading, 118.35 ± 20.3 vs. 127.11 ± 20.38; p = 0.81 at the time of FDG injection). Additionally, there was no significant difference in time to FDG injection (60.9 ± 7.6 vs. 60.0 ± 10.5; p = 0.12, respectively).

Qualitative assessment of the image quality

On the basis of visual (qualitative) analysis, 60/69 (86.96%) patients showed optimal quality FDG cardiac uptake (Fig. 1), 3/69 (4.35%) were suboptimal (Fig. 2), and uninterpretable results were found in 6/69 (8.7%) patients (Fig. 3).

Semiquantitative PET/CT analysis

An analysis was performed on the basis of fused images in all 69 patients. The available CT images allowed for the assessment of regional FDG accumulation even in patients with low myocardial uptake. Calculations were performed for the whole group and for

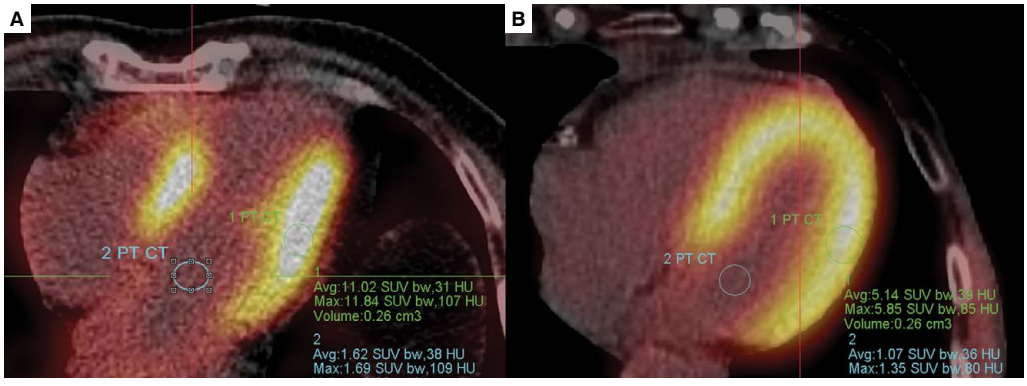

Figure 1. Myocardial viability evaluated by 18 F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) study in patients with optimal myocardial FDG uptake. **A.** A patient with previous myocardial infarction and no FDG uptake (no viability) in the apical region, myocardial to background (M/B) activity ratio (M/B index) = 7.0; **B.** A homogenous FDG uptake consistent with preserved left ventricular viability, M/B index = 4.34. SUVmaxMyo measurements in the presented scans show high SUVmaxMyo and low SUVmax LV 18 F-FDG activity

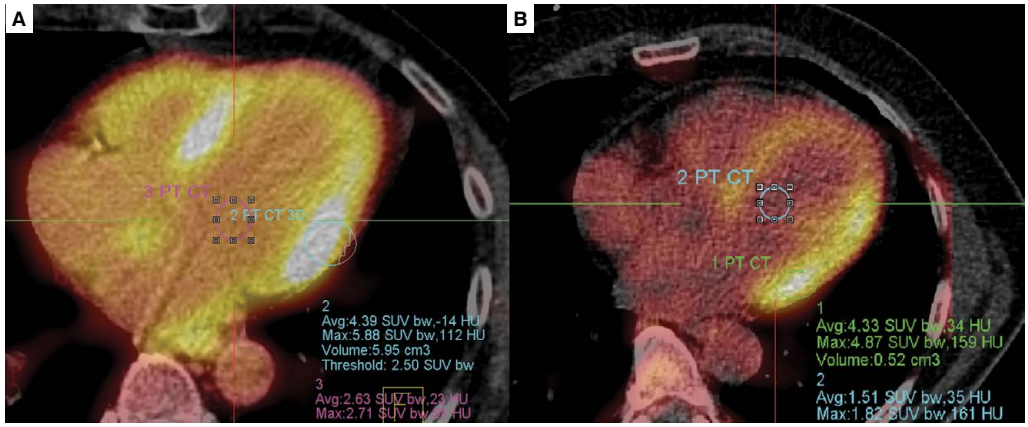

Figure 2. Myocardial viability 18F-FDG PET-CT study with suboptimal myocardial FDG uptake. Preserved heterogeneous FDG uptake pattern with high myocardial SUVmax uptake. **A.** M/B index = 2.67; **B.** M/B index = 2.18

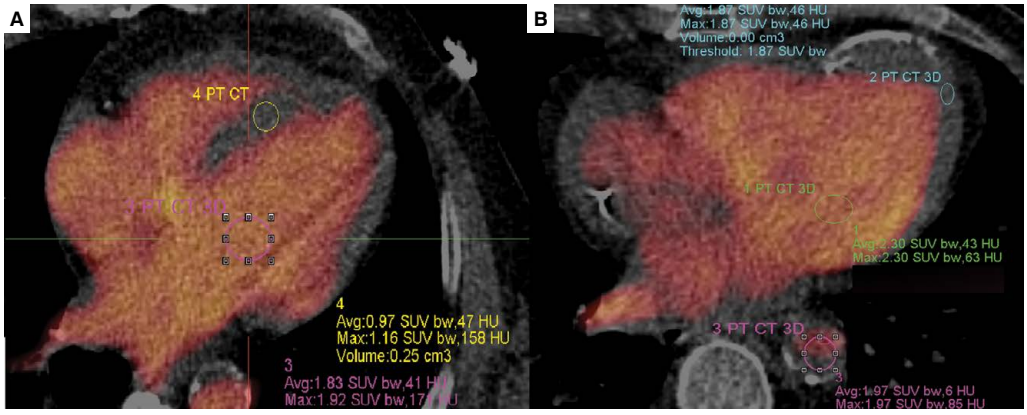

Figure 3. Myocardial viability 18F-FDG PET-CT study with uninterpretable myocardial FDG uptake. Absent FDG uptake, low myocardial SUVmax with high LV ^{18}F-FDG blood pool activity. **A.** M/B index = 0.6; **B.** M/B index = 0.81

each subgroup of patients: Group 1 (optimal images) and group 2 (suboptimal and uninterpretable images). The M/B uptake index was compared between groups and the p-value was calculated. Table 1 shows the SUVmax values of myocardial FDG uptake, background-blood pool uptake, and M/B calculated for each group of patients.

The background activity for the left ventricle and aorta were compared. There was no statistically significant difference between SUVmax in the aorta and left ventricle: 1.57 ± 0.69 vs. 1.69 ± 0.77; p = 0.18 (Table 1).

The Mann-Whitney U test showed a statistically significant difference in the mean values of M/B index comparison between group 1 and group 2 (Table 2).

The mean M/B index value for group 1 was 6.87 compared with 1.65 for group 2. The mean M/B index value was 2.23 for the images of suboptimal quality and 1.36 for images of uninterpretable quality. The highest M/B index value for the uninterpretable images was 2.2. The lowest M/B index value for the images of optimal image quality was 2.5. The index ratio of 2.2, which is consistent with the upper borderline value for visually uninterpretable images, was considered the cut-off value for differentiating between scans of optimal and non-optimal quality.

Discussion

Hybrid imaging in nuclear cardiology

Dynamic progress in medical imaging has allowed the analysis of an increasing number of parameters which may be important in understanding the mechanisms of the analyzed disease. An integrated PET/CT, where the functional scans are combined with CT is applied for many clinical purposes, including FDG myocardial viability assessment [5]. The possibility of the simultaneous analysis of perfusion or metabolism and morphological recognition of myocardial structures, such as coronary arteries, calcified plaques [6], myocardial tumors [7, 8], or epicardial adipose tissue [9, 10], allows for a more complete diagnosis. Additionally, the use of PET/CT allows for easy and accurate attenuation correction and semiquantitative calculation of glucose accumulation.

Evaluation of cardiac PET/CT image

The standard evaluation of cardiac PET/CT imaging includes always a quick check-up of the quality of the fused image performed with the general software and then the use of specific cardiac programs for further semiquantitative and qualitative evaluation. The quick assessment of general image quality is very important

Table 1. SUVmax values of myocardial FDG uptake, background-blood pool uptake, and myocardial to background index (M/B) for optimal, suboptimal, and uninterpretable visualization scans

SUVmax Mean ± SD (range)	All n = 69	Group 1 Optimal n = 60	Group 2 Suboptimal n = 3	Uninterpretable n = 6
Myocardial	8.82 ± 4.32 (1.3–19.7)	9.6 ± 4.06 (1.3–19.7)	5.2 ± 0.79 (4.6–6.1)	2.82 ± 1.11 (1.4–4.4)
Left ventricle	1.69 ± 0.77 (0.3–4.1)	1.57 ± 0.66 (0.3–3.1)	2.6 ± 1.10 (1.5–3.7)	2.42 ± 0.98 (1.3–4.1)

Table 2. SUVmax values of myocardial FDG uptake, background-blood pool uptake, and myocardial to background index (M/B) calculated for group 1 and group 2

SUVmax Mean ± SD (range)	Group 1 (optimal uptake)	Group 2 (suboptimal and uninterpretable uptake)	p
Myocardial	9.6 ± 4.06 (1.3–19.7)	3.61 ± 1.53 (1.4–6.1)	0.0001
Left ventricle	1,57 ± 0.66 (0.3–3.1)	2.48 ± 0.96 (1.3–4.1)	0.05
Aorta	1.46 ± 0.62 (0.18–2.8)	2.32 ± 0.69 (1.4–3.7)	0.03
M/B index	6.87 ± 3.99 (2.5–21.2)	1.65 ± 0.78 (0.34–3.1)	0.0001

because the study can be repeated without additional FDG injection, if the image is not optimal. This first quality control of the PET/CT image is often performed by technician performing the scan, where easy indication: "if H/B ratio is below 2.2 — repeat the scan" is clear. Further analysis express the extent and severity of metabolic defect semiquantitatively in segmental polar map as the % of maximal pixel value. A 50% threshold for viability assessment is commonly used [1, 2]. If the background activity is to high, the activity of the blood inside left ventricle increase the number of counts due to limitations of reconstruction algorithms. Since the semiquantitative image is always normalized to the pixel with highest activity and the scale of visual presentation is linear, the images of not optimal quality are overestimating the viability and underestimating the scar. In our clinical experience many myocardial scans with high background activity are not conclusive and the repeat evaluation is essential.

Quantitated myocardial FDG uptake as a monitoring tool for viability

The final PET image quality depends mostly on the myocardial and background FDG activity. There are only a few articles regarding the quantitative or semiquantitative assessment of image quality. Coulden et al. [11] suggested an SUVmax of 3.6 as the borderline for suppressed myocardium. In our group of patients, the mean value of the myocardial SUVmax in the group with uninterpretable image reached 2.82, and the highest individual value was 4.4. Despite the statistically significant difference between the myocardial SUVmax in both groups, the values were overlapping, as there were patients showing myocardial activity ranging approximately 3–6 in all the analyzed groups. Our results suggest that the relation between the myocardium and background (i.e., the M/B index) may be a better indicator than the absolute SUVmax value for image quality and reliability of image interpretation. The M/B index was previously analyzed by Bax et al. [12], who compared three preparation protocols for patients: Oral glucose load, hyperinsulinemic clamp, and nicotinic acid derivative. Image quality was expressed as the M/B activity ratio. A ratio of 2.8–2.9 (± 0.7–0.8) was considered optimal. We recorded similar results in our group of patients; optimal FDG myocardial uptake observed was 2.5. The mean value of the M/B ratio in our group of patients was 6.87 (range, 2.5–21.2; SD, 3.99). Although the patients with high myocardial FDG uptake were found in both analyzed groups, (mean values: 9.6 for optimal images and 3.61 for suboptimal and uninterpretable), the patients with suboptimal and uninterpretable image quality expressed higher background FDG activity that resulted in a significantly lower M/B index. High background (blood pool) activity reduces the image contrast, which reduces the diagnostic quality of the images.

Importance of acquisition protocol modifications for FDG PET/CT imaging

An increased blood pool activity is probably a sign of delayed clearance of the radiotracer from blood or insufficient time for clearance of the tracer. Machac et al. [13] suggested repeated imaging after 30–60 min may improve the myocardium-to-blood pool contrast. In our group of patients, double time acquisition was performed in two cases of uninterpretable scans. In these cases there was no significant improvement in image quality. The double time acquisition was in turn helpful in patient with "not optimal" image quality, where better contrast was achieved in delayed acquisition. Owing to lower density counts caused by radioactivity decay following delayed acquisition and requirement

for prolonged time, image repetition may be difficult with regard to logistic reasons. Furthermore, the increase in blood pool activity may be caused by other reasons, e.g., inadequate patient preparation with high free fatty acid and low insulin plasma levels, insulin resistance, impaired glucose tolerance, diabetes mellitus, or elevated plasma glucose concentrations. There is also a need for careful placement of the background ROI because high FDG concentration in myocardial muscle surrounding the ventricular cavity can cause false results due to partial volume defects. To avoid technical problems with the assessment of left ventricular blood activity due to the high muscle activity, in our study, the background activity was calculated and compared for two areas: Inside the left ventricle and in the descending aorta. There were no significant differences between assessments in both regions.

Importance of preparation methods for FDG PET/CT

The complexity of myocardial metabolism depends on many different factors, including substrate availability, hormones, age, BMI, and the patient's health, which influence the quality and accuracy of the study. There are two main protocols for patient preparation for FDG PET/CT studies, which are used routinely: scanning after overnight fasting used usually in oncological protocols and a glucose load protocol used in FDG myocardial viability studies. Several authors have reported varying degrees of non-specific myocardial FDG uptake despite low blood sugar levels. De Groot et al. [14] found that myocardial FDG uptake had no correlation with the fasting blood sugar level, fasting period, or age of the patient. In a similar study Kaneta et al. found a negative correlation between the blood glucose level and FDG uptake, but the fasting period and age of the patient showed no relationship [15]. We found no significant correlation between the degree of myocardial FDG uptake and the blood glucose level, either at the beginning or at the time of FDG injection. There was also no significant difference in the time from injection to image acquisition.

SUVmax calculations

Although many well known factors can affect the accuracy of SUV measurement, including patient weight, blood glucose level, length of uptake period, partial-volume effect, recovery coefficient, algorithm of reconstruction used and type of region of interest, this assessment of FDG uptake is widely used.

Many publications describing cardiac SUVmax assessment applies to the sarcoidosis [16, 17] or assessment of normal myocardial uptake [18] or the comparison of different PET acquisition methods [19]. Other studies focus on the clinical factors affecting myocardial FDG uptake [20]. Our study concerns the patients with coronary artery disease who needs semiquantitative validation of the amount of viable myocardium before the final decision of the revascularization. In our clinical experience many myocardial scans with high background activity are not conclusive and the repeat acquisition is essential.

Rahbar et al. [7] analyzed SUVmax values in a group of 24 patients with myocardial tumors and found statistically significant differences between malignant and benign tumors (2.8 vs. 8.0, respectively). However, semiquantitative assessments of myocardial FDG accumulation should be treated with caution, considering the non-specific heterogeneous uptake with the wide range of physiological myocardial SUVmax values (even in a fasting state) and poorly estimated physiologic SUVmax range of the myocardium after a glucose load protocol.

In conclusion, an M/B index of 2.2 was found to be the cut-off value for scans of optimal quality; however, their mean value was much higher (6.87). In our opinion, the assessment of the M/B index in clinical practice may play an important role, especially in semiquantitative and quantitative myocardial metabolism analyses in polar map (bulls eye) presentations. If the FDG blood pool activity is insufficiently cleared from the LV cavity, it is possible to overestimate the myocardial FDG activity due to partial volume defects. The majority of commercially available software solutions should be used with caution because they were originally developed for single positron emission CT techniques. Although they are easily applicable for quantitative and semiquantitative assessment of myocardial tracer accumulation, they may not have been validated for PET. Therefore, PET/CT image quality, as well as the SUVmax and M/B index, should be assessed before segmental calculations are applied.

Conflict of interest

The authors declare that they have no conflicts of interest.

Statement of human rights

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study, formal consent was not required and was waived by the institutional review board (IRB) of Medical University of Warsaw, Poland.

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