

# Creation of a Standardized Myocardial Perfusion Single-photon Emission Computed Tomography Database to Enhance Coronary Artery Disease Research

## Abstract

**Background:** Coronary artery disease (CAD) remains the leading global cause of cardiovascular mortality. Although single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is widely used, progress in artificial intelligence (AI)-based diagnostic tools is constrained by the limited availability of modern, high-quality, and consistently labeled imaging datasets. **Methods:** We retrospectively analyzed 144 rest–stress MIBI (99m Tc-methoxy isobutyl isonitrile) SPECT MPI studies acquired using ASNC/EANM-compliant protocols. Images were reconstructed using filtered back projection and independently interpreted by three nuclear cardiology specialists. Clinical, demographic, and imaging variables were analyzed using SPSS v26, with  $P < 0.05$  defining statistical significance. **Results:** Significant sex-specific differences in CAD presentation were observed. Women with CAD were older and more frequently demonstrated perfusion patterns compatible with microvascular dysfunction, whereas men exhibited larger territorial defects. Diabetes prevalence was significantly higher among CAD-positive patients, whereas smoking patterns differed markedly by sex. Family history of CAD was significantly more common among CAD-positive subjects. Perfusion abnormalities correlated strongly with cumulative cardiovascular risk burden. Interobserver agreement was excellent (Intraclass correlation coefficient (ICC) = 0.87). **Conclusions:** We introduce a rigorously standardized, clinically annotated SPECT MPI dataset tailored for developing and validating explainable AI models in nuclear cardiology. Its sex-stratified structure supports research into CAD phenotypes and enhances reproducibility. **Public Access:** <https://misp.mui.ac.ir/fa/t2-dual-head-spectct-coronary-artery-disease-cad>.

**Keywords:** Artificial intelligence, coronary artery disease, dataset, myocardial perfusion, SPECT

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## Introduction

Coronary artery disease (CAD) continues to be the dominant cause of cardiovascular mortality, contributing to over 18 million deaths annually according to the 2024 ESC Guidelines.<sup>[1]</sup> Myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) remains central to CAD diagnosis and risk assessment due to its prognostic accuracy, cost-effectiveness, and widespread accessibility.<sup>[1]</sup> Long-term registry studies, such as J-ACCESS, show excellent prognostic results from conventional SPECT imaging.<sup>[2]</sup> Meanwhile, contemporary hardware with radiation doses below 5 mSv achieves a spatial resolution of approximately

5 mm. Furthermore, advances in image reconstruction and processing software have significantly improved image quality and reduced the performance gap with PET imaging.<sup>[3,4]</sup> Similarly, the REFINE SPECT registry has validated quantitative SPECT metrics for predicting major adverse cardiac events across diverse populations.<sup>[5]</sup>

Despite these advances, current research is hindered by limitations in publicly available SPECT datasets. Seminal resources such as the Japanese<sup>[6]</sup> and Spanish<sup>[7]</sup> normal databases were acquired on legacy systems and lack modern demographic diversity, contemporary acquisition standards, and detailed labeling. This is particularly problematic for artificial intelligence (AI) applications, where training reliability depends on large, diverse, well-annotated

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datasets. Deep learning studies – e.g., Amini *et al.*<sup>[8]</sup> – have shown strong performance but rely on datasets that fall short of the 2022 ASNC standards<sup>[9]</sup> for:

1. Standardized SPECT acquisition and reconstruction
2. Sex-specific normal limits and diagnostic thresholds
3. High-quality clinical and quantitative annotations.

Recent studies further highlight the potential of AI in nuclear cardiology. Otaki *et al.*<sup>[10]</sup> demonstrated explainable AI models capable of predicting both epicardial CAD and microvascular dysfunction, and Liang *et al.*<sup>[11]</sup> showed that transformer networks can support low-dose SPECT imaging. However, Miller *et al.*<sup>[12]</sup> emphasized that available datasets are one to two orders of magnitude smaller than required for generalizable AI development.

To address these limitations, we developed a new, rigorously standardized SPECT MPI dataset with two innovations:

1. Sex-stratified normal limits and pathological thresholds, building on Sharir *et al.*<sup>[13]</sup> and supporting ESC-recommended sex-specific assessment<sup>[1]</sup>
2. Comprehensive expert annotation, enabling development and validation of clinically reliable, explainable AI algorithms.

This resource supports high-quality research in nuclear cardiology by integrating standardized raw projection data, sex-specific normative values, and rigorous clinical annotation. It is designed to advance precision imaging, improve diagnostic accuracy, and support regulatory-grade AI model development.<sup>[1,9]</sup>

## Methods

### Study design and population

This retrospective cohort included 144 patients undergoing rest–stress <sup>99m</sup>Tc-MIBI SPECT MPI for known or suspected CAD at Shahid Chamran Hospital, Isfahan. A schematic of the study workflow is shown in Figure 1.

All procedures adhered to the 2022 ASNC imaging standards.<sup>[9]</sup> Patients were stratified by CAD status (non-CAD vs. CAD) and sex. Inclusion and exclusion criteria were applied to ensure high imaging quality and minimize confounding by structural heart disease.

### Imaging acquisition protocol

All scans were performed using a Siemens Symbia T2 dual-head SPECT/computed tomography (CT) system following EANM guidelines<sup>[14]</sup> and a standardized two-phase protocol validated by Paul and Nabi.<sup>[15]</sup>

#### Rest phase

- Injected activity: 15–20 mCi (adjusted for body mass index [BMI])
- Imaging delay: 45 min postinjection
- Rationale: Optimal myocardial uptake and extracardiac clearance.<sup>[16]</sup>

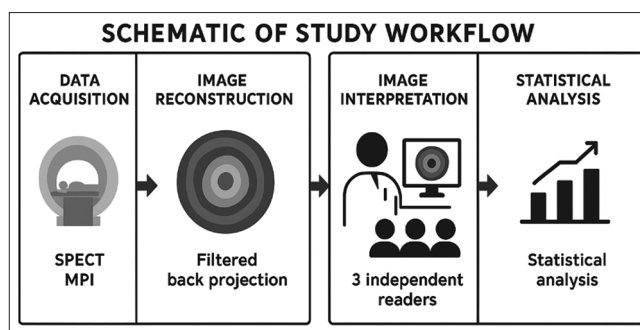


Figure 1: Schematic of study workflow

#### Stress phase

- Stress modality: Treadmill (Bruce) or dipyridamole (0.56 mg/kg over 4 min)
- Injected activity: 20–25 mCi at peak stress
- Imaging delay: 15–45 min postinjection
- Selection based on contraindications per EANM guidelines.<sup>[14]</sup>

### Inclusion and exclusion criteria

#### Inclusion criteria

1. No prior myocardial infarction
2. Ability to undergo exercise or pharmacologic stress
3. Native coronary anatomy with no history of percutaneous coronary intervention or coronary artery bypass grafting.

#### Exclusion criteria

1. Moderate-to-severe valvular disease or cardiomyopathies
2. Atrial fibrillation with R–R variability >20% or significant arrhythmias
3. Motion artifacts, myocardial-to-background ratio <2:1, or incomplete projections
4. Pregnancy or lack of expert consensus regarding image adequacy.

### Technical parameters and reconstruction

Acquisition parameters [Table 1] followed validated standards from Germano *et al.*<sup>[17]</sup> Reconstruction was performed using filtered back projection with a Butterworth filter (cutoff = 0.4 cycles/pixel; order = 5), chosen for its stability and noise performance in clinical MPI.

### Image interpretation and quality control

Three board-certified nuclear cardiologists independently evaluated each study following the standardized framework of Sharir *et al.*<sup>[13]</sup> Readers were blinded to clinical data. Discrepancies were resolved through a structured consensus review.

Quantitative perfusion analysis applied sex-specific normal limits derived from Japanese<sup>[6]</sup> and Spanish<sup>[7]</sup> reference datasets, with local adjustments. All quality control procedures adhered to EANM 2018<sup>[14]</sup> and ASNC 2022<sup>[9]</sup> standards.

### Statistical analysis

Sample size adequacy was assessed using variability estimates from REFINE SPECT<sup>[5]</sup> and J-ACCESS.<sup>[18]</sup>

- Categorical variables: frequencies and percentages
- Continuous variables: mean ± standard deviation
- Group comparisons: Student's *t*-test and  $\chi^2$  test
- Significance threshold:  $P < 0.05$
- Analyses were performed using SPSS v26 (IBM Corporation, version 26, Armonk, NY).

### Results

#### Cohort characteristics

A total of 144 patients were analyzed. Representative CAD-positive and CAD-negative SPECT images are shown in Figure 2. Demographic and clinical characteristics are summarized in Table 2.

#### Key findings

Female CAD patients were significantly older than female non-CAD patients ( $71.54 \pm 7.52$  vs.  $62.81 \pm 11.32$  years;  $P < 0.05$ ), consistent with delayed CAD onset in women.<sup>[1,19]</sup>

- Male patients were taller and heavier, but BMI was similar across all groups.

### Cardiovascular risk factor patterns

- Diabetes: markedly higher in CAD-positive patients of both sexes (48.6%–52.9%), reinforcing its role as a major risk equalizer<sup>[1,14]</sup>
- Smoking: strong sex differences; non-CAD men smoked over three times more frequently than women (50% vs. 15.6%;  $P < 0.01$ )
- Dyslipidemia: progressively increased from non-CAD females (35.9%) to CAD males (70.6%;  $P = 0.052$ ).

### Perfusion findings

- Male CAD patients exhibited significantly larger perfusion defects ( $12.3\% \pm 4.1\%$  vs.  $8.7\% \pm 3.5\%$ ;  $P < 0.05$ ), consistent with Sharir *et al.*<sup>[13]</sup>
- Female CAD patients more often demonstrated microvascular patterns with diffuse or balanced reductions, consistent with Ben-Haim *et al.*<sup>[20]</sup>
- Perfusion abnormalities correlated with cumulative cardiovascular risk ( $r = 0.62$ ,  $P < 0.01$ ) as seen in REFINE SPECT.<sup>[5]</sup>

### Familial predisposition and technical performance

- Family history of CAD was common among affected subjects, reaching 70.6% in CAD-positive males
- Interobserver reliability was excellent (ICC = 0.87)
- Reconstruction parameters showed stability across BMI ranges, confirming protocol robustness.

**Table 1: Technical specifications of the single-photon emission computed tomography acquisition protocol**

Parameter	Specification	Parameter	Specification
Radiotracer	<sup>99m</sup> Tc-MIBI	Rotation angles	90°
Matrix size	64×64	Number of projections	32 over 180°
Collimator	LEHR	Acquisition time	20 s/projection
Reconstruction method	Filtered back projection	Energy window	140 keV±20%
Patient position	Supine	Detector radius	27.5 cm

LEHR – Low-energy-high resolution; MIBI – Methoxy isobutyl isonitrile

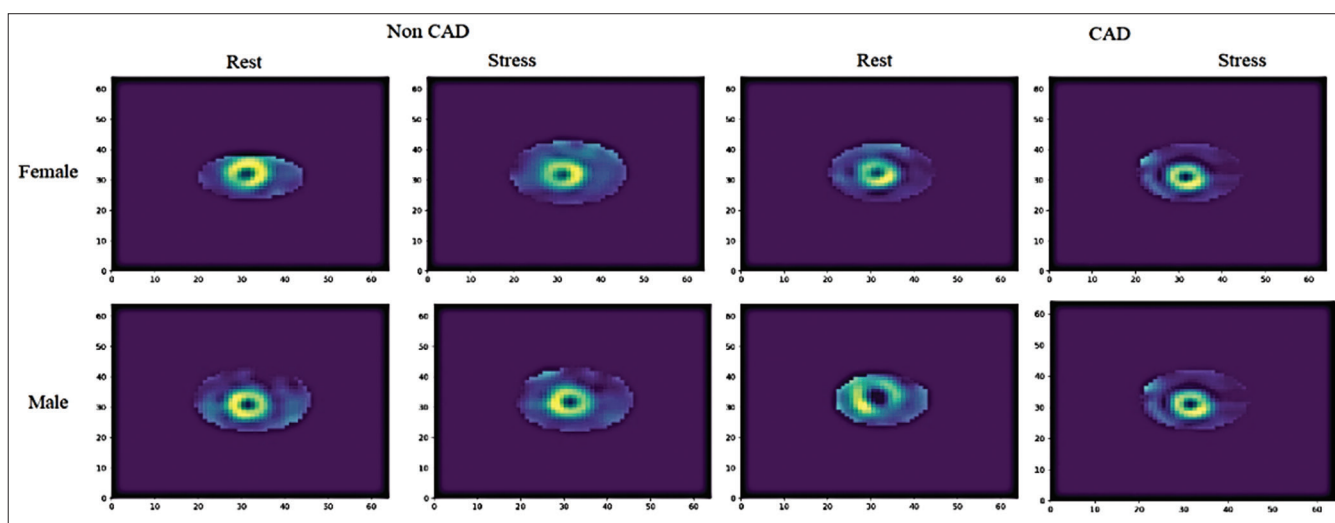


Figure 2: Indicative myocardial single-photon emission computed tomography images of coronary artery disease (CAD)-positive and CAD-negative subjects

**Table 2: Demographic and clinical characteristics stratified by coronary artery disease status and gender**

Parameter	Non-CAD		CAD	
	Female (n=64)	Male (n=26)	Female (n=37)	Male (n=17)
Age (years)	62.81±11.32	67.69±12.13	71.54±7.52*	66.82±10.27
Height (cm)	162.26±7.15	168.57±6.75	161.67±6.56	169.05±9.16
Weight (kg)	66.29±9.12	74.19±14.17	67.83±9.72	76.17±16.65
BMI (kg/m <sup>2</sup> )	25.19±3.00	25.95±3.68	26.02±3.98	26.40±3.98
Diabetes (%)	48.4	30.8	48.6	52.9
Smoking (%)	15.6	50.0 <sup>†</sup>	18.9	41.2
Hypertension (%)	62.5	69.2	73.0	58.8
Dyslipidemia (%)	35.9	57.7	56.8	70.6 <sup>‡</sup>
Family history CAD (%)	25.0	26.9	59.5*	70.6*

\*Significant differences between non-CAD and CAD groups within gender ( $P<0.05$ ), <sup>†</sup>Significant gender difference within non-CAD group ( $P<0.01$ ), <sup>‡</sup>Borderline significance ( $P=0.052$ ). CAD – Coronary artery disease; BMI – Body mass index

## Discussion

Our findings highlight significant sex-specific differences in CAD presentation, risk factor distribution, and SPECT perfusion patterns. The observed 7.3-year age gap between female CAD and non-CAD subjects reflects established sex-related pathophysiology, including higher prevalence of microvascular dysfunction and diffuse atherosclerosis in women.<sup>[6]</sup>

Risk factor analysis underscores:

- Diabetes as a major risk equalizer
- Smoking as a strongly sex-skewed risk factor
- Dyslipidemia is a progressively more prominent contributor to CAD in men.

These observations align with ESC recommendations emphasizing sex-specific diagnostic pathways<sup>[1]</sup> and with EANM procedural standards integrating clinical variables into interpretation.<sup>[14]</sup>

Our dataset also provides value for AI development. By capturing detailed clinical metadata, sex-specific reference limits, and consensus expert annotations, it addresses critical gaps identified in recent evaluations of medical AI readiness.<sup>[12,21]</sup> Its structure supports explainability, transparency, and regulatory compliance.

## Study limitations

- Single-center design limits broad generalizability, although standardized protocols mitigate this
- Predominantly intermediate-risk population
- Limited long-term follow-up; future studies should incorporate prognostic endpoints
- Lack of multicenter variability; future work will expand the dataset geographically.

## Conclusion

We developed a high-quality, standardized, sex-stratified SPECT MPI database with extensive clinical and imaging annotation, addressing major limitations in existing SPECT datasets. The dataset supports precision cardiovascular

imaging, facilitates sex-specific diagnostic research, and provides an essential foundation for reproducible and explainable AI development in nuclear cardiology. Multicenter expansion and external validation will further enhance clinical utility.

## Ethical approval

This study utilized myocardial perfusion SPECT images from patients referred to Shahid Chamran Hospital in Isfahan. No intervention was performed in the patients' treatment processes. Informed consent was obtained from all participants. The study was conducted under the ethical approval code IR. MUI. DHMT. REC.1402.074.

## Availability of data and materials

The dataset described in this study, including resting and stress myocardial perfusion SPECT images and an Excel file of patient clinical data [Table 2], is publicly available at the following links:

- <https://misp.mui.ac.ir/fa/t2-dual-head-spectct-coronary-artery-disease-cad>
- <https://kandoo.mui.ac.ir/index.php/s/5hPcmStpkOo0by0>

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## Conflicts of interest

There are no conflicts of interest.

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