ORIGINAL ARTICLE

Cardiometabolic Risk Factors in Patients With Ankylosing Spondylitis

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ABSTRACT

Objectives: This study aims to evaluate cardiometabolic risk factors in ankylosing spondylitis (AS) patients and their relationship with epicardial fat thickness (EFT).

Patients and methods: The study included 50 consecutive AS patients (29 males, 21 females; mean age 40.5±9.4 years; range 25 to 60 years) with a median disease duration of 8.3 years and 50 healthy controls (33 males, 17 females; mean age 39.8±6.4 years, range 24 to 58 years). All patients' EFT was measured with echocardiography.

Results: Both body mass index and waist circumference measurements were higher in AS patients than healthy controls (25.4±3.5. vs. 24.5±2.9 kg/m^2, p=0.005; 96.2±10.8 vs. 86.7±12.6 cm, p<0.001; respectively). Triglyceride levels were higher in AS patients than healthy controls (123.0±47.7 vs. 110.1±61.0 mg/dL, p=0.009; respectively). High-density lipoprotein cholesterol levels were lower in AS patients than healthy controls (41.3±7.0 vs. 51.9±7.0 mg/dL, p<0.001; respectively). The EFT of AS patients was greater (0.53±0.14 vs. 0.45±0.02 cm, p<0.001; respectively) and was positively correlated with age (r=0.420, p=0.002), disease duration (r=0.609, p<0.001), body mass index (r=0.419, p=0.002), waist circumference (r=0.469, p<0.001), and triglyceride (r=0.434, p=0.002) levels; and negatively correlated with high-density lipoprotein cholesterol levels (r= -0.662, p<0.001).

Conclusion: As a cardiometabolic risk factor, EFT was greater in AS patients. EFT is a noninvasive method to evaluate cardiometabolic risk factors in AS patients.

Keywords: Ankylosing spondylitis; cardiometabolic risk factors; epicardial fat thickness.

Ankylosing spondylitis (AS) is an inflammatory disease associated with metabolic syndrome and atherosclerosis.[1] In AS patients, risk factors for cardiovascular disease including valve problems, rhythm disturbances, hypertension, and atherosclerosis are increased.[2,3] Such patients suffer increased cardiovascular mortality attributable to atherosclerosis.[4] In addition, metabolic syndrome risk factors including obesity, hypertension, hyperlipidemia, disturbances of glucose metabolism, and enhanced insulin resistance are elevated in AS patients.[5]

Epicardial fat tissue (EFT) surrounds the heart and metabolically active organs. Recently, several studies have shown that excess EFT was associated with insulin resistance,[6] increased cardiometabolic risk,[7] elevated inflammatory marker levels,[8,9] and coronary artery disease.[10,11]

Nilgün et al.[12] evaluated 26 AS patients and 26 healthy controls, and they showed that although EFT was elevated in AS patients, this was not associated with either the levels of subclinical atherosclerosis markers or disease duration.

Resorlu et al.[13] studied 40 AS patients and 40 healthy controls, and they found that EFT was higher in AS patients and it was associated both with carotid intima media thickness and disease duration. Thus, this study aimed to evaluate cardiometabolic risk factors in AS patients and their relationship with EFT.

PATIENTS AND METHODS

Our study population included 50 consecutive patients with AS (29 males, 21 females; mean age of 40.5±9.4 years; range 25 to 60 years) with a median disease duration of 8.3 years, and 50 healthy controls (33 males, 17 females; mean age 39.8±6.4 years; range 24 to 58 years). All patients fulfilled the modified New York criteria for AS.[12] Detailed histories were taken and patients were comprehensively analyzed. Exclusion criteria were congestive heart failure, presence of valvular heart disease, pacemaker implantation, atrial fibrillation/flutter, frequent ventricular pre-excitation and/or abnormalities in atrioventricular conduction, renal failure, myocardial infarction, cerebrovascular accident, and/or poor echocardiographic imaging resolution.

The study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by our local ethics committee. Informed consents were obtained from all patients.

All patients underwent echocardiography. After resting for 15 minutes, all patients underwent two-dimensional and Doppler echocardiographic evaluations employing a 3.5 MHz transducer (Presoundalpha 7, IPF 1701 Model, 2009; Hitachi Aloka Medical, Ltd. Tokyo, Japan). Standard parasternal and apical echocardiograms were recorded with patients lying in the left lateral position. EFT was measured perpendicularly on the free wall of the right ventricle at end systole, over three cardiac cycles. The parasternal long- and short-axis views afforded the most accurate measurements of epicardial adipose tissue depth in the right ventricle; the cursor beam orientation was optimized for each patient. Maximum EFT was recorded at a point on the free wall of the right ventricle, along the midline of an ultrasonic beam delivered perpendicular to the aortic annulus, which served as an anatomical landmark.

Blood samples were drawn by venipuncture, after patients had fasted for at least eight hours, to measure routine parameters. Fasting blood glucose, serum creatinine, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol, and triglyceride (TG) levels were recorded using standard methods.

Statistical analysis

Statistical analyses were performed using SPSS for Windows version 15.0 software program (SPSS Inc., Chicago, IL, USA). The Student's t-test or Mann-Whitney U-test was employed to compare differences between continuous variables. The Chi-squared test was used to compare the distributions of categorical data. Pearson correlation coefficients were used between EFT values and clinical parameters. $P<0.05$ was considered as statistically significant.

RESULTS

In terms of basic clinical and demographic characteristics, both groups were similar in age, body mass index (BMI), waist circumference (WC), presence of hypertension and/or diabetes mellitus and levels of TG, HDL, total cholesterol, low-density lipoprotein cholesterol, and fasting glucose level (Table 1). Both the BMI and WC were higher in AS patients than healthy controls (25.4±3.5 vs. 24.5±2.9 kg/m², p=0.005; 96.2±10.8 vs. 86.7±12.6 cm, p<0.001; respectively). AS patients also had higher TG levels (123.0±47.7 vs. 110.1±61.0 mg/dL, p=0.009; respectively), lower HDL levels (41.3±7.0 vs. 51.9±7.0 mg/dL, p<0.001; respectively) and greater EFT values (0.53±0.14 vs. 0.45±0.02 cm, p<0.001; respectively). In AS patients, EFT was correlated with age (r=0.420, p=0.002), disease duration (r=0.609, p<0.001), BMI (r=0.419, p=0.002), WC (r=0.469, p<0.001) and TG (r=0.434, p=0.002), and HDL levels (r= −0.662, p<0.001). The correlations between EFT and disease duration, WC, and HDL level in AS patients are shown in Figure 1.

DISCUSSION

When compared with controls, AS patients had greater EFT, higher values for cardiometabolic

Table 1. Demographic and clinical characteristics of subjects

	\multicolumn{5}{c}{Ankylosing spondylitis patients (n=50)}	\multicolumn{5}{c}{Controls (n=50)}	
	n	%	Mean±SD	Median	Min.-Max.	n	%	Mean±SD	Median	Min.-Max.	p
Age (years)			40.5±9.4					39.8±6.4			0.846
Sex											
Female	21	42				17	34				0.410
Body mass index (kg/cm²)			25.4±3.5					24.9±2.5			0.005
Waist circumference (cm)			96.2±10.8					86.7±12.6			<0.001
Disease duration (years)				8.3	5-23				–	–	
Diabetes mellitus	2	4				–	–				0.153
Hypertension	4	8				–	–				0.126
Epicardial fat thickness (mm)			0.53±0.14					0.45±0.02			<0.001
C-reactive protein (mg/dL)			13.4±11.5					1.6±3.4			<0.001
Glucose (mg/dL)			96.7±11.8					97.1±8.3			0.714
Triglyceride (mg/dL)			123.0±47.7					110.1±61.0			0.009
HDL (mg/dL)			41.3±7.0					51.9±7.0			<0.001
Total cholesterol (mg/dL)			172.4±53.7					180.3±47.4			0.255
LDL (mg/dL)			122.2±33.4					126.6±34.3			0.275

SD: Standard deviation; Min.: Minimum; Max: Maximum; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

risk factors including BMI, WC, and TG levels and lower values for HDL. EFT values were correlated positively with BMI, WC, and disease duration, and negatively with HDL level. Thus, cardiometabolic risk factors were elevated in AS patients.

Ankylosing spondylitis is a chronic inflammatory disease involving both the axial skeleton and extra-articular organs including the eyes, lungs, neurological system, and heart.[15-18] Inflammatory rheumatic diseases trigger cardiovascular conditions, increasing mortality and morbidity.[19] The risk of atherosclerosis, in which inflammation plays a primary role, was increased in AS patients.

Assessment of EFT by echocardiography was validated by Iacobellis et al.[20,21] Such tissue surrounds the heart and metabolically active organs. EFT is very metabolically active, releasing atherogenic and inflammatory substrates including TNF-alpha, inhibitor of plasminogen activator, visfatin, leptin, omentin, and angiotensin.[22] Free fatty acids and adiponectin released by EFT trigger atherosclerosis of the myocardium because of the lack of any barrier between myocardial EFT and coronary vessels.[23] EFT levels were higher in AS patients than controls.

Metabolic syndrome is described as a group of various abnormal metabolic risk factors such as obesity, dyslipidemia, increased blood pressure, increased plasma glucose levels, prothrombotic condition and proinflammatory state. Metabolic syndrome was found to be more common in
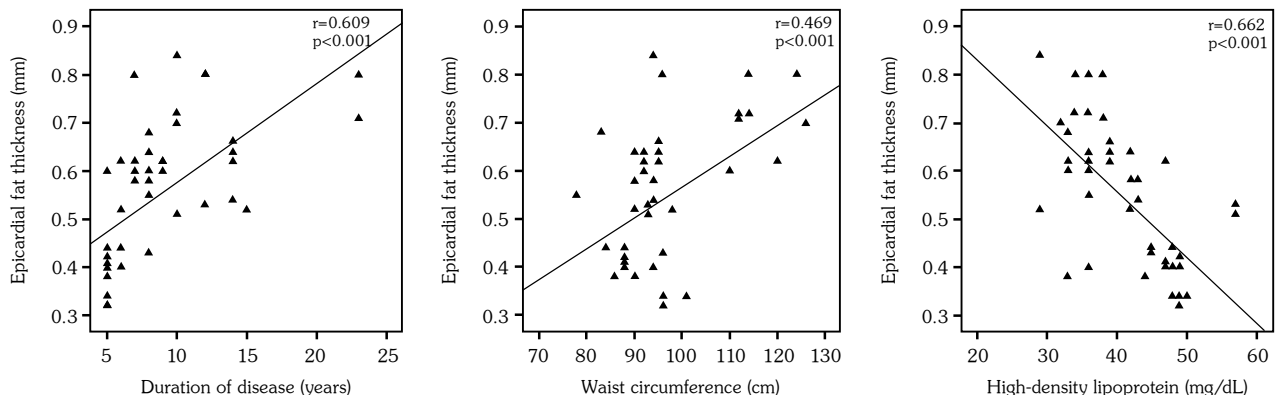

Figure 1. Correlation analyses between epicardial fat thickness and clinical parameters.

AS patients.[24,25] Malesci et al.[25] showed that the prevalence of metabolic syndrome was 46% in AS patients and 11% in others. Risk factors for metabolic syndrome, including obesity, hypertension, hyperlipidemia, disturbances in glucose metabolism, and elevated insulin-resistance, were higher in AS patients.[5] EFT surrounds both the ventricles and the coronary artery, and its extent was positively correlated with both BMI and WC, possibly contributing to the development of coronary artery disease.[26-28] Ormseth et al.[29] showed that the EFT was associated with risk factors for metabolic syndrome and cardiometabolic conditions in rheumatoid arthritis patients. In the present study, we found that BMI, WC, and TG level were elevated, and HDL level was lower in AS patients compared to controls. In addition, EFT values were correlated with BMI, WC, and disease duration, indicating that cardiometabolic risk factors were elevated in AS patients.

The principal limitation of our study was the small sample size, which afforded only a low statistical power upon equivalence testing. Thus, false-negative results were possible. Other limitations included the cross-sectional design and lack of follow-up. Comprehensive prospective studies featuring long-term follow-up are needed to determine the relationship between EFT levels and cardiovascular outcomes in AS patients. In conclusion, EFT, a cardiometabolic risk factor, was elevated in AS patients, and this may reflect subclinical cardiovascular involvement in these patients.

Declaration of conflicting interests

Funding

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