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The relationship between systemic sclerosis and hypertension and ecocardiographıc findings

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Abstract
Aims: The aim of this study was to evaluate the basic demographic and clinical features of systemic sclerosis in our patient group and to determine the relationship between the duration of disease and the development of hypertension in scleroderma patients.
Settings and Design: Systemic sclerosis is a rare, autoimmune disease with a limited or widespread involvement of connective tissue of different organs. In the literature, it is recommended that each center following the scleroderma population remove their patient data.
Methods and Material: Patients who were followed up with the diagnosis of systemic sclerosis were included in our study. The duration of the disease, the accompanying diseases, basic demographic characteristics, inflammation markers and echocardiographic characteristics of the patients were evaluated. A total of 150 patients were included in the study (87.3% female, mean age 47.7). The duration of the disease was 5.41 years.
Results: 37% of the patients had hypertension. There was a positive correlation between disease duration and hypertension (r: 0.278, p: 0.001). Echocardiographic evaluation revealed pulmonary hypertension in 10 patients. Hypertension was more prevalent in this disease group than the population with the same characteristics. As the disease duration increased, the incidence of systemic hypertension increased.
Conclusions: The first of the striking findings in our study was that the rate of pulmonary hypertension due to scleroderma was found to be similar to that in other Middle Eastern societies. In the second important finding, peripheral connective tissue involvement of scleroderma was found to be important in the development of systemic hypertension.

Keywords: systemic sclerosis, echocardiography, hypertension, regional differences

1. Introduction

Systemic sclerosis is a multisystemic chronic autoimmune inflammatory disease characterized by fibrosis, vasculopathy, extracellular matrix synthesis, and storage in the skin and internal organs. Systemic sclerosis is a chronic multisystemic disease of unknown etiology characterized by changes in the skin, circulatory system, synovium and musculoskeletal system due to fibrosis in the internal organs, especially the gastrointestinal system, heart, lung, and kidneys due to clinical connective tissue accumulation[1]. Systemic sclerosis is generally seen in women between the ages of 30-55 and has severe complications with low incidence.

Hypertension (HT), Diabetes Mellitus (DM), and renal diseases are the main systemic diseases in which differences can be observed in progression, presentation, and prognosis in the presence of systemic sclerosis. Previous studies have shown that in patients with systemic sclerosis over the age of 45, with high markers of inflammation and skin involvement, the development of HT can be predicted[2]. Hypertension causes vascular changes in a similar way to systemic sclerosis. Perivascular inflammatory infiltrates, and impaired angiogenesis and endothelial apoptosis are observed in the early stages of the disease. Data from animal models show that prolonged, uncontrolled VEGF (Vascular Endothelial Growth Factor) overexpression may have paradoxical effects on the formation of new vessels leading to capillary changes similar to those observed in Systemic Sclerosis (SSc). In addition to impaired angiogenesis, defective vasculogenesis may contribute to the vascular symptoms of SSc [3]. Cardiovascular diseases are more frequently observed in patients with rheumatoid joint disorders and individuals with systemic sclerosis [4].Systemic sclerosis may cause myocardial fibrosis, right and left ventricular systolic and diastolic dysfunction, pericardial, and endocardial involvement. Echocardiography is a contributory noninvasive test used to evaluate heart involvement [5].

This study aimed to investigate the clinical, laboratory, and echocardiographic features of systemic sclerosis patients in our center, to evaluate the relationship between hypertension and disease duration and to compare them with other population-based studies.

2. Materials and Methods

The study included 150 patients who were previously diagnosed and treated by the rheumatology clinic. They were consecutive patients. It was recommended that each center following the scleroderma population remove their patient data. This study was made retrospectively. Every patients were routinely evaluated in

terms of age, sex, laboratory findings, clinical signs and symptoms, echo findings, and concomitant diseases in our clinic. Left and right ventricular dimensions and functions, ventricular septum thickness, posterior wall thickness, systolic pulmonary artery pressures, and tricuspid gradients were routinely evaluated in the echocardiography evaluation of every patients. Pulmonary hypertension was accepted if the pulmonary artery pressure was over 40mmHg. The diagnosis of systemic sclerosis was based on EULAR and ACR systemic sclerosis criteria[6].Raynaud's phenomenon was defined using clinical (flattening of the skin of the fingers in response to exposure to cold or emotional stress) and nail-curved video capilloroscopy. The skin lesion was defined when a patient had focal swelling, stiffness, or atrophy regardless of location. Arthritis was considered as swelling and tenderness in one or more joints. In the case of dysphagia accompanied by changes in gastroscopy or barium swallowing test, gastrointestinal involvement was diagnosed. In our clinic, ESC hypertension guidelines are accepted as reference and diagnosis and treatment of hypertension are performed by this.. (Hemoglobin) Hgb values were considered as anemia in men <13 and women <12. ESR (Erythrocyte Sedimentation Rate) was determined as a limit value of 25mm / hour. Standard methods were used for CRP(C-Reactive Protein) (> 10) and (Rheumatoid Factor) RF (> 14) measurements. Proteinuria was detected by micro electrophoresis in 24-hour urine. Spot urine was searched for cylindirurea. LDL(Low-Density Lipoprotein) > 160 was accepted as the limit value for the diagnosis of hyperlipidemia.

Inclusion criteria:

- Patients who were followed up with the diagnosis of systemic sclerosis
- Exculusion criteria:
- -<18 age
- -There was a known secondary cause of cystemic hypertension other than scleroderma.

Two Patients with bilateral renal artery stenosis and 1 patients with pheochromocytoma were excluded from this study

Statistical Analysis:

Patients' history of coronary artery disease, antidiabetic, and antihypertensive treatment history were evaluated. The data obtained were evaluated using SPSS 22 program. Mean values and frequencies were used statistically. In general, descriptive statistics were used. The determinants of the study were: signs of excessive fibrosis (skin lesion, pulmonary fibrosis), symptoms of vasculopathy (hypertension, proteinuria), and signs of inflammation (arthritis, elevated CRP, RF or ESR). Statistical significance was accepted as $p < 0.05$.

3. Results

The mean age was 47.75, and the minimum age of patient was 19, and the maximum age of patient was 78 years old. The minimum duration of the disease 1 year, and maximum 11 years, and the mean disease duration was 5.41 years. Hypertension was detected in 34.7% of the patients (Table1).

In our study, the frequency of SS-associated pulmonary hypertension was 6%.

RF values were low in 52.7% and high in 47.3% of patients (Table 2).

In Echocardiographic evaluation means EF(Ejection Fraction) was 60.21, and mean SPAB(Systolic Pulmonary Artery Pressure) was found to be 31mmHg (Table 3).

Hypertension was positively correlated with disease duration (R^2: 0.278, p: 0.001) (Table 4) (figure 1).

4. Tables and Figures

Table 1: Comorbidities and laboratory assesment in systemic sclerosis

Comorbidities	Pozitif (number)	Negatif (number)	Pozitif (percent)	Negatif (percent)
Hypertension	98	52	65.3	34.7
Dm	142	8	94.7	5.3
Cad	124	26	82.7	17.3
Hyperlipidaemia	132	18	88	12
Anemia	124	26	82.7	17.3
Proteinuria	106	44	70.7	29.3
Silendiruria	139	11	92.7	7.3
Pht	149	1	99.3	0.7

Note: Dm(Diabetes mellitus), Cad(Coronary artery disease), Pht(Pulmonary hypertension)

Table 2: Inflammatory markers in systemic sclerosis patients

	Negatif (number)	Pozitif (number)	Negatif (percent)	Pozitif (percent)
Crp	141	9	94	6
Esr	116	34	77.3	22.7
Rf	79	71	52.7	47.3

Note: Crp (C- rective protein), Esr (Erythrocyte sedimentation rate), Rf (Rheumatoid factor)

Table 3: Age, disease duration and echocardiography evulation result in systemic sclerosis patients

	Number	Minimum	Maximum	mean	Std. Deviation
Age	150	19 years	78 years	47,75	13,337
Disease Duration	150	1 year	11 years	5,41	2,774
Ef	150	%35	%72	60,21	4,912
Lvedd	150	34 mm	57 mm	42,87	3,764
Lvesd	150	18 mm	41 mm	25,07	4,217
Ivs	150	7 mm	14 mm	9,91	1,636
Pwt	150	6 mm	13 mm	8,84	1,614
Rvedd	150	2 mm	40 mm	20,92	3,220
Spap	150	17 mmhg	111 mmhg	31,07	11,816
Trg	150	12 mmhg	96 mmhg	25,82	10,647

Note: Ef (Ejection fraction), Lvedd (Left ventricular enddiastolic diameter), Lvesd (Left ventricular endsistolic diameter), Ivs (Interventricular septum),Pwt (Posterior Wall thickness), Rvedd (Right ventricular enddiastolic diameter), Spap(Systolic pulmonary arterial pressure), Trg (Tricuspid regurgitant gradient)

Table 4: Hypertension was positively correlated with disease duration

		Hypertension	Time
Hypertension	Pearson Correlation	1	,278**
	Sig. (2-tailed)		,001
	N	150	150
Time Of Disease	Pearson Correlation	,278**	1
	Sig. (2-tailed)	,001	
	N	150	150

Table 5: Average range and patients with average ESR level

	Esr	N	Mean	Std. Deviation	Std. Error Mean	P value
sPAB	0	116	31,02	12,209	1,134	0.775
	1	34	31,24	10,532	1,806	

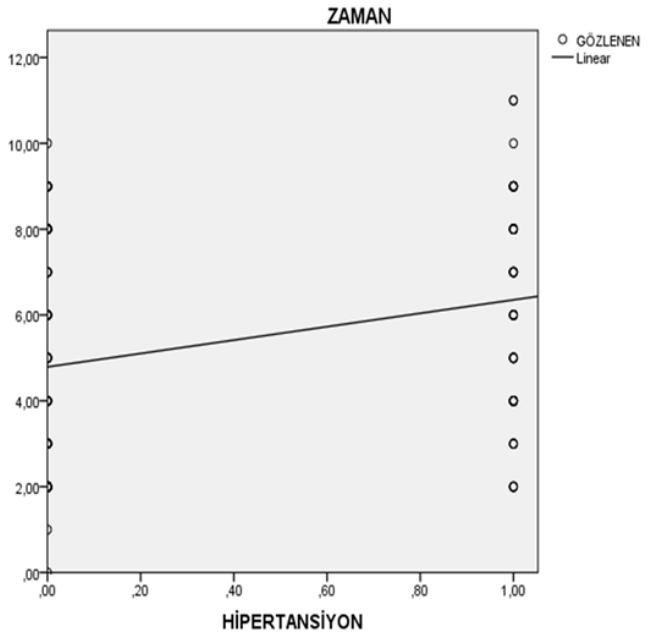

Fig 1: Hypertension was positively correlated with disease duration

5. Discussion

The mean age of the patients included in our study was found to be 47.7 and was similar to other community-based studies[2]. In the EULAR study, 87.8% of the patients were female, similarly, in our study, this rate was 87.3%, similar to the EULAR records. In our study, the frequency of SS-associated pulmonary hypertension was 6%, and in the previous prospective studies, the incidence of SS-associated pulmonary hypertension was found to be between 7.8% and 12% [7].The rate of patients with EF <55% was 3.4%, and in the EULAR-based study, this rate was 5.4%[6]. In our study, the mean SPAB was found to be 31, in a similar study [8]the mean SPAB was found to be 33.3, and the results were identical. In the same review [8] LVEDD (Left Ventricular End Diastolic Diameter), (Inter Ventricular Septum) IVS, (Posterior Wall Thickness) PWT and EF values were similar to our study. As in our study, the decrease in myocardial contractility is lower than expected in many studies and is controversial with the presence of myocardial depression in systemic sclerosis [9] [10] [11]. In most of our patients, levels of inflammation markers such as ESR and CRP were found below. In a study conducted in Japan, it was reported that elevated ESR values are strongly associated with the presence of PHT in scleroderma and may be caused by inflammation and hypergammaglobulinemia [12].In our study, pulmonary artery pressures measured echocardiographically were similar in patients with ESR above-average range and patients with average ESR level (Table 5). CRP levels were found to be high in 6% of our patients, whereas in a study on inflammation indicators [13], one-fourth of patients had high CRP values. In another study, CRP levels were found to be high in 48% of patients, and this rate reached 80% in patients with finger ulcers[14].Low ESR and CRP levels were attributed to the disease activities of the patients included in the study. Compared with the previous regional research on central Ukraine[2], anemia and CRP results were lower, and ESR was higher. Cylinderuria and proteinuria values were similar.

Hyperlipidemia was present in 12% of the patients who participated in our study and similar to previous studies, it was shown that impaired lipid profile was associated with increased macrovascular diseases in patients with systemic sclerosis[15] [16]. Unlike previous studies, we could not detect a significant relationship between DM and systemic sclerosis. It can be explained by the low number of DM patients and the short duration of DM.

Summary of key findings of our study was significant relationship between age and the presence of hypertension in systemic sclerosis. Acoording to the Framingham Heart Study, which followed patients for 30 years, agreed that systolic blood pressure (SBP) shows a continuous increase between the ages of 30 and 84 years or over [17]. Hypertension was present in 34.7% of the patients who participated in our study. We found a significant relationship between age and the presence of hypertension in systemic sclerosis. Hypertension at the onset of SSc was associated with skin lesions, arthritis, pulmonary fibrosis, abnormal platelet and ESR levels, and a higher incidence of cylinders. The rate of gastrointestinal complications was higher in hypertensive patients. The absence of hypertension was associated with a high prevalence of anemia. In hypertensive patients, the mean PAP was slightly higher, and the mean (Glomerular Filtration Rate) GFR was meaningful lower, and these results were similar to the population in central Ukraine[2].

6. Conclusion

As seen in our study, patients with systemic sclerosis in our region had similar clinical, demographic, laboratory, and echocardiographic features identical to the populations in other countries. Our study showed that a statistically significant relationship between duration of scleroderma and systemic hypertension. That correlates with the duration of the disease. The clinical doctors should be aware of the development of systemic hypertension in patients with scleroderma. Old age is a factor independent of scleroderma duration in the development of hypertension and should not be ignored.

7. Limitations

The limitations of our study were the fact that the patients included in our study were from a limited region, the age of onset of systemic sclerosis and initial symptoms were not evaluated, and diastolic evaluation could not be performed in all patients.In the future, Genetic trials may be made about devopoling systemic hypertension in systemic sclerosis patients

8.Financial support and sponsorship

Nil.

9.Conflicts of interest

There are no conflicts of interest.

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