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Original

Left ventricular wall function abnormalities in patients with ankylosing spondylitis evaluated by gated myocardial perfusion scintigraphy

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ABSTRACT

Background: Ankylosing spondilitis (AS) is a chronic inflammatory disease with prominent inflammation in joints and extraarticular organs. AS patients have approximately two times more risk of mortality than the normal population. One reason for this increase in mortality is increased cardiovascular risk. In this study, we have aimed to evaluate myocardial perfusion and left ventricular function using ^{99m}Tc-MIBI gated myocardial perfusion single photon emission computed tomography (SPECT).
Material and methods: The study group consisted of 28 AS patients (19 men, 9 women), and mean age 39.46 ± 10.98 years. All patients underwent ^{99m}Tc-MIBI gated myocardial perfusion SPECT with the same day protocol.
Results: We detected various risk factors including smoking habits in 12, family history of cardiovascular disease in 12, hypertension in 3, hyperlipidemia in 9 patients. We performed a myocardial perfusion SPECT for each patient and found normal perfusion pattern in SPECT images. Out of 28 patients, eight patients had normal perfusion but wall motion abnormalities.
Conclusion: We detected that myocardial perfusion is preserved in the patients with AS. However, left ventricular wall motion abnormalities are seen. We concluded that ankylosing spondylitis may be associated with microvascular dysfunction and gated myocardial perfusion scintigraphy could be valuable in AS patients for the evaluation of LV function even if the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score are low and the disease duration shorter.

Anomalías en la función de la pared izquierda ventricular en pacientes con espondilitis anquilosante evaluados por gammagrafía de perfusión miocárdica sincronizada

Palabras clave:
^{99m}Tc-MIBI
Gated-SPECT de perfusión miocárdica
La arteria coronaria
Movimiento de la pared
Espondilitis anquilosante

RESUMEN

Objetivo: La espondilitis anquilosante (AS) es una enfermedad inflamatoria crónica con inflamación importante en las articulaciones y los órganos extraarticulares. Los pacientes con AS tienen aproximadamente dos veces más riesgo de mortalidad que la población normal. Una de las razones de este aumento en mortalidad, es el aumento del riesgo cardiovascular. Este estudio se planificó para evaluar la perfusión miocárdica y función ventricular izquierda con ^{99m}Tc-MIBI perfusión miocárdica sincronizada computarizada por emisión de foton único (SPECT).
Material y métodos: El grupo de estudio consistió en 28 pacientes con AS (19 hombres y 9 mujeres), y la edad media de 39,46 ± 10,98 años. Todos los pacientes fueron sometidos a ^{99m}Tc-MIBI SPECT de perfusión miocárdica sincronizada con el protocolo del mismo día.
Resultados: Hemos detectado varios factores de riesgo como el hábito de fumar en 12, antecedentes familiares de enfermedad cardiovascular en 12, la hipertensión arterial en 3, la hiperlipidemia en 9 pacientes. Hemos llevado a cabo la perfusión miocárdica SPECT para cada paciente, el patrón de perfusión normal siendo en las imágenes SPECT. De los 28 pacientes, ocho pacientes tuvieron una perfusión normal, pero anomalías en el movimiento de la pared.
Conclusión: Hemos detectado que la perfusión miocárdica se preserva en los pacientes con AS. Sin embargo, se observa anormalias en el movimiento de la pared venticular izquierda. Llegamos a la conclusión que la espondilitis anquilosante pueda ser asociados con la disfunción microvascular y la gammagrafía de perfusión miocárdica sincronizada podría ser útil en pacientes con EA para la evaluación de la función del ventrículo izquierdo, aún si existe una baja puntuación en el índice de actividad de la enfermedad espondilitis anquilosante (BASDAI) y menor duración de la enfermedad.

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Introduction

Ankylosing spondilitis (AS) is a chronic inflamatory disease with prominent inflamation in spinal joints and surronding structures, affecting sacroiliac and spinal joints, causing progressive and asending bone fusion on vertebrae. This chronical inflamatory disease is seen in 1% of the population.[1] AS can affect extraarticular organs like heart and eyes.[2] AS patients have approximately two times more mortality risk than normal population. One reason of this increase in mortality is increased cardiovascular risk. Basicaly the studies are on four types of cardiovascular involvement; aortic root and valve disorders, myocardial or pericardial disorders and coronary arteries abnormalities.[3] There are many papers supporting increased risk of atherosclerosis in some inflammatory rheumatic diseases such as systemic lupus erythematosus and rheumatoid arthritis.[4,5] However, there is no enough data supporting for the relation between AS and atherosclerosis.[6]

AS has an increased mortality and morbility risk as high as psoriatic arthritis. Smoking, changeable lipid profile, hypertension, increased fibronogen and platelets, hypercoagulapathy are the major cardiovascular risk factors.[7] Male patients with AS has increased coronary heart disease risk. Systemic inflammatory mediators increase the coronary heart disease incidence by triggering atherogenesis.[6] As known, inflammation is important in pathogenesis of atherosclerosis and vascular diseases. In AS disease inflammatory mediators like C- Reaktif protein (CRP) and tumor necrosis factor (TNF)-alfa are seen in high amounts. CRP, one of the inflammatory mediators, is related to increased cardiovascular risks.

Especially, high sensitivity C- Reactive protein (Hs-CRP) is used as biomarker in cardiovascular risk assesment.[8] Inflamatory diseases causing microvascular dysfunction like AS probably provoke atherosclerosis by inducing endothelial dysfunction and in long-term may increase cardiovascular risk.[9] Aneurismatic aortic dilatation seen in AS is thought to be related to coronary artery disease (CAD). Decreased aortic elasticity induces declines in endothelial function and aortic complications.[10] In AS patients consistent to Hs-CRP and TNF-alfa, decrease in coronary flow reserve and left ventricular (LV) dysfunction is seen. Therefore, in this group of patients, in terms of occurence of cardiac complications, identification of decrease in coronary flow reserve is important.[11] In this study, we planned to evaluate myocardial perfusion and LV function using ^{99m}Tc-MIBI (methoxyisobutylisonitrile) gated myocardial perfusion single photon emission computed tomography (SPECT) in patients with AS.

Material and methods

Study subjects

The study group consisted of 28 AS patients (19 men, 9 women), aged 22- 62 years, and mean age 39.46 ± 10.98 years. The patients were selected among adult (>18 years) AS patients. Individuals with a past or present history (angina pectoris, myocardial infarction, by-pass surgery, peripheral artery disease and stroke) and/or symptoms of cardiovascular diseases were excluded. According to inclusion criteria above, we included the AS patients consecutively into the current study. All patients agreed to participate in this study and signed the written informed consent document after we gave the necessary information about the study. The study protocol was approved by the ethics committee of our institution.

After inclusion of the patients consecutively into the study according to criteria, we completed their detailed physical examination. The disease severity was quantified using the Bath Ankylosing Spondilitis Disease Activity Index (BASDAI). We measured blood pressure, body mass index (BMI) and determined all risk factors for cardiovascular diseases including smoking habits, family history of cardiovascular disease, hypertension, plasma level of glucose, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and Hs-CRP. Patients those had LDL cholesterol or total cholesterol levels higher than 160 mg/dl or 200 mg/dl, respectively, were considered as dislipidemic. Body mass index (BMI) was calculated as the ratio of weight (kg) to height (m) squared (kg/m^2). Hs-CRP values were classified according to Ridker classification.[12] After completion of the initial physical and laboratory evaluation of the study population, gated ^{99m}Tc-MIBI myocardial perfusion SPECT was performed at rest and peak exercise stress.

Gated ^{99m}Tc-MIBI myocardial perfusion SPECT

All patients underwent ^{99m}Tc-MIBI gated myocardial perfusion SPECT with the same day protocol. As stress modality, treadmill exercise test with Bruce protocol was used. Exercises study were achievement of at least 85% age-predicted heart rate, severe chest pain, significant ECG changes (ST depression ≥2 mm), development of significant arrhythmia, or blood pressure changes (hypertension, diastolic blood pressure ≥120 mmHg or systolic blood pressure ≥240 mmHg; hypotension, decrease in systolic blood pressure ≥30 mmHg compared to basal value). At peak exercise, 925-1295 MBq (25-35 mCi) Tc-^{99m}-MIBI was injected and patients were asked to continue exercise for a period of up to 1.5 min. Myocardial perfusion SPECT imaging was begun 45 min after the injection of 370 to 555 MBq (10-15 mCi) Tc-^{99m}-MIBI at rest and 1 h after the injection of 925-1295 MBq (25-35 mCi) Tc-^{99m}-MIBI at stress. There was at least a 4-hour interval between the rest and stress imagings.

Gated SPECT studies were acquired with a dual-head gamma camera (Siemens, Symbia S, Germany) equipped with a low energy all purpose collimator and the energy was centered on 140 keV with a 20% window. Images were acquired using a step and-shoot circular orbit starting from the 45° right anterior oblique to the 135° left posterior oblique projection. Thirty-two projections were obtained using a 64 × 64 matrix for 25 sec per frame. Tomographic images were reconstructed using a ramp filter with a Butterworth filter (order, 8; cutoff frequency, 0.34 cycle/ cm for gated study and 0.47 cycle/cm for nongated study).

All gated myocardial perfusion SPECT images were assessed by two blinded experienced observers.

The software programs used for quantitative analysis were quantitative perfusion single photon emission computed tomography (QPS), and quantitative gated single photon emission computed tomography (QGS) (Cedars-Sinai Medical Centre, Los Angeles, California USA). Wall motion is obtained by measuring the excursion of the endocardium from end-diastole to end-systole. The scores were obtained as a sum of all left ventricle (LV) regions in a 20-segment model, on a 5-point scale for each segment and sum thickening scores (STS) and sum motion scores (SMS) were used.[13]

Statistical analysis

Continuous data are expressed as the mean ± standard deviation (SD), and categorical variables are expressed as percentages.

A stepwise model of multiple linear regression analysis was used to assess independent associations between the wall motion abnormality and other clinical and laboratory parameters. Two-sided P -values of less than 0.05 were considered statistically significant. The statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS) version 15 (SPSS, Chicago, IL).

Table 1
Demographic, clinical and laboratory features of the patients.

	Patients ($n = 28$)
Age (year)	39.46 ± 10.98
Male/female (number)	19/9
Disease duration (year)	7.96 ± 6.14
BASDAI	2.80 ± 41.48
BMI (kg/m^2)	25.62 ± 3.43
Smoking (number)	12
Hs-CRP	0.825 ml/dl
Total cholesterol (mg/dl)	190.3 ± 46.7
LDL cholesterol (mg/dl)	133.8 ± 43.4
HDL cholesterol (mg/dl)	31.5 ± 5.9
Triglyceride (mg/dl)	112.3 ± 58.0
Medical treatment (number)	
None	1
Sulfasalazine	20
Anti TNF-alpha	7

Data are mean ± SD.

Results

A total of 34 consecutive patients with AS were admitted. 6 patients were excluded from the study, including 3 with a past cardiovascular event, 3 who have diabetes mellitus. The remaining 28 patients with AS were evaluated in this study. The main demographic, clinical, and laboratory features of the patients are shown in Table. The mean Hs-CRP level of the study patients was 0.82 ± 0.81 mg/dL. According to the risk estimate of Ridker for cardiovascular disease, 21 of our patients are classified in "highest" risk group, 3 in "high", 2 in "moderate" and remaining 2 in "low" risk group.[12] Mean disease duration in the patients was 7.96 ± 6.14 years. Twenty patients were on sulfasalazine, 7 patients were on anti-TNF- alpha treatment and 1 of the patients was not taken any treatment. According to blood pressure recordings which were performed after 10 minutes resting period for each patient, hypertension was detected in 3 patients. BMI was also calculated in all patients. 8 of our patients had overweight and 4 patients were detected to have obesity in the current study. Nine patients were found to be dislipidemic.

There was neither previously documented cardiac disease including CAD nor related medications in all patients.

Gated ^{99m}Tc-MIBI myocardial perfusion SPECT findings

Gated myocardial perfusion SPECT was completed for each patient. All patients tolerated the

diagnostic test without any complication including symptomatic hypotension or significant ventricular arrhythmia during the exercise stress test. All patients reached the heart rate of more than 85% of target at peak stress. There was no any ST segment shift during the test in all patients. In the myocardial perfusion SPECT, normal coronary perfusion pattern (fig. 1A) was detected in all patients. Out of 28 patients eight patients had normal perfusion but wall motion abnormalities. In 3 patients wall motion abnormalities was localised on lateral wall, in 3 on septum, in one on anterior and lateral walls and in one on inferior and septal walls. The results were calculated for SMS and STS as 11 ± 3, 8 ± 2, respectively (mean ± SD) (fig. 1B). The calculated mean ± SD values of gated myocardial perfusion SPECT EF (%) was 68 ± 11 at stress.

Multiple linear regression analysis showed an independent association between Hs-CRP and cardiac wall motion ($p = 0.016$).

Discussion

AS is the most common form of the spondyloarthropaties. It affects between 0.2% and 0.9% of the population.[1] Male are more influenced by this chronic rheumatological disease. AS involves mostly sacroiliac and spinal joints. Apart from skeleton involvement, AS also affects extraskeletal organs. The most common extraskeletal involvement is uveitis, however the most frequent cause of death in this group of patients is related to cardiac involvement.[2–14,15] In the literature, 20-40% mortality rate related to cardiovascular disease is reported among AS patients.[3,16] In this study, we evaluated the myocardial perfusion and LV function with gated myocardial perfusion scintigraphy. We detected that coronary perfusion is preserved in these patients, but abnormalities in LV function is observed in eigth patients.

In some studies with small number of patients, it is reported that there is approximately 20% increased hypertension risk.[17] On the other hand due to small number of patients in these studies, it is difficult to say that there is a relation between hypertension and AS. In our study similar to previous studies, there were 3 patients with hypertension. In the literature, there many papers related to cardiovascular disease in AS. Some of these studies are showing the LV diastolic dysfunction. Brewerton's study is the first study which indicated diastolic dysfunction in AS patients. In this study, with 74 AS patients, they found no differences in systolic echocardiogaphic parameters however elongation in early diastolic decelation times and myocardial relaxation times.[18] In the following studies the diastolic dysfunction is seen around 26% of AS patients.[19] Although most studies indicate diastolic dysfunction, there are also publications reporting 5-42% pericardial effusion in AS patients. Shah et al. studied 24 patients without clinical sign of pericarditis. They concluded that although these patients have no left ventricular dysfunction, they have pericardial effusion.[20] There is no precise data supporting increase CAD in AS. Due to the pathogenesis of AS and one and a half times more mortality than normal population in these patients, there is high probability that AS has a relation with atherosclerosis.[16] Although, it is known that coronary flow reserve is decreased in AS, increased incidence of CAD in AS is not proven.[17] In recent publications, endothelial dysfunction, subclinic atherosclerosis, diastolic dysfunction abnormalities in AS have gained more importance. One of the finding related to cardiac involvement of AS is LV function. In a study performed by Ribero and et al, twenty-eight AS and fourteen Reiter patients were evaluated with echocardiography and in 18% of AS patients decrease in LV contraction function is seen.[21] There is kindly development in myocardial scintigraphy in recent years. The development especially in gating myocardial perfusion scintigraphy gives information about perfusion as well as objective data on the function of the myocardium in the same study.[22,23] With this imaging technique we can evaluate global and regional LV functions in addition to perfusion.[24,25] In the comparison of echocardiography and gated SPECT good correlation results were obtained for LVEF, volumes, and regional wall motion.[26,27] In our study, we performed gated SPECT in 28 AS patients and evaluated the LV function with QGS software program. In this study, we detected preserved coronary perfusion pattern in all patients and decided that there is no coronary flow limiting stenosis in our study group. Nevertheless, existence of mild wall motion abnormalities in some patients could be related to microvascular dysfunction abnormality. Inflamatory process in chronic inflamatory diseases may results in microvascular dysfunction in correlation to Hs-CRP. We did not recognize wall motion abnormalities in resting echocardiography, however this finding is more apparently detected under stress since myocardial motion is possibly affected by stress-induced microvascular perfusion abnormalities.[28–30]

The BASDAI score and CRP are the parameter showing disease severity in AS disease. When the demographic and clinical data of the patients with LV abnormalities were analysed, we observe that there were no relation between the BASDAI score, CRP level, disease duration of these patients and LV motion abnormalities.

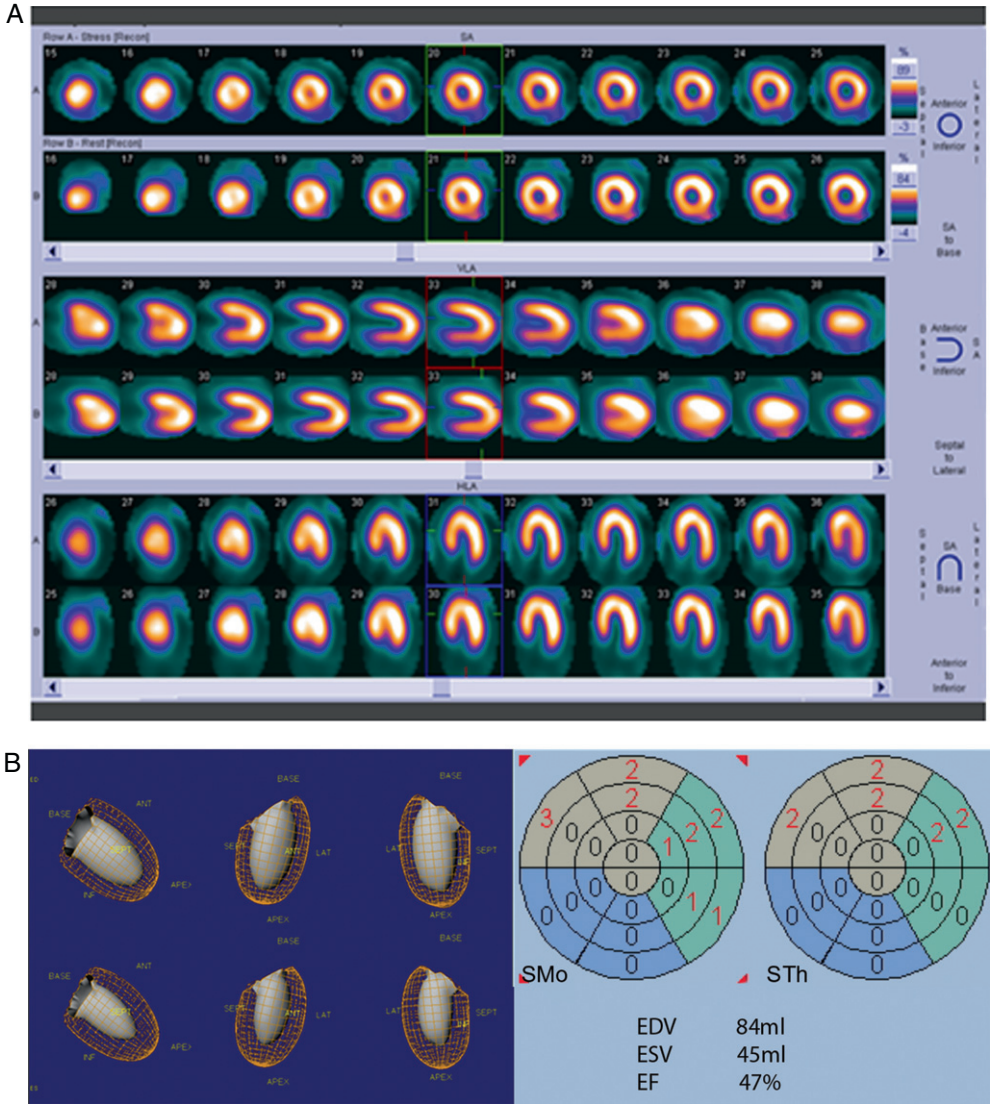

Figure 1. A) Myocardial perfusion SPECT image shows a normal perfusion pattern in a patient with ankylosing spondilitis. B) The semiquantitative analysis of the same patient's gated SPECT study reveals wall motion (SMo) and thickening (STh) abnormalities with scores calculated as 14 and 10, respectively. The calculatated ejection fraction values was 47%.

However there were a correlation between Hs-CRP values and wall motion abnormalities. The relationship between wall motion abnormality and inflammatory process that has been shown by increased inflammatory marker Hs-CRP was meaningful, because the myocardial perfusion was in normal limits in our study, we concluded that AS is possibly associated with microvascular dysfunction and gated myocardial perfusion scintigraphy could be valuable in AS patients for the evaluation of LV function even they have low BASDAI score and shorter disease duration.

Conflict of interest

Authors state that they don't have any conflict of interest.

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