**Original**

# The accuracy of myocardial perfusion SPECT imaging in the evaluation of coronary artery disease in women and men

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## Abstract

BACKGROUND: The purpose of this study is to compare sensitivity, specificity and accuracy of myocardial perfusion SPECT for the detection of coronary artery disease (CAD) in women and men.

MATERIAL AND METHODS: 588 patients (455 males and 133 females, 273 after a previous myocardial infarction) underwent stress myocardial perfusion SPECT. The accuracy of myocardial perfusion SPECT was proved by coronary angiography (stenosis > 50% was considered as a CAD).

RESULTS: The sensitivity of SPECT was slightly higher, but statistically not significant, in men than in women (94% versus 91%, p > 0.05). The specificity was higher in women than in men (93% versus 82%), but this difference was not statistically significant either (p > 0.05). The accuracy of SPECT was the same for both sexes (92%). In angiographically verified group of patients the selection bias was obvious — patients with CAD dominated (74%) and the fraction of patients with CAD in men's group (83%) was significantly higher than in women's group (50%), p < 0.05.

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CONCLUSIONS: No significant difference was revealed in the accuracy of myocardial perfusion SPECT in men and women. Our results are in accordance with the prevailing opinion in literature that discovered differences in sensitivity, specificity and diagnostic accuracy are usually not statistically significant or that they can be explained by the selection bias of patients in angiographically verified groups (significantly higher fraction of patients with CAD in men's group).

**Key words: SPECT, myocardial perfusion, coronary artery disease, men and women**

## Introduction

Stress myocardial perfusion scintigraphy performed by SPECT is an examination used routinely in patients with suspected or known coronary artery disease (CAD) [1–5]. Cost-effectiveness studies showed that rational utilisation of this non-invasive procedure resulted in a significant saving of means. In previous papers we proved the high diagnostic accuracy of myocardial SPECT for the detection of CAD in our group of patients verified angiographically and the significant role of this examination in risk stratification [10–12]. In accordance with literary data we did not find any significant difference in the diagnostic accuracy of myocardial SPECT using Tl-201 or Tc-99m labelled radiopharmaceuticals and various imaging protocols in the patients with and without previous myocardial infarction [10]. The work of other authors did not evidence the affecting of sensitivity and specificity by various sorts of stress and the choice of 50% or 70% of stenosis as a criterion for CAD [13, 21].

Nevertheless, in literature there remains an open question concerning a comparison of the diagnostic accuracy of myocardial SPECT in women and men. According to some articles, diagnostic accuracy was lower in women [14, 15] but other authors did not find a significant difference in diagnostic accuracy between the genders [16–18]. Therefore, the aim

of this paper is to evaluate retrospectively the sensitivity, specificity and diagnostic accuracy of myocardial SPECT for detection of CAD in men and women in our group of patients verified angiographically.

## Materials and methods

**Patient population.** In our department the study population comprised 588 patients prospectively selected from patients referred for exercise myocardial perfusion SPECT who underwent coronary angiography. The patient population included 133 females and 455 males, including 273 after myocardial infarction (MI). The age ranged from 31–79 years (mean 56). Their demographic data are summarised in Table 1.

**Exercise testing.** The exercise test was performed on a bicycle ergometer with the patient in the upright position. Blood pressure and a 12-lead ECG were recorded at rest and at each minute of exercise. Each patient exercised to 85% of the age-predicted maximal heart rate or the onset of angina pectoris, dyspnoea or fatigue, dizziness, frequent (> 10/min) multifocal or paired ventricular extrasystoles, ST segment depression (> 0.2 mV) or decrease in blood pressure of 10 mm Hg below the peak value of the previous stage.

**Dipyridamole Test.** Dipyridamole was administered intravenously at a standard dose of 0.56 mg/kg body weight and over a 4-min period to the patients who could not achieve maximal predicted heart rate.

**Imaging Procedure.** 271 patients after myocardial infarction (MI) were examined with the Tl-201 stress-redistribution-reinjection study: A dose of 74 to 111 MBq (2 to 3 mCi) Tl-201 was injected in the patient 1 minute before the stress was stopped, and tomographic imaging was performed 5 minute (stress) and 4 hours (redistribution) later. Tl-201 (37 MBq; 1 mCi) was reinjected when an irreversible defect on stress-redistribution imaging was seen.

317 patients without prior MI underwent the 2-day protocol with Tc-99m MIBI or tetrofosmin: on Day 1, 740 MBq (20 mCi) Tc-99m MIBI or tetrofosmin dose was injected at peak exercise, with SPECT imaging performed 15 min after injection. On Day 2, the same dose of tracer was injected at rest with 1 hour before SPECT imaging was performed.

Images were acquired with an Elscint Helix scintillation camera equipped with a low-energy all-purpose parallel-hole collimator. Thirty projections were obtained over a 180° arc from 45° right anterior oblique to 45° left posterior oblique using a 64 x 64 matrix. Images were reconstructed with a filtered back-projection using a Butterworth filter (order, 5; cut-off frequency 0.35 cycle/pixel for Tl-201 and 0.4 cycle/pixel for Tc-99m-labelled tracers). Paired images of stress and rest short-axis and horizontal and vertical long-axis slices were generated for visual analysis.

Myocardial uptake was assessed by consensus of two expert observers who were unaware of coronary angiography results. SPECT patterns were divided into normal scan fixed defects and reversible or combined i.e. fixed plus reversible defects.

**Coronary angiography.** Quantitative analysis was used to determine the severity of coronary stenosis. Angiographically significant CAD was defined as 50% or more luminal diameter stenosis of epicardial coronary arteries or their major branch. Fifty percent or more luminal diameter stenosis in the grafts, in the bypassed vessel distal to the graft insertion or in an unbypassed artery was considered significant when patients had had prior coronary artery bypass surgery.

**Statistical analysis.** Sensitivity, specificity and accuracy were calculated globally and by gender. Chi-square testing was used to compare the results between these groups. A p value < 0.05 was considered to be indicative of a significant difference.

## Results

444 patients were proved to have a significant stenosis of the arterial lumen (above 50%), of them 116 patients had one-vessel disease, 122 two-vessel disease and 206 three-vessel disease. 144 persons exhibited the normal finding or nonsignificant stenosis on coronary angiography. Table 2 contains a correlation of stress tomographic myocardial perfusion and coronary angiography in men, women and in the total population.

Coronary angiography confirmed CAD in 444 patients and we have proved reversible ischaemia on SPECT in 414 of them (sensitivity 93% in the total population). The sensitivity of SPECT was slightly higher, but statistically not significant, in men than in women (94% versus 91%, p > 0.05). Normal perfusion or fixed defects only were in 125 from 144 patients with normal or not significant coronary angiography patterns (total specificity 87%). The specificity was higher in women than in men (93% versus 82%), but this difference was statistically not significant either (p > 0.05). The accuracy of SPECT was the same for both genders (92%) (Fig. 1).

## Discussion

Although the first results of the Framingham study suggested CAD to be a relatively benign disease, this idea has not been confirmed in the course of the following 30 years of the follow-up [19, 20]. CAD is the leading cause of mortality of women in all developed countries and only in the USA it brings about 250 thousand deaths of women yearly. One of the most important pieces

**Table 1. Clinical characteristics in men and women**

|  | Total population (n = 588) | Men (n = 455) | Women (n = 133) |
|---|---|---|---|
| Mean age | 56 | 55 | 58 |
| History of infarction | 273 (46%) | 233 (51%) | 40 (30%) |
| History of revascularisation | 59 (10%) | 51 (11%) | 8 (6%) |
| Prior angioplasty | 40 | 33 | 7 |
| Prior bypass grafts | 19 | 18 | 1 |

**Table 2. The correlation of myocardial perfusion SPECT imaging and coronary angiography (the coronary angiography was considered as a "gold standard")**

|  | TP | TN | FP | FN |
|---|---|---|---|---|
| Men | 354 | 63 | 14 | 24 |
| Women | 60 | 62 | 5 | 6 |
| Total | 414 | 125 | 19 | 30 |

TP — true positives, TN — true negatives, FP — false positives, FN — false negatives

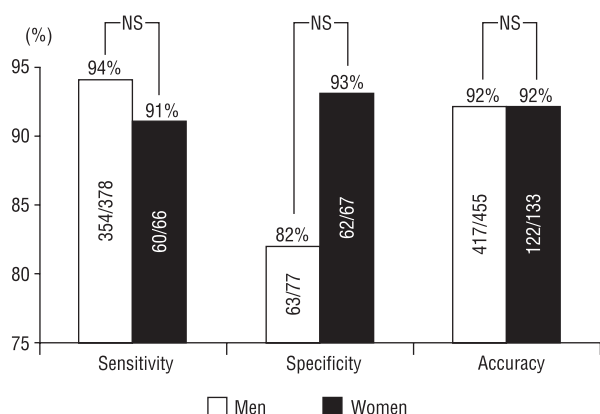Milan Kamínek et al., The accuracy of myocardial perfusion SPECT imaging...



**Figure 1.** The comparison of sensitivity, specificity and accuracy of myocardial perfusion SPECT imaging in men and women. Sensitivity = TP/(TP + FN), specificity = TN/(TN + FP), accuracy = (TP + TN)/total population.



**Figure 2.** Incidence of CAD in the population of patients verified by coronary angiography — the significantly higher incidence in men.

of knowledge is that CAD prevalence in women is, in contradiction to men, more dependent on age and that substantial acceleration of the disease occurs gradually after menopause.

Diagnostics of CAD in women is not easy. Due to its availability and low cost, stress electrocardiography remains the most frequent stress test. However, a series of papers proved the lower diagnostic accuracy of ST segments depression in women then in men (21, 22). Also, it was found that the patient's gender influenced significantly the physician's decision to indicate coronary angiography and that this examination is in women indicated less than needed. It results in a relatively lower frequency of revascularisation in women and later in their higher mortality. On the other hand, the invasive procedure was asked for a significant fraction of women who had the subsequent angiographic finding negative [22]. Thus, the necessity is obvious for a non-invasive test with high diagnostic accuracy as the "gatekeeper" of an invasive examination.

Diagnostic accuracy of myocardial perfusion SPECT for CAD detection was reported to be typically in the range of 91–96% [2–4, 10]. However, some authors pointed out that the diagnostic accuracy of this examination was lower [14, 15] but others did not prove a significant difference in the diagnostic accuracy of this examination between both genders. The differences were given rather by selection of patients in angiographically verified groups with a higher fraction of patients with CAD in men [13, 16–18]. Specifically, coronary angiography is indicated mainly in the patients with positive finding on stress test [21]. This selection is unambiguously evident in our group of patients, too. Of a total number of 588 persons examined, 444 patients had CAD (76%); in men the fraction of patients with CAD was significantly higher (83%) in comparison with the women's group (50%) (Fig. 2). As is possible to derive from the Bayes theorem, the sensitivity of examination is increased if the fraction of persons with CAD in the study population is higher [19, 20].

In interpreting a finding it is necessary to pay regard to the particular anatomic diversities of both genders and the patient's habits. Gamma-rays registered during scintigraphy are absorbed in the tissue situated between myocardium and body surface. In men there is a serious problem of the correct assessment of a finding on t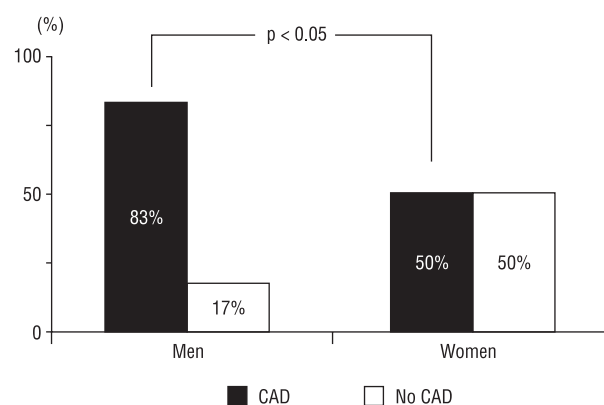he inferior wall where gamma rays are substantially attenuated due to diaphragmal and adipose tissue. On the contrary, in women gamma-rays are attenuated by breast tissue.

There is a series of ways how to improve the interpretation of findings on the myocardial SPECT. One of them is a comparison of own findings with a gender-stratified normal database. The choice of an optimal reference population has been disputed for years. Both subjects with a low likelihood for CAD and patients with normal findings on coronary angiography have been used as the reference population. However, both of these criteria of normality have been criticised, since patients referred to angiography had some reasons for the referral and might not be representative of the healthy reference population. On the other hand, the subjects with a low likelihood of CAD <5% according to Diamond and Forrester [19] may represent a too healthy part of the population. The commercially available databases should be used with caution. The false-positive defects were shown in a large age- and gender-stratified group of healthy subjects undergoing myocardial SPECT assessed by comparison with two databases [23]. The false-positive response rate was 12% when compared with CEqual database and 29% when compared with the Cedars-Sinai program. Defects occurred more often in women than in men but the difference did not attain statistical significance. The distribution of defects was independent of age. The results of the recent study suggest that normal angiography should be preferred as the reference standard in myocardial scintigraphy when a patient is examined for CAD prior to possible angiography [24].

Prone projection, attenuation correction or gated SPECT are other very useful methods for the identification of attenuation artefacts [25–28]. Gated myocardial perfusion SPECT imaging represents one of the most powerful weapons available to nuclear cardiology. By comparison, no other cardiac imaging modality is currently capable of routine clinical assessment of left ventricular perfusion and function [28, 29]. Industry data indicated that over 66% of all SPECT studies in the United States in 1999 were performed using the gated acquisition technique, up from only about 3% in 1993 [29]. In our department we have been using gated SPECT routinely since 1998. While it was initially held that gated SPECT acquisitions were only possible in conjunction with Tc-99m-tracers, recent published experience indicated that gated Tl-201 SPECT imaging is feasible [28, 29].

In women with a small cavity of the left chamber of the heart, the further possibility of the use of gated SPECT appears as promising — the evaluation of the perfusion directly in the end-diastole phase. End-diastolic frames could present a better image resolution by reducing the blurring effect of cardiac motion on the final perfusion study, especially in patients with small or hyperdynamic hearts. In a group of 53 women, Taillefer et al. [30] proved more ischaemic defects and better sensitivity in end-diastole perfusion images — 84% (32/38) - than in standard ungated images — 74% (28/38); however, the difference was not statistically significant with regard to the low number of examined patients.

## Conclusions

We proved myocardial SPECT to be a non-invasive examination with high sensitivity, specificity and diagnostic accuracy for the detection of ICHS in men and women; we did not find a statistically significant difference in the detection of ICHS in the two genders. Our results are in accordance with the prevailing opinion in literature. If differences in sensitivity, specificity and diagnostic accuracy are found, they are usually not statistically significant or they can be explained by the selection of patients in angiographically verified groups (considerably higher fraction of patients with CAD in men's group).

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