Residual Activity Correction in Quantitative Myocardial Perfusion $^{13}$N-Ammonia PET Imaging: A Study in Post-MI Patients

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Abstract  Background/Introduction/Aim: Positron emission tomography (PET) is the gold standard for the quantification of myocardial blood flow (MBF). A standard PET scan is acquired in two phases (rest and pharmacological stress). $^{13}$N-ammonia is a perfusion radiotracer that may show residual activity, which may affect MBF estimation during the second phase of the scan. An algorithm for residual activity correction (RAC) is available when reconstruction is performed using Syngo MBF (by Siemens). The aim of this study was to evaluate differences in MBF estimation with and without RAC by Syngo MBF in patients with a previous MI using $^{13}$N-ammonia PET.

Methods: MBF was evaluated by $^{13}$N-ammonia PET in a group of 25 patients with a history of MI. Dynamic MBF measurements were analyzed with Syngo Dynamic PET, with and without RAC, and the results were evaluated with statistical methods.

Results: Significant differences in stress phase MBF after RAC were identified in the left anterior descending coronary artery (LAD) territory ($p=0.0425$) and the right coronary artery (RCA) territory ($p=0.004$). A trend towards significance was identified in the global polar plot ($p=0.049$). No statistically significant difference was found in the left circumflex artery (LCx) territory ($p=0.333$).

Conclusion: Syngo Dynamic PET, through its RAC function, can be a useful adjunct in assessing second-phase MBF of primarily the RCA territory and secondarily the global polar plot and LAD territory but not the LCx territory.

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1. Introduction

Based on current estimations from the World Health Organization, cardiovascular disease causes the most deaths worldwide and is expected to cause deaths in excess of 23.6 million until the year 2030.¹ Heart failure (HF) is itself a growing global epidemic, causing considerable increases in mortality and in healthcare costs, while affecting more than 15 million people worldwide.²,³ A considerable proportion of HF cases arise from chronic myocardial ischemia. Ischemic HF may present after a variable interval following myocardial infarction (MI).

Numerous current international guidelines, including those from the European Society of Cardiology, emphasize the need for prognosis assessment and risk stratification in HF patients.⁴ Positron emission tomography (PET) is an imaging modality that allows for identification of non-viable myocardium.⁵ It represents a helpful tool for the diagnosis of residual ischemia and for risk stratification in HF, as it constitutes the gold standard for the quantification of myocardial blood flow (MBF) and myocardial perfusion reserve (MPR) in absolute terms.⁶

The positron-emitting radiotracers used in PET cardiac imaging include rubidium-82 (⁸²Rb), nitrogen-13 ammonia (¹³N-ammonia) and oxygen-15 water (¹⁵O-water). Different tracers also have different half-lives, ranging from 76 seconds for ⁸²Rb to 9.96 min for ¹³N-ammonia.⁷ Traditionally, a perfusion PET scan includes two phases, during which a separate dose of radiotracer is administered. Most commonly, the first scanning phase is performed at rest, while the second phase is acquired during pharmacologically induced stress.

In shortened protocols with ¹³N-ammonia,⁷ there is potential for residual radiotracer activity from the first scan phase to persist during the second phase, and recently, a method to estimate and correct the residual activity (residual activity correction [RAC]) for MBF estimation has been made available (embedded in the Syngo MBF software package).⁸ However, it is still unknown whether estimates of MBF with RAC may be significantly different from uncorrected values in scans performed in patients with evidence of a previous MI. This becomes relevant when considering that these patients are the most likely to benefit from state-of-the-art non-invasive imaging modalities such as PET.

Therefore, the aim of this study was to evaluate global and regional differences in ¹³N-ammonia PET-derived MBF and between stress phase scans with and without RAC in patients with a previous MI.

2. Patients/Methods

A retrospective study was performed on a group of 25 patients (18 males and 7 females) that were referred for a rest/adenosine stress ¹³N-ammonia PET scan for the evaluation of residual ischemia at the National Autonomous University of Mexico. Approval was obtained for the conduction of the study from the local institutional ethics committee.

All patients had a history of previous MI documented clinically and confirmed by the results of the perfusion scan as fixed perfusion defects.

2.1. PET Acquisition and Reconstruction

All image data were acquired in list mode on a Siemens Biograph-16 TruePoint PET/CT (Siemens Healthcare, Knoxville, USA) with the TrueV option (the axial field of view of 21.6 cm). This 3D system consists of a 16-slice CT and a PET scanner with 4 rings of lutetium oxyorthosilicate (LSO) detectors. Patients were instructed to fast overnight and to avoid the consumption of methylxantine- and caffeine-containing beverages or medications for 24 h before the study. Prior to the rest perfusion phase of the scans, a CT-based transmission scan (130 kVP; 25 mAs; helical scan mode with a pitch of 0.95) was obtained during normal breathing for the correction of photon attenuation for all acquisitions. The automatic coregistration of the CT attenuation map with the PET images was verified visually, and alignment was corrected when necessary by an expert nuclear medicine technician. During rest, myocardial perfusion was assessed using 300 MBq of ¹³N-ammonia. Imaging lasted for 12 minutes and began simultaneously with the peripheral injection of the radiotracer. The ¹³N-ammonia was administered as a single intravenous bolus (8–10 s with infusion rate 0.4 ml/sec) followed by a 10-ml saline flush. Pharmacologic stress imaging was performed one minute later and began with a 6-min adenosine infusion through a peripheral vein (140 μg/kg/min). A second dose of 400 MBq ¹⁴N-ammonia was injected in the fourth minute of the adenosine administration and image acquisition was started in the same way, simultaneously with the radiotracer bolus. Static, dynamic and 16-bin ECG-gated images were generated from the list mode data. Patient emission data were reconstructed using 3D attenuation weighted ordered subsets expectation maximization (OSEM3D) reconstruction with a 168×168 matrix, zoom 2, Gaussian filter with a full width at half maximum of 5 mm, 2 iterations and 21 subsets for gated and dynamic images and TrueX (OSEM3D with PSF) reconstruction with a 256×256 matrix, zoom 2, Gaussian filter of 4 mm, 4 iterations and 8 subsets for static images. CT-based attenuation, scatter, decay, and random corrections were applied to the reconstructed images. Dynamic images were reconstructed with 25 frames for rest (1×10 sec, 12×5 sec, 2×10 sec, 7×30 sec, 2×60 sec, 1×180 sec) and 26 frames for stress (delay 90 sec, 1×30 sec, 1×10 sec, 12×5 sec, 2×10 sec, 7×30 sec, 2×60 sec, 1×180 sec).

RAC was applied for dynamic images obtained during pharmacological stress to exclude the influence of residual ¹³N-ammonia activity from the rest phase. The average time between the rest and stress phases was 26.040 ± 4.745 minutes. Dynamic data sets were processed by subtracting the residual activity present in the first frame of the stress study (acquired directly before the stress phase) from the time activity curves using the RAC method integrated into Syngo MBF (Siemens Healthcare, Knoxville, Tennessee, USA). Quantitative perfusion estimates were derived as follows: left ventricular contours were detected.

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automatically with minimum observer intervention. With a previously described 2-compartment kinetic model for $^{13}$N-ammonia, stress and rest flow values in mL/g/min were computed for each sample on the polar map through the resulting time-activity curves for global quantification. Rest MBF was corrected for the rate-pressure product (RPP) as previously described. Perfusion variables were calculated globally (for the whole left-ventricular region) and regionally (based on three vascular territories as usual [LAD, LCx and RCA]).

2.2. Statistical Analysis

All continuous variables are described as the means ± standard deviation. Within-groups comparisons (between the scans of the same patients, with and without RAC) were made using the paired-sample t-tests after assessing the normality of the distribution. A p-value < 0.05 was considered significant. All statistical analyses were performed with SPSS (Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp., USA).

3. Results

The patients were of Mexican descent, with a mean age of 66 years (standard deviation ± 11 years).

Significant differences in MBF after RAC were identified in rest-phase dynamic MBF measurements in the left anterior descending coronary artery (LAD) territory (p = 0.0425) and right coronary artery (RCA) territory (p = 0.004) (see Figure 1). A trend towards significance was identified in the global polar plot (p = 0.049). No statistically significant difference was found in the left circumflex artery (LCX) territory (p = 0.333). Detailed results are presented in Table 1.

4. Discussion

In our study, we identified a significant difference in stress phase MBF values of the LAD and RCA territories, while values in the global polar plots trended towards significance after using the RCA function of Syngo Dynamic PET. On the other hand, no significant difference was observed in stress phase MBF values in the LCX territory. Our data strongly indicates that Syngo MBF is a valuable tool to accurately quantify rest phase MP. Through the use of RAC, the overestimation of stress-phase MBF can be avoided, which can consequently improve the diagnostic capabilities and accuracy of MBF PET.

Quantitative myocardial perfusion PET has the potential to enhance the detection of early stages of atherosclerosis or microvascular dysfunction, the characterization of flow-limiting CAD and the identification of balanced ischemia due to multivessel stenosis, which provides valuable functional information of pathophysiologic importance. By adding to the visual interpretation of myocardial perfusion, the quantification of MBF can potentially a) identify subclinical CAD, b) better characterize the extent and severity of CAD burden, and c) assess "balanced" decreases of MBF in all 3 major coronary artery vascular territories. Recent investigations have demonstrated that PET-determined reductions in hyperemic MBF in patients with subclinical or clinically manifested CAD are predictive of an increased relative risk of future cardiovascular events and clinical outcomes. Quantifying MBF with PET enables the evaluation of coronary vasodilatory dysfunction as an early precursor of CAD and facilitates the long-term follow up of risk factor modification. Furthermore, PET image quantification can promote personalized treatment and prevention.9 The evaluation of software such as PMOD and FlowQuant (Lortie model) showed that they can be used interchangeably for quantification in daily practice.10 Additionally, another study using 10 software packages (SPs) based on 8 tracer kinetic models found that they may be used interchangeably to process data acquired with a common imaging protocol.11

Figure 1  Myocardial blood flow (MBF) without residual activity correction (RAC) (Left) in a patient with anterior myocardial infarction. MBF after RAC in the same patient (Right) showing significant differences in MBF. Both images are of the second scan phase (stress phase).
of MBF by Syngo Dynamic PET. The publication by Slomka et al compared quantitative results obtained from 3 software tools (QPET, Syngo MBF, and PMOD); the publication by Sunderland et al studied healthy controls to identify normal MBF values with Syngo MBF, PMOD, and FlowQuant software.

To our knowledge, this is the only study to evaluate the use of RAC in the correction of second-phase residual activity in MBF PET. In this context, our data are of significant value, as they offer the opportunity to correct the overestimation of second-phase MBF, which can potentially lead to inaccurate diagnosis and risk stratification. It is of note that significant differences in our data were observed only in the LAD and RCA and not in the LCX. This can be potentially explained by the fact that the lateral wall (officially considered an LCX domain) can also be perfused by branches of the LAD. Anatomically, there is considerable variation and overlap between the areas perfused by the LAD and LCX. An additional explanation might be the fact that patient motion or spillover can potentially affect the LCx results. Overall, the global polar plot has a trend towards significance when using RAC to correct rest MP, which indicates that the RAC function of Syngo Dynamic PET can be used efficiently for correcting MBF quantification in this context.

It could be argued that the use of RAC in MBF quantification is of little use, as one might argue that it is easier to simply wait for the natural decay of the injected radiotracer. However, RAC could potentially have a use in high-patient-flow PET centers, where scan time efficiency would be significantly hampered if sufficient time for the natural decay of radiotracers was to be allotted appropriately. Consequently, the number of scans per day would decrease, leading to reduced productivity as well as reduced cost-effectiveness. However, it is understandable that further research is required before the wider adoption of the RAC function of Syngo Dynamic PET can be successfully applied in clinical practice.

5. Limitations

1. The patient population was too small to allow for sufficient evaluation of Syngo performance in patients with different severities of CAD.
2. Syngo results were not compared with other software already approved for RAC.
3. The effect of RAC on long-term patient-related decision making was not evaluated.

6. Conclusion

In conclusion, through its RAC function, Syngo Dynamic PET can be a useful adjunct in correcting for residual activity in second-phase MBF quantification of primarily the RCA territory and secondarily the global polar plot and LAD territory. However, this is not the case for the LCX territory. The study of RCA and LAD territories with the concomitant use of RAC can guarantee the unimpeded and accurate measurement of second phase MP and has the potential to promote more accurate decision making.

Conflict of interest

There is no disclosure on behalf of any of the authors.

References


