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GENDER DIFFERENCES IN DETECTING CORONARY ARTERY DISEASE WITH DIPYRIDAMOLE STRESS MYOCARDIAL PERFUSION IMAGING USING ^{99m}-Tc SESTAMIBI GATED SPECT

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A b s t r a c t. There are some specifics in the presentation of coronary artery disease (CAD) in women compared with men that may cause diagnostic pitfalls. The accuracy of noninvasive diagnostic testing in women tends to be lower than that in men. Stress myocardial perfusion imaging with ^{99m}-Tc sestamibi gated SPECT is an accurate technique for detecting CAD. Only a few studies have compared dipyridamole stress imaging according to gender.

The aim of the study was to compare the diagnostic value of dipyridamole myocardial perfusion imaging with ^{99m}-Tc sestamibi gated SPECT in detecting CAD among patients of both sexes.

We studied 62 consecutive patients (38 men, 24 women) using ^{99m}-Tc sestamibi gated SPECT and dipyridamole stress to detect CAD. All the patients also underwent coronary angiography. Overall regional sensitivity was significantly lower in women compared with men (71.4% vs. 92.7%, p = 0.039). There were no significant differences for detecting CAD in individual coronary arteries, although regional sensitivity in all three vascular territories was higher in men compared to women. The lowest sensitivity in women was found in the LAD territory (66.6%). Overall regional specificity in men and women was similar and did not reach statistical significance (88.7% vs. 94.7%). Significantly lower specificity in men was found only in the RCA territory (79.1%), compared with that in women (100%).

Our results confirmed that there are certain gender differences in the diagnostic performance of dipyridamole stress myocardial perfusion imaging with ^{99m}-Tc sestamibi gated SPECT which are assigned to the characteristics of the female population. However, the diagnostic accuracy is also quite high in women, which makes this technique efficient enough in detecting CAD among this population.

Key words: coronary disease, diagnostic imaging, sex characteristics.

Introduction

Coronary artery disease (CAD) continues to be a leading cause of death among women [1]. It is well known that there are age differences at the time of detection of the disease in women as opposed to men, also the clinical presentation is different. Women have a higher frequency of angina/chest pain than men; however, they have a lower prevalence of obstructive CAD compared with men with similar symptoms [2].

Women with acute coronary syndromes are less likely to receive an effective acute diagnostic approach and treatment than men [3]. They experience a significantly worse outcome compared with men with regard to prognosis after myocardial infarction or myocardial revascularization [4].

Bearing in mind all these facts and characteristics of CAD in women, it is clear that choosing an appropriate, accurate and noninvasive diagnostic test would be of great importance. The most widely used test today, the exercise treadmill test (ETT), has limited diagnostic accuracy in detecting CAD in women. According to the CASS Study data, its sensitivity was 76%, and specificity only 64% [5].

Stress myocardial perfusion imaging (MPI) with radionuclides is an accurate technique for detecting CAD. However, some authors have reported a lower efficacy of the testing in women, compared with men [6]. Others have obtained comparable results for both women and men [7]. Only a few studies have compared the results of pharmacological stress with dipyridamole in these two groups [8].

Therefore, the aim of our study was to compare the diagnostic power of myocardial perfusion imaging with ^{99m}-Tc sestamibi in identifying coronary artery stenosis in women, compared with men.

Methods

Study population

This prospective study involved 62 consecutive patients (38 men, 24 women) suspected of having CAD or with previously confirmed CAD, who were referred for dipyridamole stress myocardial perfusion imaging between

September 2000 and October 2002 at the Institute of Pathophysiology and Nuclear Medicine, Medical Faculty, Skopje.

Dipyridamole as a pharmacological stressor was used in all patients because they were unable to exercise for various reasons (e.g. poor condition, older age, comorbidity).

A detailed questionnaire which included clinical, historical and vasodilator stress data was filled in, with particular attention to the risk factors for CAD, previous myocardial infarction (MI) and results of other relevant examinations.

At the end of the study all the patients underwent coronary angiography within 3 months of myocardial perfusion imaging.

Dipyridamole myocardial perfusion protocol

A one day rest-stress protocol with ^{99m}-Tc sestamibi was performed in all patients. They were instructed not to consume caffeine-containing products for 24 hours before testing and nitrates and beta-blockers were discontinued 24 and 48 hours before testing, respectively. For the rest study 10–12mCi of the tracer was injected intra-venously, in fasting conditions. Imaging started at least 1 hour later.

For the stress study dipyridamole infusion in doses of 0.56mg/kg per body weight was given for 4 minutes. At peak vasodilator effect (3 minutes after the end of the infusion), 25mCi of the tracer was injected. Two to three minutes later patients were given aminophyllin as an antidote (125 to 250mg). Readings of blood pressure and 12-lead electrocardiograms were recorded at 2-minute intervals. Stress imaging started at least 1 hour after the application of the radiopharmaceutical.

Single photon emission computerised tomography (SPECT) acquisition protocol

Both studies, rest and stress, were acquired as tomographic ECG-synchronised – *gated SPECT* studies with a rotating single-detector gamma camera (SMV Vision DS–7). A low energy all-purpose (LEAP) collimator was used with a step-and-shoot approach for 32 projections over a 180° noncircular orbit around the patient′s body, beginning at 45° right anterior oblique projection and ending at 45° left posterior oblique. Each projection lasted 25 seconds and gating was done with 8 frames per cycle.

Image interpretation

Stress and rest images from the short-axis, horizontal long-axis and vertical long-axis slices were compared by four experienced readers. Perfusion defects were classified as fixed (defect in both studies), reversible (defect only on stress images) and reverse (defect only on rest images).

The left ventricle was divided into 17 segments (9). Each segment was scored using a 5-point scoring system as following: 0-normal (80–100% tracer uptake), 1-slightly reduced (65–80%), 2-moderate (50–65%), 3-severe (30–50%) and 4-absent (0–30%). A summed stress score (SSS) was obtained by means of adding the scores for the 17 segments of the stress images. A summed rest score (SRS) was similarly obtained by means of adding the scores for the 17 segments of the rest images. The sum of the difference between the stress and rest scores was defined as the summed difference score (SDS) or reversibility score, an index of jeopardized myocardium.

The ejection fraction of the left ventricle was measured in both stress and resting conditions with the MultiDim software package.

Correlation with coronary angiography

The severity of the stenosis was determined visually from the coronary angiographic films by an experienced observer, blind to nuclear data. A luminal narrowing of 70% or greater was considered significant. Abnormal vascular territories identified by perfusion defects (reversible or fixed) were correlated with stenosed coronary arteries.

Results

Patients characteristics

Characteristics of the 38 men and 24 women studied are shown in *Table 1*. The two groups did not differ significantly in age, presence of previous myocardial infarction, number of risk factors, presence of left bundle-branch block (LBBB) or in the sum difference score. The ejection fraction of the left ventricle in resting conditions measured by gated SPECT tended to be lower in men (47.3 % vs. 56.4%, $p = 0.053$).

Compared with women, men had significantly more frequent coronary artery disease detected by coronary angiography (68.4% vs. 37.5%), those who had the disease were significantly younger (53.8 for men vs. 61.7 years for women) and in men summed stress and rest scores were significantly higher (all $p < 0.05$). Compared with men, women had significantly more frequent atypical angina (67% vs. 37%, $p < 0.01$).

Diagnostic power of the myocardial perfusion imaging

The results of detecting coronary artery disease in men and women with dipyridamole stress myocardial perfusion imaging using ^{99m}-Tc sestamibi gated SPECT are shown in *Table 2* and *Figure 1*.

Table 1–Табела 1

Patients' characteristics
Карактеристики на пациентите

Variables	men (n=38)	women (n=24)	p value
Age (y)	52,76 ± 8,87	56,04 ± 8,43	0.15
Atypical angina	14/38 (37%)	16/24 (67%)	0.004*
Previous MI	14/38 (37%)	6/24 (25%)	0.33
Risk factors	2 ± 1,11	2,5 ± 1,14	0.09
LBBB	9/38 (23,6%)	6/24 (25%)	0.906
CAD	26/38 (68,4%)	9/24 (37,5%)	0.016*
Age (in CAD+)	53,8 ± 6,8	61,7 ± 9	0.03*
EF%	47,32 ± 14,97	56,4 ± 14,54	0.053
SSS	11,45 ± 11,35	5,04 ± 7,40	0.017*
SRS	7,6 ± 10,33	2,70 ± 5,89	0.039*
SDS	3,84 ± 5,57	2,33 ± 5,31	0.294

MI – myocardial infarction; LBBB – left bundle-branch block; CAD – coronary artery disease verified with coronary angiography; EF – resting ejection fraction of the left ventricle with gated SPECT; SSS – summed stress score; SRS – summed rest score; SDS – summed difference score

Table 2 – Табела 2

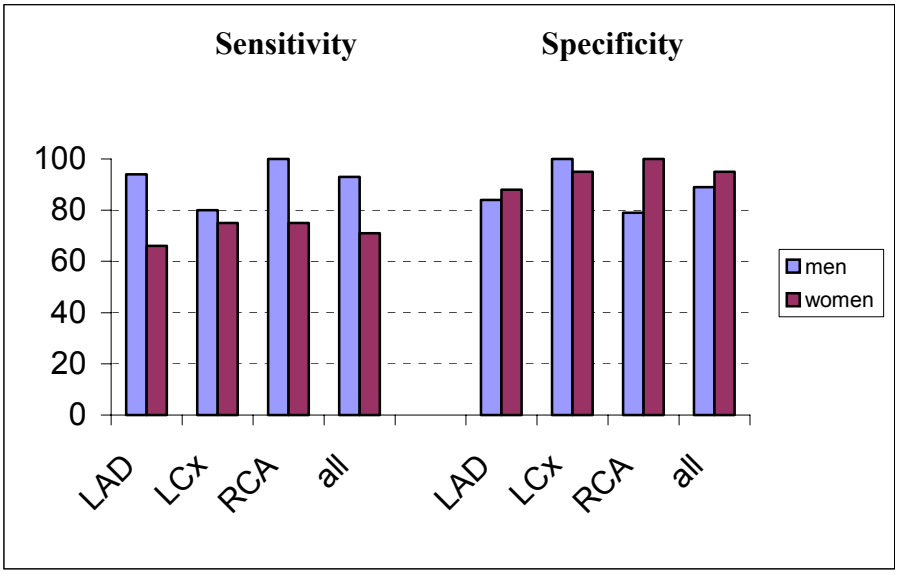
Regional diagnostic power of dipyridamole stress myocardial perfusion imaging (MPI) with ^{99m}-Tc sestamibi gated SPECT according to the gender

Регионална дијагностичка моќ на дипиридамолскаша стрес миокардна перфузија (МП) со ^{99m}-Tc sestamibi gated SPECT според половаша припадност

MPI	Gender							
	male				female			
	LAD	LCx	RCA	all	LAD	LCx	RCA	all
TP	16/17	8/10	14/14	38/41	4/6	3/4	3/4	10/14
TN	16/19	28/28	19/24	63/71	15/17	19/20	20/20	54/57
FP	3/19	0/28	5/24	8/71	2/17	1/20	0/20	3/57
FN	1/17	2/10	0/14	3/41	2/6	1/4	1/4	4/14
SN	94,1%	80%	100%	92,7%	66,6%	75%	75%	71,4%

SP	84,2%	100%	79,1%	88,7%	88,2%	94,7%	100%	94,7%
Accuracy	88,9%	94,7%	86,8%	90,1%	82,6%	91,6%	96%	90%
PPV	84,2%	100%	73,7%	82,6%	66,6%	75%	100%	77%
NPV	94,1%	93,3%	100%	95,4%	88,2%	95%	95,2%	93%

TP – true positive; TN – true negative; FP – false positive; FN – false negative; SN – sensitivity; SP – specificity; PPV – positive predictive value; NPV – negative predictive value; LAD – left anterior descending coronary artery; LCx – left circumflex; RCA – right coronary artery



Sensitivity	Specificity
LAD p = n.s. (0,08)	LAD p = n.s.
LCx p = n.s.	LCx p = n.s.
RCA p = n.s. (0,053)	RCA p = 0,03*
All p = 0,039*	All p = n.s.

Figure 1 – *Gender differences in detecting CAD with dipyridamole stress myocardial perfusion imaging using ^{99m}-Tc sestamibi gated SPECT in individual vascular territories*

Слика 1 – *Полови разлики во детектирањето на КАБ со дипиридамолската стрес миокардна перфузија користејќи ^{99m}-Tc sestamibi gated SPECT за поединечните васкуларни територии*

Overall regional sensitivity was significantly lower in women compared with men (71.4% vs. 92.7%, p = 0.039). There were no significant differences in detecting CAD in individual coronary arteries, although regional sensitivity in all three vascular territories was higher in men compared to women, especially in the LAD and the RCA territory (p = 0.08 and 0.053 respectively). However, the number of coronary arteries with stenosis in women was rather small (6 for LAD, and 4 for LCx and RCA). The lowest sensitivity in women was found in LAD territory (66.6%).

Overall regional specificity in men and women was similar and did not reach statistical significance (88.7% for men vs. 94.7% for women). The lowest specificity in men was found in the RCA territory (79.1%), and it was significantly lower than that in women (100%). There were no significant differences in specificity for the other two vascular territories (LAD and LCx). Women had the lowest specificity in the LAD territory (88.2%).

Discussion

Diagnostic evaluation of women with suspected CAD continues to be a major challenge because of many gender-specific issues. Some studies have suggested that CAD was subdiagnosed and subtreated in women and that women with angina and chest discomfort were less often referred to diagnostic tests and therapeutical interventions compared with men [10].

According to the data from the CASS Study women were 5–10 years older, on average, at the time when CAD was diagnosed [5]. In our study, although on a smaller number of patients, this observation was confirmed. The mean age of women with CAD was 61.7 years, and for men it was 53.8 years (p < 0.03). Women more often have atypical symptoms, a fact that many authors have pointed out [11]. We found atypical angina in 67% of women compared with 37% men. However, women have a lower prevalence of obstructive CAD compared with men with similar symptoms [2]. CAD was present in 26/38 men (68.4%) and in 9/24 women (37.5%) in our study, which was a significant difference (p = 0.016).

Several meta-analyses have shown that the accuracy of a certain diagnostic test in women is lower than that found in men [12]. However, the results from the few studies that have considered gender differences in the diagnostic accuracy of the stress myocardial perfusion imaging are conflicting [6,7].

When we compared overall regional sensitivity in the two groups, we found significantly lower values in women compared with men (71.4% vs. 92.7%). Generally, in all the three vascular territories (LAD, LCx and RCA), women had lower sensitivity, but not significantly. Taillefer [13] analysed in a

prospective study 115 women by using ^{99m}-Tc sestamibi gated SPECT, and found a sensitivity of 80.4% and a specificity of 92%. Santana-Boado [14] reported a lower sensitivity of ^{99m}Tc sestamibi SPECT in women compared with men (85% vs. 93%, p = 0.01), whereas there was no significant difference for specificity (91% vs. 89%). We also did not find any significant difference in overall regional specificity (94.7% vs. 88.7%), but in the RCA territory men had a significantly lower specificity (79.1% vs. 100%).

Several explanations for the results of our study could be proposed. Most of the differences appear to be due to the generally smaller heart size in women and therefore a relatively greater effect of imaging blurring, which makes the detection of the perfusion defects difficult [6].

Particular test artifacts should also be taken into consideration. Breast attenuation in women was suggested as one of the major limitations for correct interpretation of the perfusion images. This could cause false-positive results in the anterior wall, as well as false-negative results when a true perfusion defect is misjudged as an artifact [15]. The use of gated SPECT in our study enabled high specificity, but it is possible that some milder perfusion defects were incorrectly classified as breast attenuation, resulting in a lower specificity in the LAD territory in women.

The better specificity in women in the inferior wall (RCA territory) could be explained with the lower incidence of diaphragmatic attenuation in this group, a problem that is frequently encountered in men.

The study has certain limitations. The number of analysed coronary arteries with significant stenosis among women was rather small. This could have influenced the statistical data.

In conclusion, there are certain gender differences in the diagnostical performance of dipyridamole stress myocardial perfusion imaging with ^{99m}-Tc sestamibi gated SPECT, which are assigned to the specifities of the female population. However, the diagnostic accuracy is high enough in women, which makes the use of this technique efficient in detecting CAD among this population.

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Резиме

ПОЛОВИ РАЗЛИКИ ВО ОТКРИВАЊЕТО НА КОРОНАРНАТА АРТЕРИСКА БОЛЕСТ СО ДИПИРИДАМОЛСКАТА МИОКАРДНА ПЕРФУЗИЈА КОРИСТЕЈЌИ ^{99m}-Tc SESTAMIBI GATED SPECT

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Постојат специфики во клиничката слика на коронарната артериска болест (КАБ) кај жените споредено со мажите, кои се доволни да предизвикаат потешкотии во откривањето на болеста. Од друга страна, познато е дека неинвазивните дијагностички тестови кај жените имаат тенденција кон помала точност споредено со мажите. Стрес миокардната перфузија со ^{99m}-Tc sestamibi gated SPECT е ефикасна метода за откривање на КАБ. Само мал број на студии ги компарирале резултатите кај пациенти од двата пола кога како стресор е користен дипиридамол.

Цел на нашата студија беше да се спореди дијагностичката вредност на дипиридамолската стрес миокардна перфузиона томосцинтиграфија со ^{99m}-Tc sestamibi gated SPECT во откивањето на КАБ помеѓу пациентите од двата пола.

Беа иследени 62 последователни пациенти (38 мажи, 24 жени) користејќи ^{99m}-Tc sestamibi gated SPECT и дипиридамолски стрес за да се детектира КАБ. Сите пациенти на крајот од студијата имаа направено и коронарна ангиографија. Општата регионална сензитивност беше сигнификантно помала кај жените споредено со мажите (71,4% наспроти 92,7%, p = 0.039). Немаше сигнификантни разлики во детектирањето на КАБ на индивидуалните коронарни артерии, иако сензитивноста во сите три васкуларни територии беше повисока кај мажите. Најниска сензитивност од 66,6% кај жените се доби за васкуларната територија на левата антериорна десцендентна артерија (ЛАД). Општата регионална специфичност кај двата пола беше слична и статистички незначајна (88,7% наспроти 94,7%). Единствено сигнификантно помала специфичност кај мажите беше најдена за васкуларната територија на десната коронарна артерија (79,1%), споредено со таа кај жените (100%).

Нашите резултати потврдија дека постојат одредени полово условени разлики во дијагностичките можности на дипиридамолската стрес миокардна перфузија со ^{99m}-Tc sestamibi gated SPECT, кои може да се препишат на карактеристиките на женската популација. Сепак дијагностичката точност и кај жените е висока, што ја прави примената на оваа техника доволна ефикасна во откривањето на КАБ кај оваа популација.

Клучни зборови: коронарна болест, дијагностички визуелизациони техники, полови карактеристики.