Diagnostic Performance of PET vs. SPECT Myocardial Perfusion Imaging in Patients with Smaller Left Ventricles: a Substudy of the ^{18}F-Flurpiridaz Phase-III Clinical Trial

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ABSTRACT

The performance of SPECT myocardial perfusion imaging (MPI) may deteriorate in smaller hearts, primarily due to the lower resolution of conventional Anger cameras. ^{18}F-flurpiridaz is a novel PET MPI agent with superior image and defect resolution. We sought to determine the diagnostic performance of ^{99m}Tc-labeled SPECT MPI compared to ^{18}F-flurpiridaz PET MPI according to left ventricular (LV) size.

Methods

We conducted a substudy of the phase-III clinical trial of flurpiridaz (n=750) and stratified diagnostic performance according to the median PET LV end-diastolic volume (LVEDV), with smaller LV's defined as LVEDV <113 mL (n=369), and larger LV's as LVEDV ≥113 mL (n=381). Images were interpreted by the majority rule of three independent blinded readers. The reference standard was quantitative invasive angiography with ≥50% stenosis in ≥1 coronary artery considered significant.

Results

SPECT performance decreased significantly from an area under the curve (AUC) =0.75 in larger LVs to 0.67 in smaller LVs (P=0.03), whereas PET performance was similar in larger or smaller LVs (AUC=0.79 vs. 0.77, P=0.49). Accordingly, in smaller LVs, PET had a higher AUC=0.77 than the SPECT AUC=0.67 (P<0.0001), a phenomenon driven by female patients (P<0.0001). There was a degradation of sensitivity of SPECT in smaller LVs that was highly significant (P<0.001), whereas there was no significant change in PET sensitivity according to LV size (P=0.07). Overall, PET had significantly higher

sensitivity than SPECT in both smaller (67% vs. 43%, $P<0.001$) and larger LVs (76% vs. 61%, $P<0.001$). The specificity of PET and SPECT was similar in larger LVs (76% vs. 83%, $P=0.11$). While SPECT specificity improved in smaller compared to larger LVs (90% vs. 83%, $P=0.03$), the PET specificity did not change with LV size (76% vs. 76%, $P=0.9$).

Conclusion

The diagnostic performance of ^{18}F-flurpiridaz PET MPI is not affected by LV size and is superior to SPECT MPI in patients with smaller LVs, highlighting the importance of appropriate test selection in these patients.

Keywords

Diagnostic performance; Left ventricle size; SPECT MPI; PET MPI; Flurpiridaz

INTRODUCTION

Left ventricular volumes vary significantly with body size, height, gender, and across ethnic groups, such as between Caucasian and Asian populations *(1-5)*. An ideal non-invasive imaging test should have preserved diagnostic value irrespective of left ventricular size. However, using receiver operating characteristic (ROC) analyses, the diagnostic performance of single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) for detection of coronary artery disease (CAD) has been reported to be lower in smaller hearts *(1)* in the setting of suboptimal spatial resolution and low myocardial extraction fractions of Technetium-based radiopharmaceuticals, leading to limitations in defect resolution *(6)*. The suboptimal spatial resolution of SPECT is further demonstrated by spuriously high determinations of ejection fraction *(7,8)*.

Positron emission tomography (PET) MPI is increasingly being used in clinical practice *(6,9-11)* and further allows for the accurate quantitation of myocardial blood flow *(12)*. ^{18}F-flurpiridaz is a novel PET MPI agent that has undergone phase-II *(13)* and -III *(14)* trial evaluation. Flurpiridaz has a high image resolution due to the short positron range of F-18, the improved spatial resolution of PET over SPECT, routine attenuation correction for PET, and a superior defect resolution due to the elevated myocardial extraction fraction of this radiopharmaceutical *(9,11,12)*.

Large meta-analyses suggest superior diagnostic performance in global populations of PET compared to SPECT MPI *(15,16)*, in addition to significantly reduced radiation

exposure *(17)*. However, in patients with smaller hearts being tested for CAD, the nuclear cardiology modality with the highest diagnostic yield is unknown. To help fill this gap in knowledge and clinical care, we sought to systematically compare the diagnostic performance of ^{99m}Tc-labeled SPECT MPI and ^{18}F-flurpiridaz PET obtained sequentially in the same 750 patients enrolled in the phase-III trial of flurpiridaz, with results stratified according to left ventricular size.

MATERIAL AND METHODS

Patient Population

In the present study, all n=755 patients from the 1st phase-III trial of ^{18}F-flurpiridaz PET were evaluated (14). Five studies with corrupt gated data were excluded (final n=750). The trial design was a prospective, open-label study comparing the performance of ^{99m}Tc-labeled SPECT MPI vs. ^{18}F-flurpiridaz PET in patients referred for invasive coronary angiography (ICA) (ClinicalTrials.gov: NCT01347710). The study was approved by local institutional review boards, and all patients provided written informed consent. Briefly, eligible patients had known or suspected CAD, and either had SPECT and PET MPI done prior to ICA, or alternatively underwent ICA without intervention following which both nuclear imaging tests were obtained. Both MPIs were performed within 60 days of ICA. Significant exclusion criteria included myocardial infarction/unstable angina within 6 months, percutaneous coronary intervention within 6 months, history of coronary artery bypass grafting, New York Heart Association class III/IV heart failure, non-ischemic cardiomyopathy, symptomatic valvular disease, significant congenital heart disease, history of heart transplantation, or transient ischemic attack/cerebrovascular accident within 3 months.

Study Protocol

The mode of stress was either exercise (n=221, 29%) or pharmacological (n=534, 71%), with identical stress modality used in both SPECT and PET studies of each patient. SPECT MPI was performed without attenuation correction, as per common clinical practice. Flurpiridaz doses were pre-specified as 2.5-3.0 mCi for rest, 9.0-9.5 mCi for

exercise stress (≥60 minutes rest-stress interval), and 6.0-6.5 mCi for pharmacologic stress with regadenoson, adenosine, or dipyridamole (≥30 minutes rest-stress interval) *(16)*. Raw data was submitted to a central laboratory (BioClinica, Inc., Newtown, PA) for quality control and processing for blinded interpretation by 3 independent expert readers, coordinated and conducted by the core laboratory. The reference standard was quantitative ICA assessed by the clinical trial core lab in a blinded manner (PERFUSE Core Laboratory, Boston, MA), with significant disease defined as ≥50% stenosis in at least one coronary artery.

Left Ventricular Volumes

Left ventricular end-diastolic volumes (LVEDV) were determined from gated rest ^{18}F-flurpiridaz PET images using Corridor4DM software (Ann Arbor, MI). Studies were divided into sub-groups according to the median LVEDV=113 mL or by quartiles. Smaller ventricles were defined as LVEDV<113 mL (n=369 patients), and larger ventricles as LVEDV≥113 mL (n=381 patients). The diagnostic performances of PET and SPECT, defined as ROC areas under the curve (AUC), were then compared according to LV size.

MPI Analyses

The primary efficacy read for MPI status was the overall qualitative diagnosis determination based on the independent read by each reader using perfusion and gated image data only. Reads were dichotomized as MPI negative (normal) or MPI positive for each patient. The majority rule was used for sensitivity and specificity, where at least 2 readers had the same interpretation. The semi-quantitative read was conducted using

the 17-segment LV model with a multipoint grading scale (0-4). Summed stress scores were used to derive ROC curves for SPECT and PET. ROC analyses of AUC's were performed using the median value of the resulting SSS for each patient and imaging modality. ROC curves are presented as AUC and 95% Wald confidence intervals (CI).

Statistical Analyses

Patient characteristics were compared using the χ^2 test for categorical variables and the t-test for continuous variables. A Spearman's rank correlation was performed to determine the relationship of LVEDV with baseline characteristics. Sensitivity and specificity comparisons were performed using 2-sided McNemar's test at α=0.05. The differences in ROC AUC with associated *P*-value were performed by χ^2 analyses. A *P*-value <0.05 was considered significant. SAS version 9.3 was used for analyses.

RESULTS

Patient Characteristics

The distribution of patient characteristics according to LV size categories is shown (Table 1). Patients were divided according to the median LVEDV, leading to n=369 patients in the smaller LV group (LVEDV<113 mL), and n=381 patients in the larger LV group (LVEDV≥113 mL). Other than age and tobacco use history, traditional cardiovascular risk factors were distributed similarly between groups. Patients with smaller LVs had smaller height, weight, body mass index (BMI), and body surface area (BSA).

LVEDV Distribution and Correlation with Patient Parameters

The distribution of LVEDV and corresponding patient numbers is illustrated (Fig. 1a). The median LVEDV was 113 mL with an interquartile range of 92-143 mL, and minimal-maximal value spread of 41-423 mL. The correlation of LVEDV with pertinent patient parameters is further presented (Table 2). The lowest correlation was observed with BMI (r=0.24), with significantly higher correlations observed with weight (r=0.51), height (r=0.54), and BSA (r=0.59) (all with P<0.0001). The parameter value correlating with the median LVEDV=113 mL was 1.73 m for height, 89.4 kg for weight, 30 kg/m^2 for BMI, and 2.03 m^2 for BSA, respectively. N=332 (44%) of all study subjects had a BSA≤2.0 m^2. The correlation plot between BSA and LVEDV is illustrated (Fig. 1b).

Diagnostic Performance of SPECT vs. PET MPI According to LV Size

ROC curves of SPECT vs. PET in smaller and in larger LVs were derived (Fig. 2). In smaller LVs (Fig. 2a), PET had a higher AUC=0.77 (CI=0.72-0.82) compared to the SPECT AUC=0.67 (0.62-0.72, P<0.0001). In larger LVs (Fig. 2b), PET similarly had a higher AUC=0.79 (0.75-0.84) compared to the SPECT AUC=0.75 (0.70–0.79), however this was borderline not significant (P=0.06). We additionally explored the diagnostic performance of SPECT vs. SPECT and PET vs. PET according to LV size (Suppl. Fig. 1). SPECT performance decreased significantly from larger to smaller LVs (P=0.03) (Suppl. Fig. 1a). On the other hand, PET had a similar performance in larger and in smaller LVs (P=0.49) (Suppl. Fig. 1b). Our findings indicate that while there was a significant decline in the diagnostic performance of SPECT in smaller ventricles, the diagnostic performance of PET did not change significantly with LV size. In cases where PET correctly identified perfusion defects (true-positives) and SPECT did not (false-negatives), the prevalence of multi-vessel CAD was similar between smaller (n=11, 30%) and larger (n=14, 36%) LVs (P=0.63) (Suppl. Table 1). Taken together, these results demonstrate the superior diagnostic performance of PET over SPECT which is most pronounced in smaller ventricles.

We subsequently stratified the diagnostic performance of SPECT vs. PET by quartile groupings of LV size (Fig. 3). In patients with very small LVs (Fig. 3a, quartile 1: LVEDV ≥41 – <92 mL), the PET AUC=0.74 (0.66-0.81) was superior to the SPECT AUC=0.64 (0.57-0.71) (P<0.05). Similarly, in patients with LVs in quartile 2 (Fig. 3b, LVEDV ≥92 – <113 mL), the PET AUC=0.79 (0.73-0.86) was greater than the SPECT AUC=0.70 (0.63-

0.77) (*P*<0.01). Even in patients whose LV's were larger than the median (Fig. 3c, quartile 3: LVEDV ≥113 – <143 mL), the diagnostic performance of PET (AUC=0.75, 0.68-0.81) was superior to SPECT (AUC=0.67, 0.60-0.74) (*P*<0.05). Only in patients with the largest ventricles (Fig. 3d, quartile 4: LVEDV ≥143 – ≤423 mL) was the diagnostic performance of PET (AUC=0.83, 0.77-0.89) similar to SPECT (AUC=0.82, 0.77-0.88) (*P*=0.85).

Sensitivity and specificity of SPECT and PET based on dichotomous visual reads and stratified according to LV size is additionally presented (Fig. 4). There was a highly significant degradation of SPECT sensitivity in smaller vs. larger LVs (43% and 61%, respectively, *P*<0.001). However, there was no significant change in PET sensitivity according to LV size (67% in smaller vs. 76% in larger LVs, *P*=0.07). Thus, PET had significantly higher sensitivity than SPECT in both smaller (67% vs. 43%, respectively, *P*<0.001) and in larger LVs (76% vs. 61%, respectively, *P*<0.001) (Fig. 4a). On the other hand, the specificity of SPECT and PET was similar in larger LVs (76% vs. 83%, respectively, *P*=0.11), and the specificity of SPECT was superior to PET in smaller LVs (90% vs. 76%, respectively, *P*<0.001) (Fig. 4b). Of note, this was driven by a significant improvement of SPECT specificity in smaller compared to larger LVs (83% vs. 90%, respectively, *P*=0.03), whereas PET specificity did not change with LV size (76% vs. 76%, *P*=0.9).

We further scrutinized the diagnostic performance of SPECT vs. PET in smaller LVs according to gender (Fig. 5). In males (Fig. 5a), PET had a similar AUC=0.75 (0.68-0.82) compared to the SPECT AUC=0.71 (0.65-0.77, *P*=0.24). In females (Fig. 5b), PET had

a significantly higher AUC=0.76 (0.68-0.84) compared to the SPECT AUC=0.61 (0.52–0.70, *P*<0.0001).

Case Examples of Discrepant MPI Studies

Pharmacological stress MPI results of a 66 year-old female with LVEDV=82 mL are presented (Fig. 6). Her SPECT MPI (Fig. 6a) was interpreted as definitely normal, whereas her PET MPI (Fig. 6b) was deemed definitely abnormal. ICA demonstrated 2-vessel disease with left anterior descending (LAD) 82%, left circumflex (LCx) 54%, and right coronary artery (RCA) 43% stenoses.

We further depict the pharmacological stress MPI results of a 72 year-old male with LVEDV=88 mL (Suppl. Fig. 2). His SPECT MPI (Suppl. Fig. 2a) was reported as definitely normal, whereas his PET MPI (Suppl. Fig. 2b) was assessed as definitely abnormal. ICA demonstrated significant CAD with LAD 46%, LCx 0%, and RCA 100% stenoses.

DISCUSSION

At present, societal guidelines and appropriate use criteria (18,19) do not favor selecting different cardiac imaging modalities based on LV size to enhance diagnostic performance and optimize patient risk stratification, in part due to a paucity of robust data. An early study by Hansen *et al.* using [201]Thallium SPECT MPI demonstrated that smaller chamber size was associated with a significant detrimental effect on diagnostic performance (1). Further, cardiac MRI measures of LV volumes differ significantly according to body size in addition to gender (2). Interestingly, quantitative SPECT MPI studies using commercial software packages in Japanese (3) and Chinese (4) populations demonstrated a loss of diagnostic performance in such patients, proposed by the investigators to be driven at least in part by smaller hearts compared to Western patients, and independent of gender.

Factors affecting PET image resolution include the positron range, with higher positron emission energies such as that of [82]Rb associated with higher positron ranges and image blurring (9). In addition, routine attenuation correction and reduced prevalence of artifacts further enhance the diagnostic performance, risk stratification, and predictive ability of PET MPI (20). To date, this has been particularly demonstrated in obese patients (21). Indeed, higher image resolution and routine measurement of attenuation correction in PET MPI decrease false-positive studies, particularly in the presence of breast tissue or significant adipose tissue, thereby increasing specificity (11). In addition, higher spatial and contrast resolution, and elevated PET radiopharmaceutical myocardial extraction fraction – particularly with ^{18}F-flurpiridaz (22) – improve the detection of perfusion abnormalities, thereby decreasing false negative studies and increasing sensitivity

(10,12,13). Furthermore, PET MPI permits identification of cardiac function at peak vasodilatory stress *(23)* and is ideally suited for absolute myocardial blood flow quantitation *(12,24,25)*, both of which are associated with enhancement of diagnosis and also contribute to prognostic determination. Thus, PET MPI permits integration of perfusion, flow, and cardiac function.

Flotats *et al.* reported that [82]Rb-chloride PET MPI offers higher image quality and interpretation confidence compared to ^{99m}Tc-labeled SPECT MPI with or without attenuation correction, obtained in the same patients *(26)*. Similarly, the image quality and diagnostic certainty with ^{18}F-flurpiridaz was found in phase-II *(13)* and -III *(14)* trials to be superior to ^{99m}Tc-labeled SPECT MPI obtained in the same patients. Meta-analyses of SPECT vs. PET MPI for the detection of CAD with ICA as the reference standard *(15,16)* have confirmed the superior diagnostic performance of PET in global patient populations. Whether this remains true in patients with smaller ventricles has not been appropriately studied. Bateman *et al.* compared ^{99m}Tc-sestamibi SPECT vs. [82]Rb-chloride PET MPI in separate but matched patient populations, concluding that diagnostic performance was higher in PET independent of gender and BMI *(27)*. Their results however were not stratified according to LV size.

To the best of our knowledge, no prior large study has looked at the diagnostic performance of SPECT vs. PET MPI in smaller vs. larger ventricles in a systematic manner and in the same patients, similar to our current study. Our results indicate the superiority of PET over SPECT not only in patients with smaller LVs (defined as being

smaller than the study population median), but also in very small LVs (1st-24th percentile) as well as in somewhat larger LVs (51st-74th percentile). Indeed, only in patients with the largest LVs (75th-100th percentile) was the diagnostic performance of SPECT similar to PET. Further, we present observations with flurpiridaz which permits both pharmacological and exercise stress, not routinely performed in clinical practice due to the short half-lives of the currently available PET radiopharmaceuticals *(9)*. Importantly, only 59% of obese patients with a BMI≥30 kg/m^2 in our study had a small LV, suggesting that the benefit from PET in this patient population is largely due to soft tissue attenuation correction. Furthermore, our study indicates that there is a significant benefit of PET in female patients with smaller LVs, likely driven at least in part by breast and adipose tissue attenuation correction.

Several factors may have influenced the diagnostic performance of SPECT and PET MPI in the phase-III clinical trial of flurpiridaz *(14)*. There are no prior clinical trials comparing the performance of SPECT and PET MPI in the same patients prior to or after ICA. Thus, our results may differ from observations in the published literature *(15,16)*. Overall sensitivity may have been somewhat lower given potential safety concerns in delaying coronary revascularization in patients with high-risk CAD determined during ICA, or a very abnormal SPECT MPI scan, leading to such patients not being enrolled in the trial. The reference standard was % stenosis by ICA, which has a poor relation with the functional significance of CAD by fractional flow reserve *(28)* or MPI *(29)*, thus adversely affecting both sensitivity and specificity.

16

Analyses from the 1st phase-III trial of flurpiridaz demonstrated that blinded visual analysis of SPECT was skewed towards higher specificity and lower sensitivity *(14)*. This bias is obviated by ROC AUC analyses which provides an objective assessment of diagnostic performance. A 2nd phase-III trial of flurpiridaz is ongoing (ClinicalTrials.gov: NCT03354273). Recognizing the subjectivity of direct comparison of PET vs. SPECT MPI, the primary outcome measure will be the diagnostic performance of ^{18}F-flurpiridaz PET MPI in the detection of significant CAD defined as ≥50% stenosis. Comparison of the diagnostic performance of PET vs. SPECT MPI will be a secondary outcome measure.

Identifying the ideal non-invasive test for the appropriate patient is paramount, as smaller hearts are associated with a lower sensitivity to detect obstructive CAD *(1,3,4)*. Our current imaging strategies for detection of CAD thus require further refinement. The present body of work supports PET MPI to play an expanded role compared to SPECT MPI in the diagnosis of CAD in patients with smaller LVs. Importantly, our findings further add to the body of work supporting ^{18}F-flurpiridaz as an ideal PET perfusion tracer with superior diagnostic performance *(9,13,14,24,25,30-33)*.

Limitations

Reference ranges for cardiac volumes derived from PET MPI are not well defined. For example, a study comparing 4 different commercial software packages demonstrated that LV volumes derived from gated ^{82}Rb-chloride PET MPI varied considerably *(34)*. Future studies will need to establish the correlation of cardiac volumes obtained by ^{18}F-flurpiridaz

with the reference standards of cardiac magnetic resonance imaging and transthoracic echocardiography, and ideally compare results with other available PET radiopharmaceuticals. To reflect routine clinical practice, SPECT MPI was conducted without CT attenuation correction, which may have affected SPECT sensitivity and specificity. Finally, our results need to be tested prospectively in future studies to be appropriately validated and potentially integrated into routine clinical care. To facilitate such studies and assist physicians in the selection of the most appropriate imaging modality, we determined the association of patient characteristics routinely obtained during a clinical visit with LVEDV. Of height, weight, BMI, and BSA, the best correlation was between BSA and LVEDV.

Conclusions

The present study compared the diagnostic performance of SPECT vs. PET according to LV size. The diagnostic performance of ^{18}F-flurpiridaz PET MPI for detection of CAD is not significantly affected by LV size. The superior performance of ^{18}F-flurpiridaz PET compared to ^{99m}Tc-labeled SPECT is more pronounced in smaller ventricles and is driven by female patients, underscoring the added value of intrinsic attenuation correction in addition to the higher spatial resolution of PET. Future studies should prospectively analyze whether patients with smaller LVs benefit more from PET than SPECT MPI.

DISCLOSURES

ACKNOWLEDGEMENTS

KEY POINTS

Question

What is the diagnostic performance of ^{99m}Tc-labeled SPECT MPI compared to ^{18}F-flurpiridaz PET MPI in patients with smaller left ventricles (LVs)?

Pertinent Findings

Whereas the performance of SPECT MPI decreases significantly in smaller compared to larger LVs, it is similar in PET MPI regardless of LV size. Unlike SPECT MPI, there is no degradation of sensitivity in smaller LVs with PET MPI.

Implications for Patient Care

PET MPI is not affected by LV size, is superior to SPECT MPI in patients with smaller LVs, and should be the preferred method for the detection and evaluation of coronary artery disease in such patients.

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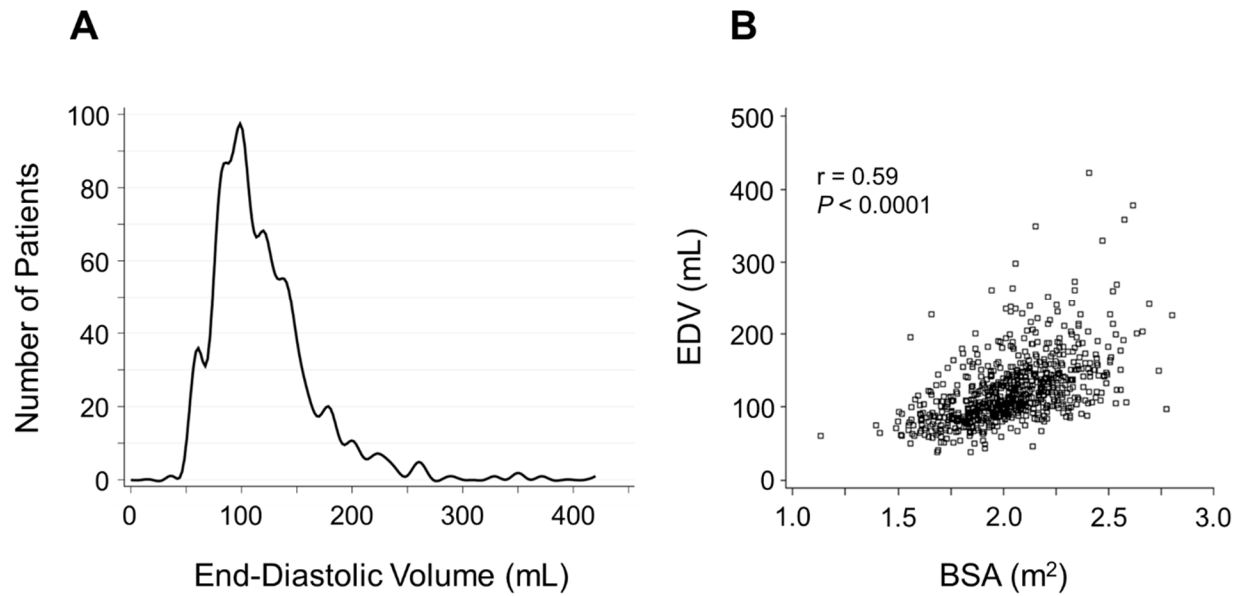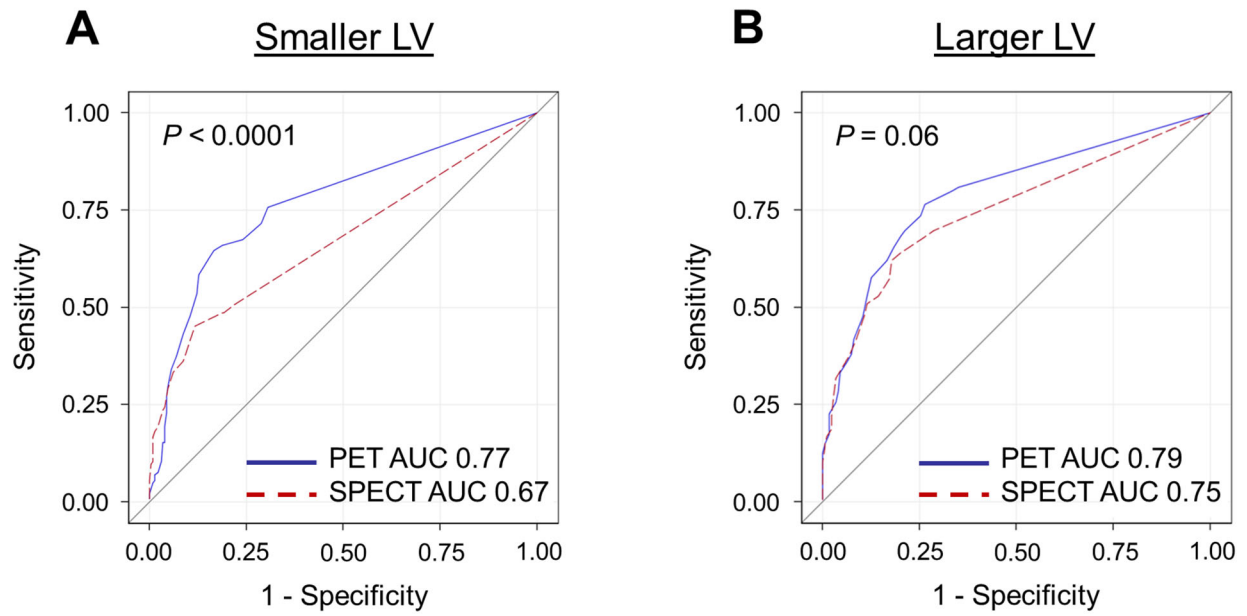
A

B

Figure 1. Distribution of Left Ventricular End-Diastolic Volumes in the Trial Population (A) and Spearman Correlation of BSA with LVEDV (B). BSA: body surface area. EDV: left ventricular end-diastolic volume.

A   Smaller LV

$P < 0.0001$

PET AUC 0.77
SPECT AUC 0.67

B   Larger LV

$P = 0.06$

PET AUC 0.79
SPECT AUC 0.75

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Figure 2. Diagnostic Performance of SPECT vs. PET According to LV Size. The performance of both imaging modalities against each other is compared in smaller (A) and in larger (B) LVs.

28
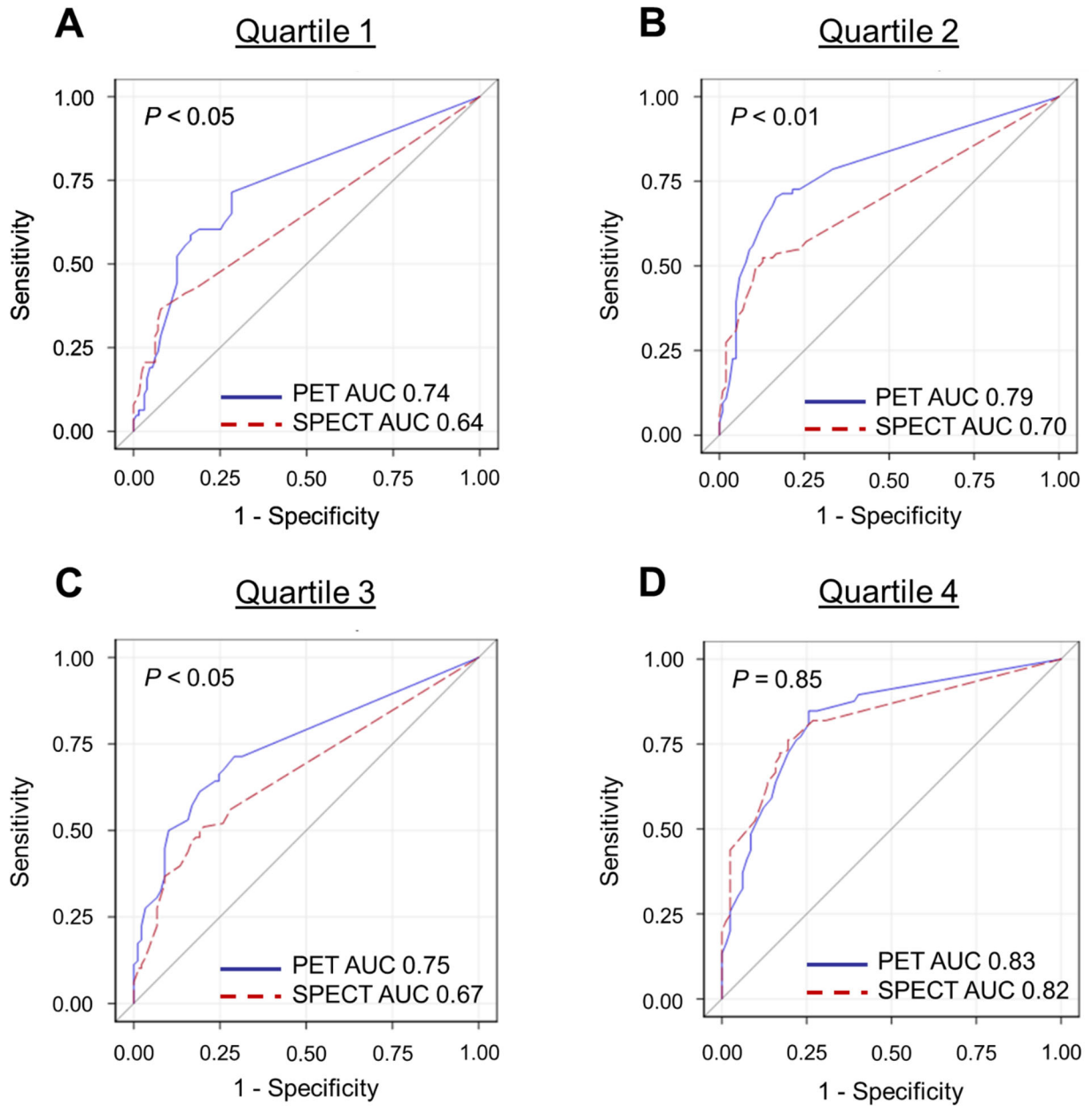
Figure 3. Diagnostic Performance of SPECT vs. PET According to Quartiles of LV Size.

The performance of both imaging modalities against each other is compared in quartiles

1 (A), 2 (B), 3 (C), and 4 (D).
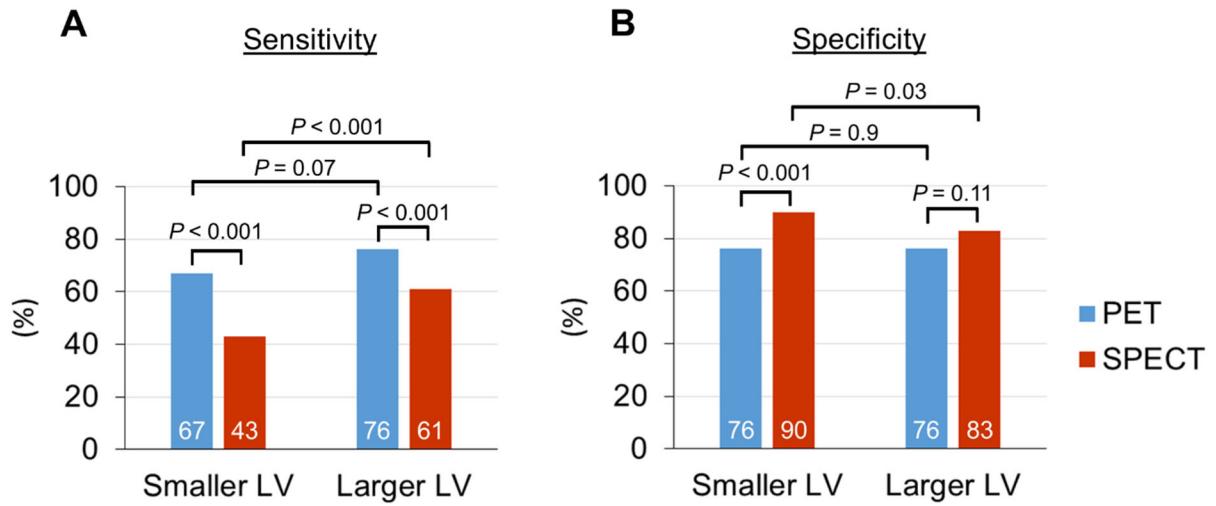
Figure 4. Sensitivity and Specificity of SPECT and PET in Smaller and in Larger LVs.

The sensitivity (A) and specificity (B) of both imaging modalities compared to each other

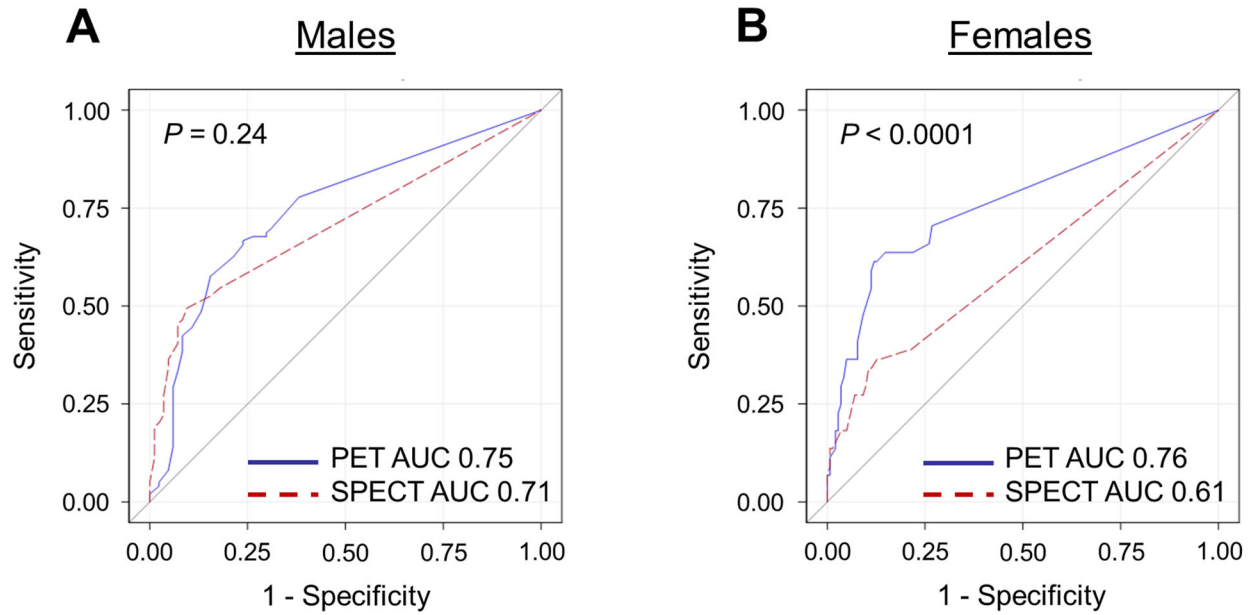in smaller and in larger LVs is presented.

Figure 5. Diagnostic Performance of SPECT vs. PET in Smaller LV's According to Gender. The performance in smaller LV's of both imaging modalities against each other is compared in males (A) and in females (B).
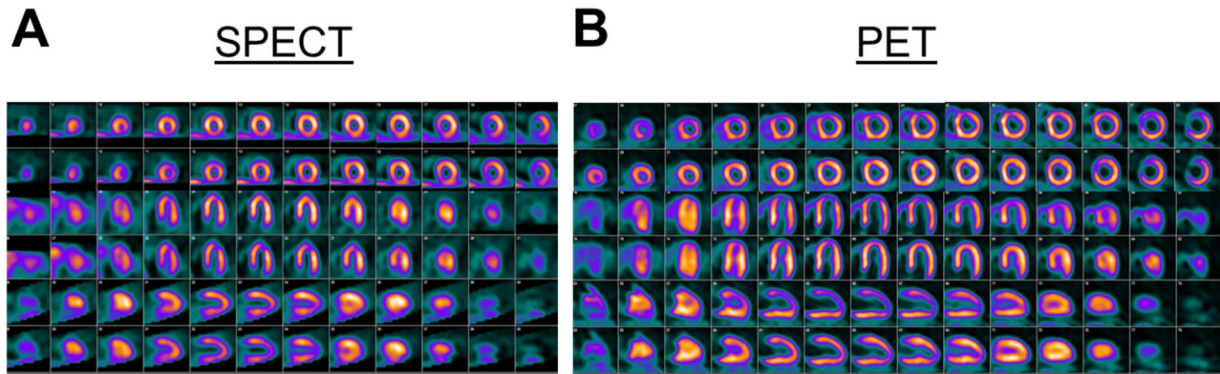
A SPECT

B PET

Figure 6. Case Example, Patient 301-139-008. Reformatted myocardial perfusion images (stress images above the corresponding rest images) of a 66 year-old female with LVEDV=82 mL. While the SPECT images (A) were interpreted as normal, the PET images (B) demonstrated anterior and lateral wall stress-inducible defects, consistent with underlying 82% stenosis in the LAD and 54% stenosis in the LCx.

	Smaller LV (n = 369)	Larger LV (n = 381)	P-value
Age, years	64.2 ± 9.7	60.6 ± 9.0	< 0.0001
Gender, male	185 (50)	335 (88)	< 0.0001
Hypertension	305 (82)	315 (83)	0.80
Dyslipidemia	323 (87)	328 (86)	0.77
Diabetes mellitus	124 (33)	134 (35)	0.60
Tobacco use history	196 (53)	255 (67)	< 0.0001
Family history of CAD	230 (62)	212 (56)	0.09
Height, m	1.68 ± 0.1	1.76 ± 0.09	< 0.0001
Weight, kg	83.5 ± 17.7	99.6 ± 19.0	< 0.0001
Body mass index, kg/m^2	29.8 ± 6.2	32.3 ± 6.8	< 0.0001
Body surface area, m^2	1.9 ± 0.2	2.2 ± 0.2	< 0.0001

Table 1. Patient Characteristics. Patient characteristics according to LV size. Values are presented as mean ± standard deviation or n (%). For body surface area (BSA) calculations, the Du Bois formula was used, where BSA=0.007184 x Height $(m)^{0.725}$ x Weight $(kg)^{0.425}$. CAD: coronary artery disease. LV: left ventricle.

|	Correlation with EDV	
	Spearman r	***P*-value**
Height	0.54	< 0.0001
Weight	0.51	< 0.0001
Body mass index	0.24	< 0.0001
Body surface area	0.59	< 0.0001

Table 2. Correlations of Patient Parameters with End-Diastolic Volumes. EDV: end-diastolic volume.
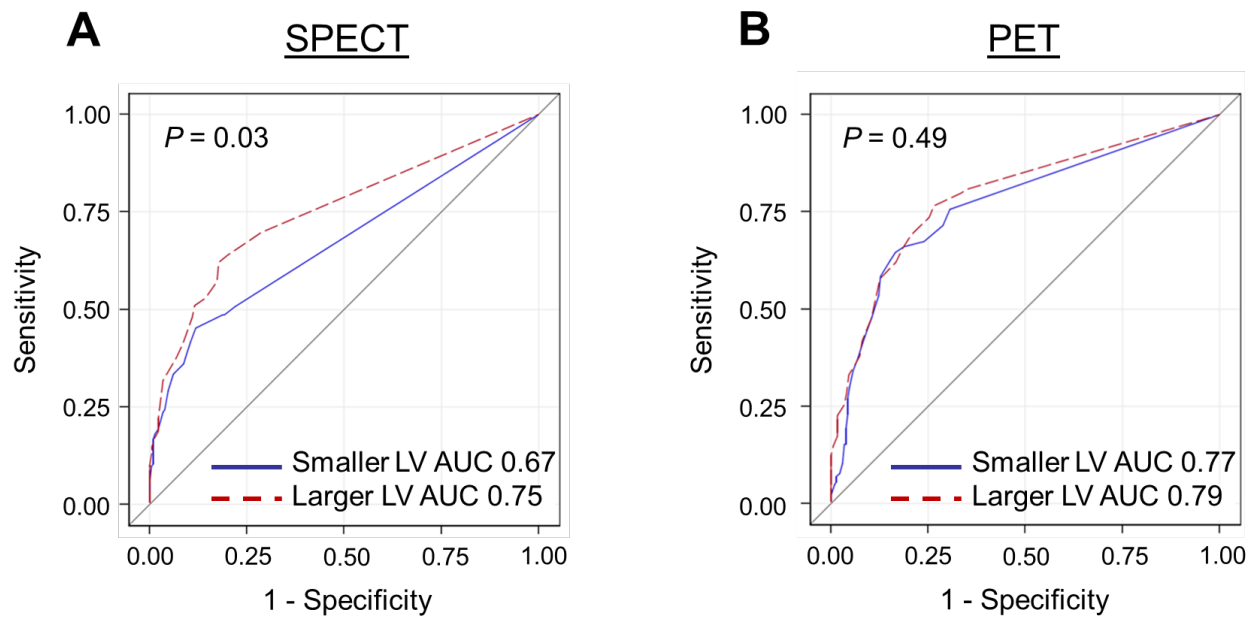
A SPECT

B PET

Suppl. Figure 1. Diagnostic Performance of SPECT vs. SPECT and PET vs. PET According to LV Size. The performance of PET (A) and SPECT (B) in smaller vs. larger LVs is depicted. AUC: area under the curve. LV: left ventricle.
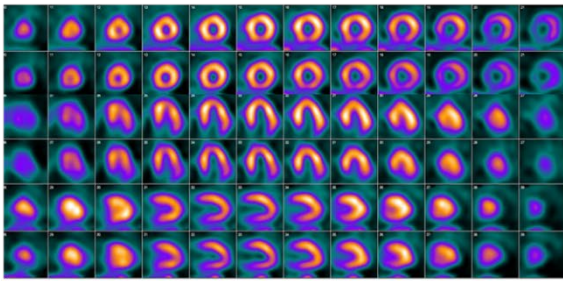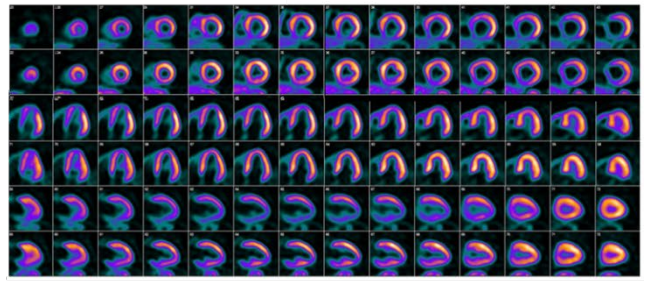
Suppl. Figure 2. Case Example, Patient 301-260-001. Reformatted images of a 72 year-old male with LVEDV=88 mL. The SPECT scan (A) was interpreted as normal. The PET images (B) however were deemed to have significant disease, most pronounced in the anterior and inferior walls, in the setting of LAD 46% stenosis and RCA 100% stenosis.

	Smaller LV		Larger LV	
	CAD	Multi-Vessel CAD	CAD	Multi-Vessel CAD
True-Positive PET	95	45 (47)	156	94 (60)
False-Negative SPECT	82	26 (32)	81	30 (37)
True-Positive PET and False-Negative SPECT	37	11 (30)	39	14 (36)

Suppl. Table 1. Discrepant PET and SPECT cases in smaller and in larger LV's, stratified according to single- or multi-vessel CAD. Values are presented as n (%).