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Short communication

# Myocardial perfusion in women with systemic lupus erythomatosus and no symptoms of coronary artery disease

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## Abstract

BACKGROUND: The aim of the study was to assess myocardial perfusion in women with systemic lupus erythomatosus (SLE) and no symptoms of coronary artery disease (CAD).
MATERIAL AND METHODS: Twenty two women with SLE of mean age 40.5 ± 7.2 were enrolled in the study. The average duration time of the disease was from 2 to 19 years, mean 8 ± ± 4.6 years. The inclusion criterion was the absence of stenocardial symptoms. The myocardial perfusion was studied by using Single Photon Emission Computerized Tomography (SPECT) utilising $^{99m}$Tc-MIBI ands a triple-head gamma-camera. We also analyzed risk factors of heart ischemic disease in our group.
RESULTS: Myocardial perfusion stress scanning showed abnormal perfusion in 12 patients, 54.5% of the whole group, mostly in the anterior wall. At rest hypoperfusion abnormalities were found in 7 individuals. In patients with positive myocardial perfusion, out scanning, risk factors of CAD were more pronounced than in a sub-group with a negative result of myocardial perfusion scanning.
CONCLUSIONS: In young women with SLE and no symptoms of coronary artery disease, myocardial pefusion defects may be detected by means of myocardial perfusion scintigraphy. Exercise and resting electrocardiography tests could be not sufficient for CAD diagnosis in women with SLE. The presence of coronary artery disease risk factors in women with SLE could be an indication to perform myocardial perfusion SPECT scanning.

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## Introduction

The prevalence of systemic lupus erythematosus (SLE) is considered to be 1 in 500 to 1000 women. Clinical symptoms may involve many organs. Along with the introduction of new treatment methods, the clinical image and causes of mortality have changed. Until now renal failure and infections were the most common causes of death in SLE. A rapid decrease in mortality in SLE was caused by intensive immunosupressive therapy and a wide use of antibiotics [1]. At the same time an increase of cardiovascular complications was observed [2]. Ischaemic heart disease has been described in young women with SLE from the early 70s. In 1976 Urowitz stated that cardiac deaths occur in the early acute phase of the disease or after many years duration [3]. Cardiovascular mortality is considered to be 9–45% of all deaths in patients with SLE [2]. This affects mostly young women. It is suspected that the rate of CAD is much higher, as most of patients have no symptoms of disease. This theory was confirmed by post mortem studies [4]. The aim of this study was to assess the prevalence of asymptomatic cardiac ischemic disease and risk factors of CAD in women with SLE utilizing myocardial perfusion $^{99m}$Tc-MIBI SPECT.

## Material and methods

Twenty two women with SLE of mean age 40.5 ± 7.2 mean were enrolled in the study. Systemic lupus erythomatosus was diagnosed based on the criteria of American Rheumatic Association (ARA). The average duration time of the disease was from 2 to 19 years, mean 8 ± 4.6 years. The inclusion criterion was the absence of stenocardial symptoms. The severity of SLE was calculated based on SLEDAI scale. All enrolled women had low SLE

activity with a mean SLEDAI score 4.2 ± 3.1. Of other clinical symptoms, skin changes were seen in 13 patients, arthritis in 7, thrombocytopenia in 5, myositis, phlebitis and haemolytic anaemia in 2.

All women were on steroid therapy in support doses varying from 10 to 20 mg/48 h; some of them were also on chlorochinine or azathioprine treatment. All patients had resting electrocardiography (ECG), echocardiography and exercise electrocardiography prior to our study. Romhilt-Estes and Sokolow-Lyon indexes were used to assess heart muscle hypertrophy. Myocardial perfusion scanning was performed in the Department of Nuclear Medicine of the Medical University of Gdańsk in two days protocol after i.v. administration $^{99m}$Tc-MIBI (FAM, Łódź, Poland), of activity 20 mCi (740 MBq). An exercise test was performed 30 minutes after the administration of the radiotracer, using the modified treadmill Bruce protocol. The rest test was performed 60 minutes after the administration of the radiotracer. SPECT scanning was performed using a three-head gammacamera Multispect-3 (Siemens, Erlangen, Germany). The data were collected into a 64 × 64 matrix.

Plasma levels of cholesterol and its fractions, plasma glucose, homocysteine, antiphospholipid antibodies and/or lupus anticoagulant (LAC) were assessed. We also checked the blood pressure values in each patient. Each woman was asked about tobacco smoking habits and menopausal age.

The study protocol has been approved by the local Ethics Committee. Written informed consent was obtained from all subjects.

## Results

No ischemic or heart muscle hypertrophy changes were found in the rest electrocardiography examination. The ECG exercise test was positive only in one case. In echocardiographic study the segmental hypokinetics of the heart muscle was observed in 5 patients.

### *Myocardial SPECT*

SPECT stress scanning showed abnormal myocardial in 12 patients, 54.5% of the whole group. At rest hypoperfusion abnormalities were found in 7 patients. Localization of heart perfusion abnormalities is shown in Table 1.

**Table 1. Localization of heart perfusion abnormalities SPECT in 12 women with systemic lupus erythomatosus and positive myocardial perfusion SPECT scanning**

| Pt. no. | Inferior wall | Anterior wall | Septum |
|---|---|---|---|
| 1. | + | + | |
| 2. | | + | + |
| 3. | | | + |
| 4. | + | + | |
| 5. | | + | |
| 6. | | + | |
| 7. | | + | |
| 8. | + | + | |
| 9. | | | + |
| 10 | | + | |
| 11. | | + | |
| 12. | + | + | |

### *Risk factors*

Two women were moderately hypertensive, both with SPECT changes. The cholesterol level was moderately higher in patients with a positive SPECT examination compared to those, without any abnormalities in coronary flow, but no relevant statistical difference was found. The plasma levels of LDL and triglycerides level was higher in subjects with abnormal myocardial perfusion. The plasma homocysteine level was higher only in women with positive antiphospholipid antibodies. The risk factors in women with and without myocardial SPECT changes are shown in Tables 2 and 3.

Six women were cigarette smokers; 4 of them had perfusion abnormalities in myocardial SPECT scanning. Nine women (age 36–49 years) were climacteric; 7 of them had changes in SPECT scanning. Elevated titres of antiphospholipid antibodies and/or lupus anti-coagulant (LAC) were found in 7 cases; in 6 of them heart perfusion changes were observed. Those risk factors are shown in Table 3.

## Discussion

Our study showed abnormal myocardial flow in 12 individuals, more than half of the whole group. At rest, fixed myocardial perfusion abnormalities were found in 7 individuals. In all these cases no clinical symptoms and signs of coronary artery disease were present. Similar studies were by Bruce et al [5, 6]. In this group 38% of the 129 asymptomatic patients had myocardial perfusion SPECT abnormalities. 90% of patients had reversible and 20% irreversible changes [6].

Assessing myocardial blood flow is useful in detecting heart ischemia, depicting the extent of disease, prognosing and

**Table 2. Comparison of laboratory findings in patients with and without myocardial perfusion SPECT changes**

| | Group with SPECT changes n = 12 | Group without SPECT changes n = 10 |
|---|---|---|
| Cholesterol [mg/dl] | 244.0 ± 56.09 | 207.0 ± 33.24 |
| LDL [mg/dl] | 155.0 ± 51.79 | 123.1 ± 25.44 |
| HDL [mg/dl] | 58.5 ± 11.8 | 63.0 ± 3.3 |
| Triglycerides [mg/dl] | 123.5 ± 47.4 | 93.5 ± 46.11 |
| Homocysteine [μmol/l] | 13.7 ± 4.4 | 13.5 ± 3.5 |

LDL — low density lipoprotein; HDL — high density lipoprotein

**Table 3. Risk factors in women with SLE**

| | Group with SPECT changes n = 12 | Group without SPECT changes n = 10 |
|---|---|---|
| Smoking (%) | 4 (30%) | 2 (20%) |
| Climacterium | 7 (58%) | 2 (20%) |
| Antyphospholipid antibodies | 5 (42%) | 1 (10%) |
| LAC | 1 (8%) | 0 |

LAC — lupus anticoagulant

assessing the treatment efficiency in CAD. The assessment of myocardial perfusion in women with SLE is far more complicated than in other patients. Women more frequently complain of atypical rest pain provoked by stress. Typical symptoms of coronary artery disease in common are: fatigue, general weakness, malaise and chest pain [7]. In women with SLE non-ischemic chest pain is also common, which makes the diagnostic even more complicated. The causes of non-ischemic chest pain may be caused by joint and/or muscular pain, pleural involvement and pain linked with the thoracic vertebral column. Using commonly available diagnostic tests, such as: electrocardiography and echocardiography, asymptomatic CAD can be detected in about 16% SLE patients [5, 6]. The diagnostic value of resting electrocardiography and echocardiography in detecting coronary artery disease without heart infarction is limited even in patients with arteriosclerotic changes in coronary arteries [7]. In our study all patients with changes of myocardial perfusion detected by SPECT had normal resting electrocardiography. The value of exercise ECG testing especially in young women is controversial as well. This is due to the high prevalence of false positive results. In our study ECG exercise test had no diagnostic value (apart from one case). Performing dobutamine echocardiography instead of ECG test may help to exclude false positive results, especially in women [8].

Another problem of CAD in SLE is its pathology. Although in autopsy, computed tomography and magnetic resonance imaging arteriosclerotic plaques dominate as the most frequent finding, others mechanisms causing changes in coronary arteries cannot be excluded [4, 9]. This could be vasculopathy due to antiphospholipid syndrome and the formation of small blood clots in arteries. This may stimulate arteriosclerotic changes and may have an important impact on choosing the treatment methods.

In our study only women with asymptomatic coronary disease were enrolled. The aim of early treatment of CAD is the modification arteriosclerosis risk factors, which are different in different age groups and between sexes. Risk factors like hypertension, diabetes mellitus and obesity are far more common in women with SLE, even in the pre-menopausal period; the use of corticosteroids and limited physical activity are additional risk factors. There are many indicative parameters linked with premature arteriosclerosis in women with SLE such as increased levels of homocysteine, heat shock proteins (HSP), $\beta_2$-glicoprotein I, antiphospholipid antibodies and oxLDL antibodies [10, 11]. Lupus erythomatosus itself as the inflammatory disease is regarded to be an independent risk factor of arteriosclerosis. In the active inflammatory phase of the disease the arterial intima is affected and that is the triggering point of the immunological reaction which initiates plaque formation arthrosclerosis.

In our study we found that a sub-group with changes in myocardial perfusion had increased risk factors for CAD [7]. Most CAD-asymptomatic women with myocardial perfusion SPECT changes were climacteric, cigarette smokers and had positive antiphospholipid antibodies or a high cholesterol level. These findings should be confirmed in larger population studies. In young women with SLE different risk factors of arteriosclerosis should be taken into consideration, before treatment is started. In patients with impaired myocardial flow arteriosclerosis prophylaxis should be initiated as soon as possible.

Therefore, it seems that non-invasive diagnostic procedures should be performed selectively in all SLE patients with risk factors. A separate issue, which is worth further study, is the role of myocardial SPECT scanning in the risk stratification of patients with SLE.

## Conclusions

In young women with SLE and no symptoms of coronary artery disease myocardial pefusion defects may be detected by means of myocardial perfusion scintigraphy. Exercise and resting electrocardiography tests may not be sufficient for CAD diagnosis in women with SLE. The presence of coronary artery disease risk factors in women with SLE could be an indication to perform myocardial perfusion SPECT scanning.

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