



ABSTRACT

Background: Our aim was to develop a normal database to be used for quantification of myocardial perfusion and diagnosis of obstructive coronary artery disease (CAD) using 3D PET-CT.

Methods: From a record of 1501 patients, 78 were identified as having low-likelihood (LLK) of coronary artery disease. Forty LLK patients were used to construct a normal database using 4DM-PET, the remainder used as validation. A group of 45 CAD patients who had invasive coronary angiography (ICA) and PET-CT scans were used to evaluate the accuracy of the database for detecting CAD using the sum stress score. The effect of different exclusion criteria and the inclusion of LLK patients on the results were evaluated.

Results: The normal database for CAD detection had a normalcy rate of 95%. Sensitivity was 100% and specificity was 87% for 50% stenosis when detecting global disease. For localizing disease to the LAD, LCX, and RCA, sensitivity ranged from 59% to 68%, while specificity ranged from 87% to 89%.

Conclusions: A normal database containing the relative perfusion scores of patients without obstructive CAD can be used to accurately diagnose obstructive CAD using Rb-82 with 3D PET-CT imaging.

INTRODUCTION

Myocardial perfusion imaging using Rubidium-82 positron emission tomography (PET) is a powerful tool for diagnosing obstructive coronary artery disease (CAD) because of its consistently high accuracy [1].

Previous studies have described the development of 'normal databases' characterizing relative perfusion data for patients with a low-likelihood (LLK) of obstructive CAD [2,3].

Most of the previous studies that have developed low-likelihood normal databases have done so only in the context of SPECT or 2D PET myocardial perfusion imaging. There is a need for the development of additional low-likelihood normal databases for 3D rubidium-82 PET MPI.

OBJECTIVES

To describe the development of a database populated with patients having a LLK of obstructive CAD using 3D hybrid PET-CT imaging, and evaluate its accuracy for the diagnosis of obstructive CAD.

METHODS

- Using a record of 1501 patients who had scans between July 2009 to December 2010 (inclusive), a group of patients with a low-to-medium likelihood (LLK) of obstructive coronary artery disease (CAD) was identified based on their Morise score [4]. 76 eligible patients were identified
- Twenty male and twenty female patients were randomly selected from the eligible LLK group with scans acquired on the Discovery 690 PET-CT system (GE Healthcare, Milwaukee, WI) to become the normals database.
- The remaining 36 LLK patients were used as external validation
- Using the same patient record, any patient who had a PET scan followed by an invasive coronary angiogram (ICA) performed within 6 months after the PET was considered for inclusion
- Exclusion criteria were: percutaneous coronary intervention (PCI) performed within 6 months prior to the PET scan, history of a coronary artery bypass graft (CABG), history of intervened myocardial infarction (MI), or left ventricular ejection fraction (LVEF) under 40%
- To determine the effect of patient population on results, we also examined the results when patients with LVEF < 40% and history of intervened MI were included
- The sum stress score (SSS) was calculated in a 17-segment model using 4DM-PET (v2010) clinical interpretation software (INVIA, Ann Arbor, MI).
- The defect scores in each segment were summed in order to obtain the SSS. Based on the SSS, each patient was classified into one of the following four groups. For a SSS of 0 to 3, the patient was considered not to have significant disease. The SSS values of 4-7, 8-11 and ≥ 12 were considered mild, moderate and severe disease respectively.
- Transient ischemic dilatation (TID) was used in conjunction with SSS as a marker of obstructive CAD in order to account for the possibility of triple-vessel disease
- Using the standard American Heart Association 17-segment model, the territories supplied by each major vessel were defined according to Figure 1
- The cutoffs for localizing disease were the same as those used for global disease (0-3, 4-7, 8-11, ≥ 12), expecting that global disease should be localized in one of the coronary territories.
- Sensitivity, specificity, accuracy, and prevalence were all calculated for 50% stenosis criteria.
- For the univariate analysis of continuous demographic measures, Wilcoxon rank sum tests were used while for categorical measures, Fisher exact tests were performed using SAS 9.2 2002-2008 (SAS Institute Inc., Cary, NC, USA).
- Results were found to be statistically significant for $p < 0.05$

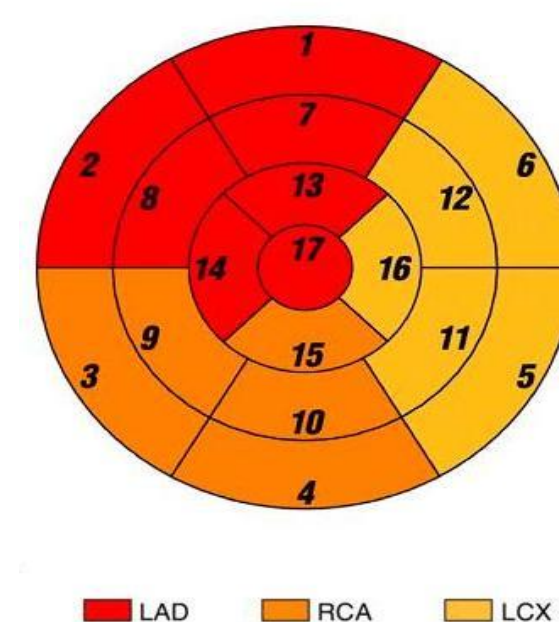


Fig 1. American Heart Association model of coronary artery territories in 17-segment model

Disease

RESULTS

- Demographic characteristics** were not significantly different between database normals and validation normals. However, the angiogram group had a significantly greater number of males, patients with dyslipidemia & hypertension, and cardiac history (MI, PCI). This was reflected in the increased Morise risk score ($p < 0.05$).

- Normals Database** results are illustrated in Fig. 2. The normalcy rate (SSS ≤ 3) of the database was 95%, with 38/40 of the LLK patients having a normal scan interpretation based on SSS. Normalcy was also assessed for the validation group and was found to be 94.4% (34/36)

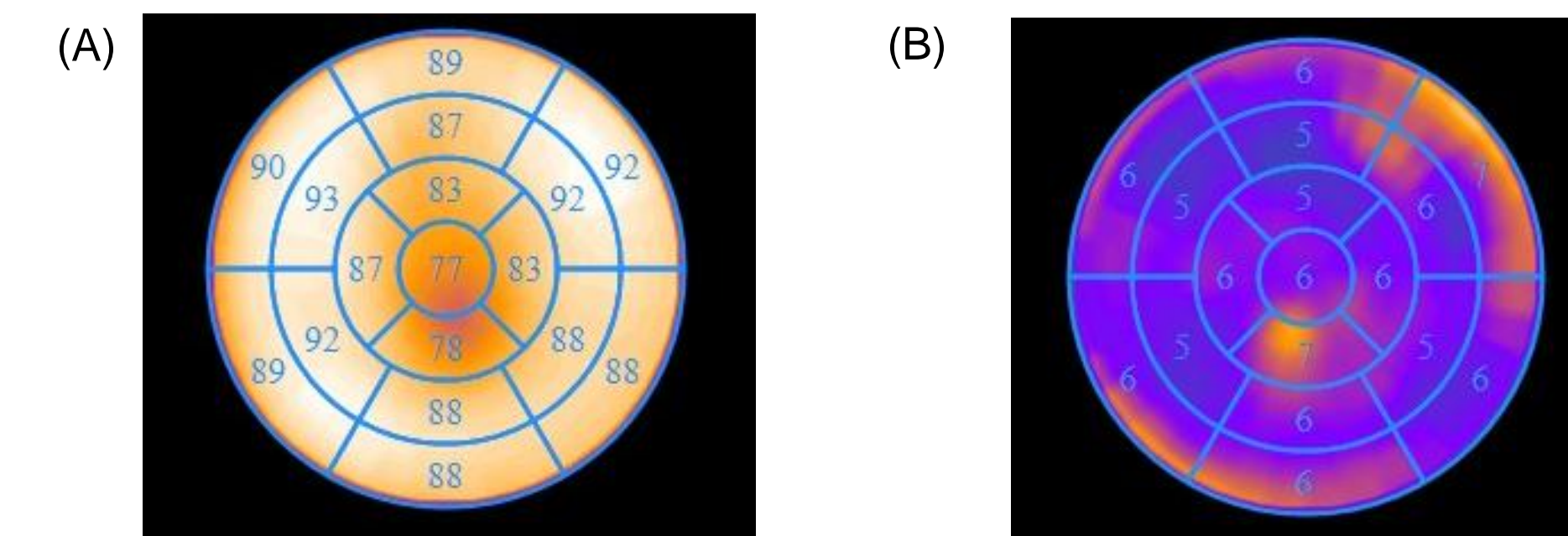


Fig 2. Stress normal database mean (a) and standard deviation (b) polar maps with relative perfusion average values in each segment (%).

- Global disease detection** of the normals database is shown in Fig. 3. As expected, including patients with history of intervened MI or LVEF < 40% decreased the specificity/accuracy of the results. Similarly, when the 36 LLK validation normals were included in the results specificity/accuracy improved.

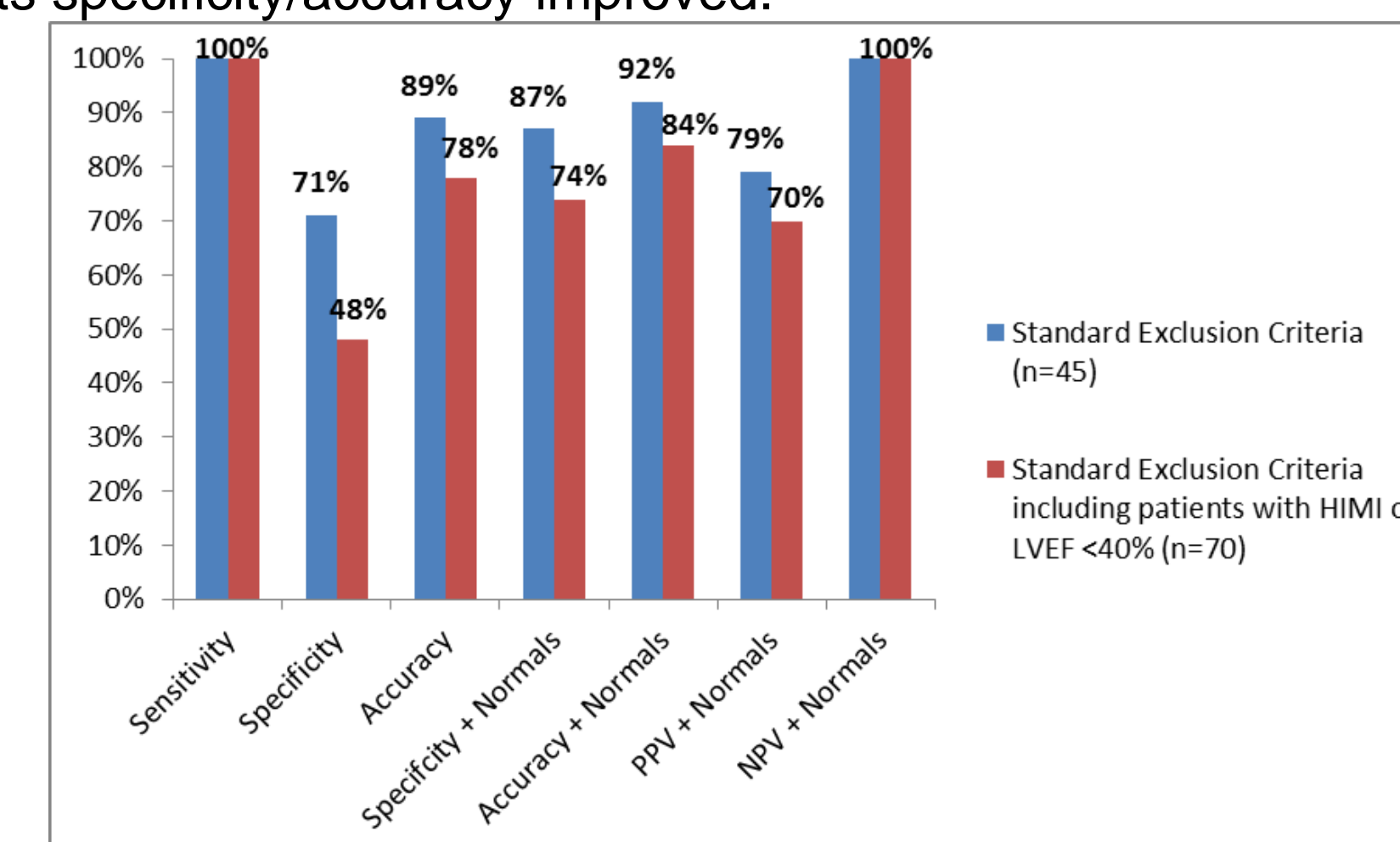


Fig 3. Normal database detection of global obstructive CAD at 50% stenosis. Standard criteria excluded patients who had PCI within 6 months of PET, any history of CABG, ejection fraction < 40%, or history of intervened myocardial infarction. '+Normals' indicates the 36 low-likelihood validation normals are included in the reported values. PPV is positive predictive value, NPV is negative predictive value, HIMI is history of intervened myocardial infarction, and LVEF is left ventricular ejection fraction.

- Regional disease localization** of obstructive CAD to the three great vessels compared to global disease detection demonstrates decreased sensitivity, and preserved specificity. LLK patients were included and standard exclusion criteria was used. (Fig. 4)

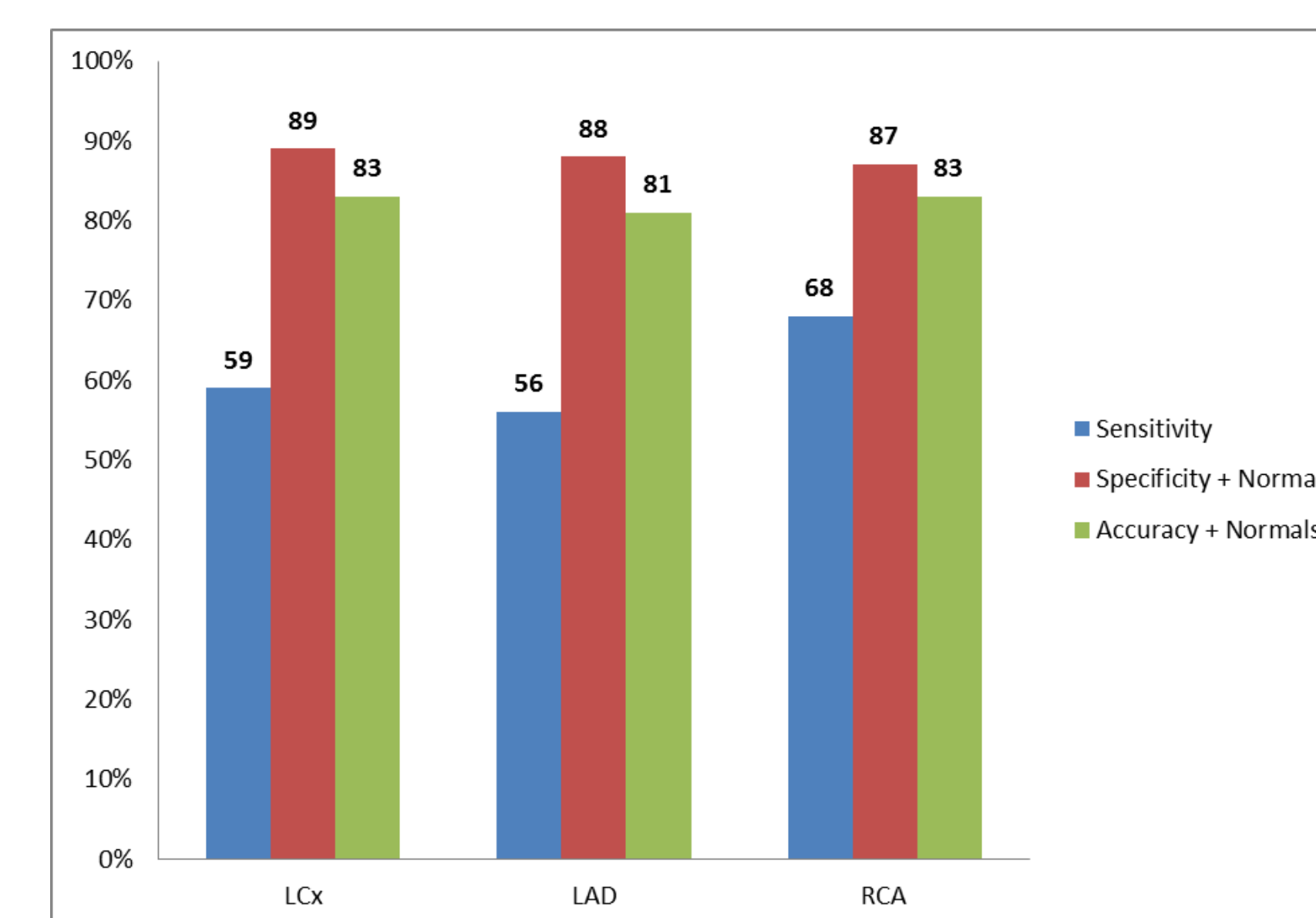


Fig 4. Normal database localization of obstructive CAD at 50%. Sensitivity, specificity and accuracy are presented for each of the three main coronary vessels using the standard exclusion criteria. '+Normals' indicates 36 low-likelihood validation patients included in the calculations.

- Receiver operating characteristic curves** demonstrate the impact of including patients with history of intervened MI or LVEF < 40% (Fig 5).

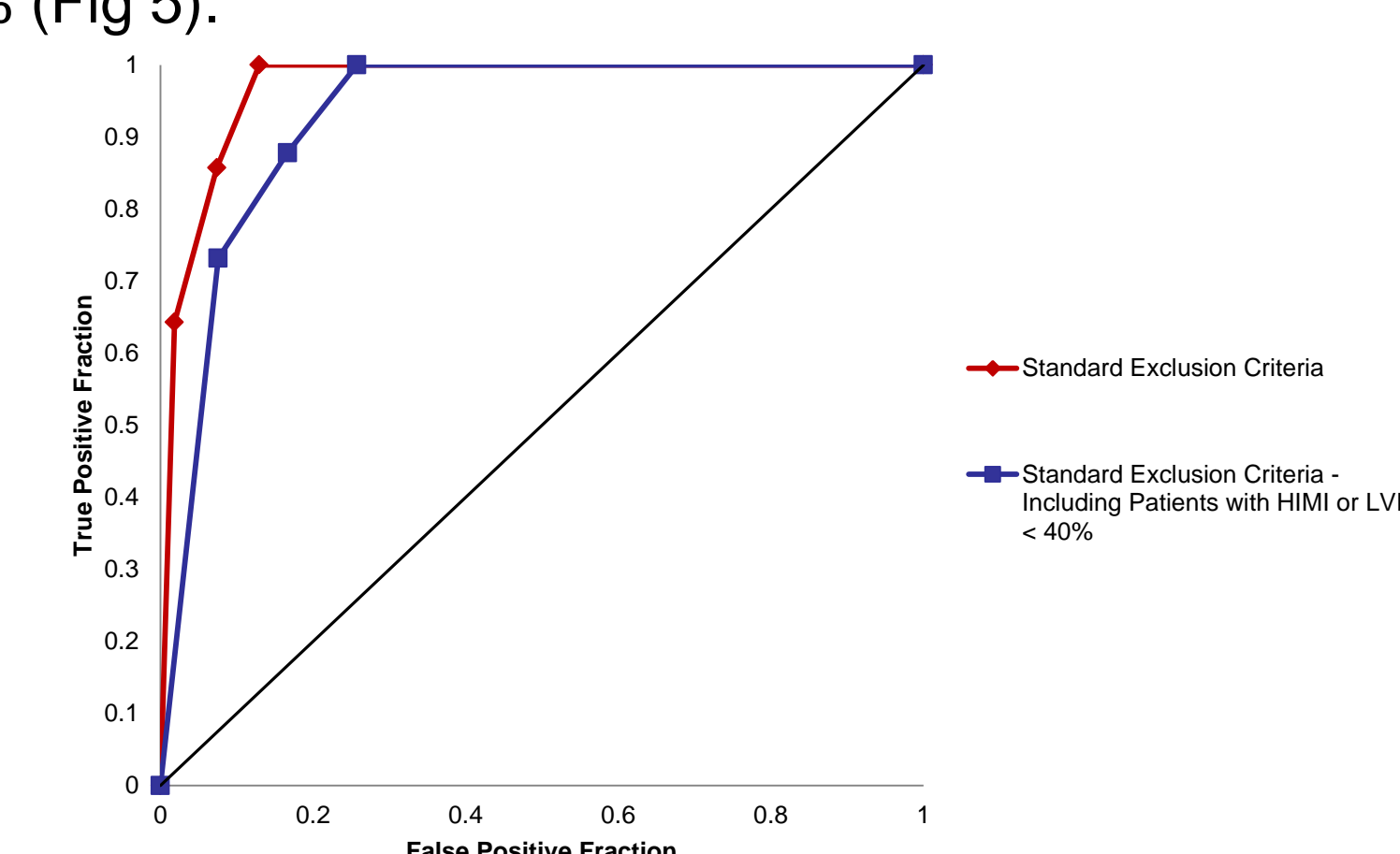


Fig 5. Receiver operating characteristic (ROC) curves for detection of CAD at 50% stenosis severity. SSS ≥ 4 was used as the cutoff point for determining presence of CAD. The 36 LLK normals were included in the results. AUC is area under curve.

CONCLUSIONS

This study suggests that a database containing the relative perfusion scores of patients without obstructive CAD can be used to accurately diagnose obstructive CAD using 3D Rb-82 PET-CT imaging. This type of semi-quantitative analysis using a normal database may be useful as an adjunct to the standard visual clinical interpretation of myocardial perfusion.

REFERENCES

- Bateman et al., Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: Comparison with ECG-gated Tc-99m sestamibi SPECT. J Nucl Cardiol 2006; 13:24-33.
- Santana et al., Quantitative (82)Rb PET/CT: Development and validation of myocardial perfusion database. J Nucl Med 2007; 48:1122-8.
- Nakazato et al., Automated quantitative 82 3D PET/CT myocardial perfusion imaging: Normal limits and correlation with invasive coronary angiography. J Nucl Cardiol 2011; Online First.
- Morise AP., Comparison of the Diamond-Forrester method and a new score to estimate the pretest probability of coronary disease before exercise testing. Am Heart J 1999; 138:740-5.

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