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Dermatochalasis: A potential risk factor for cardiovascular diseases

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Abstract

To examine the cardiac parameters of patients with dermatochalasis by echocardiography to analyze whether there is a relationship between dermatochalasis and cardiac disorders. This prospective comparative study included 132 (57 male, 75 female) patients with dermatochalasis with an average age of 47.09±9.53 years and 77 (34 male, 43 female) healthy controls with an average age of 47.31±4.23 years. Each participant was examined by 2-dimensional, M-mode, and color-flow Doppler, pulsed-wave (PW) Doppler, and tissue Doppler imaging (TDI) echocardiography. In patients with dermatochalasis, PW Doppler transvalvular mitral flow measurements showed higher late diastolic flow velocity (A) but lower early diastolic flow velocity (E) and E/A ratio compared to the control group (p=.056, p=.02, and p=.04, respectively). Similarly, TDI measurements showed lower lateral and septal early diastolic myocardial velocities (E'), and higher lateral and septal late diastolic myocardial velocities (A), and E/E' ratios in patients with dermatochalasis compared to the control group (p=.03, p=.01, p=.09, p=.04, p=.02, and p=.01, respectively). In this study, we discovered that patients with dermatochalasis have abnormal left ventricular diastolic function. It indicates that dermatochalasis may be responsible for subclinical cardiac involvement.

Keywords: Dermatochalasis, left ventricular diastolic dysfunction, cardiac involvement, tissue Doppler echocardiography, pulsed-wave Doppler

Introduction

Dermatochalasis is a common disorder defined as drooping of the eyelid skin and orbital tissue due to the age-related reduction in tone and elasticity of the eyelids. Dermatochalasis affects approximately 16% of individuals over the age of 45 [1]. Histopathological research on dermatochalasis revealed an increase in the number of dilated lymphatic vessels and a decrease in the density of collagen and elastin fibers [2-5]. In addition, degradation in elastin and collagen fiber structure and fragmentation were observed in dermatochalasis specimens [2-4]. The increase in lymphangiectasia in dermatochalasis was attributed to inflammation-induced loss of elastin and collagen fibers [4,6,7].

The cardiovascular system is one of the areas in the body with the highest concentration of collagen and elastin fibers. The subendothelial, subepicardial, and epicardium layers of the heart, as well as heart valves, contain an abundance of type 1, 2, 3, and 4 collagen and elastin fibers [8-10]. The special configuration of these fibers in the heart improves the heart's resistance to stretching while maintaining its flexibility, relaxation, and current form [11-13].

We suspect that the considerable loss of elastin and collagen fiber found in the eyelids may also occur in the cardiovascular system of patients with dermatochalasis. Therefore, we aimed to assess the cardiac parameters of patients with dermatochalasis by echocardiography. As far as we are aware, it is the first investigation to examine the association between dermatochalasis and cardiac disorders.

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Material and Methods

Ethical approval

This study was approved by the Sancaktepe Sehit Prof. Dr. Ilhan Varank Training and Research Hospital's ethics committee in compliance with the principles of the Helsinki Declaration.

Study population

This prospective comparative study included 77 healthy control subjects and 132 dermatochalasis patients over the age of 40, who sought medical attention in the ophthalmology department between April 2021 and October 2021 due to symptoms of drooping and heaviness in the upper eyelids. An experienced ophthalmologist (S.K.) identified the healthy control subjects, ensuring the absence of eyelid drooping or deformations, as recommended by Jacobs et al. [1].

Each participant in both groups provided detailed information about their medical history, which was then cross-validated using medical data recording systems. Subjects with a history of cardiovascular diseases (such as hypertension, coronary artery disease, valvular disease, pericardial disease, heart failure, cardiac surgery, etc.), a history of systemic diseases (such as diabetes mellitus, connective tissue disease, renal-hepatic failure, malignancy, etc.), a history of chronic medication use, other eyelid diseases (such as entropion, ectropion, trauma, etc.), a history of prior eyelid or intraocular surgery, and subjects older than 55 years were excluded from both groups. Patients who had previously received dermatochalasis surgery or cosmetic laser treatments such as Plexr were also excluded.

All the patients with dermatochalasis in the study group had complained of eyelid drooping for less than two years. We excluded patients with dermatochalasis who had a prior history of cardiac disease. Our intention in excluding individuals with known heart disease was to eliminate the potential confounding effect caused by heart diseases unrelated to dermatochalasis. Based on this premise, our objective was to investigate the subclinical effects of recently diagnosed dermatochalasis on cardiac tests in patients who do not show any clinically apparent cardiac disease. Therefore, 7 dermatochalasis patients with hypertension and 1 dermatochalasis patient with heart valve disease were excluded from the study.

Ophthalmalogical examination

An experienced opthalmologist performed a comprehensive ophtalmological examination on each participant, which included measurements of best-corrected visual acuity, spherical equivalent, slit-lamp biomicroscopy, intraocular pressure (IOP), and central corneal thickness (CCT). Refractive measurements were made by autokeratorefractometry (Topcon KR-800, Topcon Medical Systems, Inc. Fukuoka, Japan). Goldmann applanation tonometry was used to assess IOP, and a non-contact tonopachymeter (NT-530P, Nidek CO. Gamagori, Japan) was used to assess CCT. The mean marginal rim distance (MRD) was measured for each participant.

The participants were classified phenotypically into four levels by two experienced opthamologists (S.K., M.K.) in accordance with the recommendations of Jacobs et al [1]. Grade 1 is normal (the skin of the superior eyelid does not reach the eyelashes), grade 2 is mild (the skin of the superior eyelid slightly brushes the eyelashes), grade 3 is moderate (the skin of the superior eyelid drops over the eyelashes), and grade 4 is severe (the skin of the superior eyelid drops onto the eye). The study group consisted of patients with bilateral grade 2, 3, and 4 dermatochalasis, while the control group consisted of age- and gender-matched healthy subjects without drooping eyelids, as recommended by Jacobs et al. [1].

Physical examination

All participants' heights and weights were measured with a digital scale and a Harpender stadiometer that was mounted on the wall. The body mass index (BMI) value was measured for each participant by dividing the body weight in kilograms by the square of the height in meters (kg/m^2). Blood pressure was calculated three times with 15-minute rest intervals utilizing the automated sphygmomanometer (Omron M2 HEM7121E, Omron Healthcare Co, Japan). The average of three consecutive measurements was used to assess blood pressure. Serum glucose levels, lipid levels, and renal function tests were assessed using Cobas 6000 Roche. A total blood count test was performed using an auto hematology analyzer (BC6800 Mindray Medical Electronics Co. Shenzhen, China).

Transthoracic echocardiography

Echocardiographic assessments were performed by the Philips Affinitti 70 ultrasound system (Medical Healthcare Solutions, Inc.; Andover, MA, USA) with an S4-2 transducer probe. A competent cardiologist (E.A.) who was blind to research groups performed the transthoracic echocardiographic measurements. Single-electrode echocardiographic recordings were collected simultaneously with echocardiographic measurements. Current recommendations were followed for doing a 2-dimensional, M-mode, and color-flow Doppler echocardiography [14]. Left ventricular end-diastolic diameter (LVeDD), left ventricular end systolic diameter (LVsDD), interventricular septum thickness (IVS), and left ventricular posterior wall thickness (LVPW) were calculated from parasternal long-axis, apical four- and five-chamber views, and their means were measured. The Biplane Simpson technique was used to calculate the left ventricular (LV) ejection fraction (EF) in the apical four-chamber view.

Diastolic function was assessed using mitral inflow parameters and tissue Doppler imaging (TDI) data. At the end of the mitral valve cusp, the early diastolic flow velocity (E) and late diastolic

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flow velocity (A) waves were recorded using apical four-chamber pulse-Doppler (PW) imaging. The E/A ratio was then used to look at the mitral inflow characteristics.

The research also produced TDI images of myocardial diastolic velocities. According to the current guidelines, PW TDI was conducted via modifying the spectral pulsed Doppler signal filters to achieve a Nyquist limit of 15-20 cm/s and utilizing the least optimum gain. A pulsed wave Doppler sample (gate 2 mm) was put directly below the lateral mitral annulus and the basal septal region to measure TDI velocities from the apical four-chamber view. The lateral and septal early diastolic myocardial velocities (E') in addition to the lateral and septal late diastolic myocardial velocities (A) were all assessed. The lateral E/E' ratio and the septal E/E' ratio were then computed [14].

Statistical analysis

Statistical analysis was performed using IBM SPSS for Windows version 23.0 (Statistical Package for Social Sciences, Chicago, Illinois, USA). The Kolmogorov-Smirnov test was conducted to analyze the normality of the variable distribution. The variables with a normal distribution were assessed using an independent sample Student's t-test and described as mean±standard deviation, while variables with a non-normal distribution were assessed using the Mann-Whitney U test and represented as median (25%-75%). The categorical variables were assessed using the chi-squared test and described as numbers and percentages.

Results

This study included 132 patients with dermatochalasis (57 males, 75 females) with an average age of 47.09±9.53 years and 77 healthy controls (34 males, 43 females) with an average age of 47.31±4.23 years. There was no statistically significant difference in mean age and gender distrubition between the two groups (p=.84, and p=.50, respectively). The study group consisted of 44 mild (grade 2), 56 moderate (grade 3), and 32 severe (grade 4) cases of dermatochalasis. Patients with dermatochalasis reported an average duration of drooping eyelids for 1.6±0.3 years, and none had symptoms for more than 2 years. The MRD was 1.6±0.9 mm in the study group and 2.9±0.3 mm in the control group, showing a statistically significant difference between the two groups (p=.002). Table 1 presents some of the demographic and clinical characteristics of both groups.

There was no statistically significant difference in hemoglobin, serum creatinine, total cholesterol, LDL, or glucose levels between the two groups (p=.16, p=.47, p=.42, p=.16, and p=.88, respectively). We did not find a statistically substantial difference in EF, LVeDD, LVsDD, IVS, and LVPW between the two groups (p=.53, p=.06, p=.35, and p=.31, respectively) (Table 2).

When comparing patients with dermatochalasis to the control group, we discovered significant differences in the E wave, A wave, E/A ratio, septal and lateral E' waves, A waves, and E/E' ratios. A substantial decrease in E, septal E', and lateral E' waves (p=.02, p=.01, and p=.03, respectively) and a significant rise in A, septal A, and lateral A waves were observed in patients with dermatochalasis (p=.056, p=.04, and p=.09, respectively). Furthermore, the decrease in the E/A, and the increase in the septal E/E' and lateral E/E' ratios of patients with dermatochalasis were significant (p=.04, p=.01, and p=.02, respectively) (Table 2).

Table 1. Demographic and clinical characteristics of the study groups

Variables	Mean of study population	Dermatochalasis group (n=132)	Control group (n=77)	p
Male/Female	91/118	57/75	34/43	.50*
Age (year)	47.17±7.99	47.09±9.53	47.31±4.23	.84**
Smoking (n)	89	55	34	.52*
Systolic blood pressure (mmHg)	115.35±12.61	114.46±12.4	116.88±12.9	.18**
Diastolic blood pressure (mmHg)	71.69±8.52	71.18±8.14	72.57±9.12	.25**
Heart beat (per minut)	73.3(65.8-84)	72(66-83)°	70(65-80)°	.85***
BMI (kg/m²)	27.89±4,81	27.77±4.56	28.01±4.99	.15**
Seq (diopter)	0.29(0.18-1.13)	0.25(0.14-1.02)	0.36(0.22-1.06)	.24***
BCVA	0.94±0.14	0.93±0.13	0.96±0.12	.74**
CCT (µm)	552.58±29.74	548.8±25.6	556.2±38.6	.43**
IOP (mmHg)	15.23±3.7	15.6±3.8	14.8±3.4	.08**
MRD (mm)	2.66±0.65	1.6±0.9	2.9±0.3	.002**

Seq: sferik equivalants, BCVA: best corrected visual aquity (Snellen), CCT: central corneal thickness, IOP: intraocular pressure, MRD: marjinal rim distance
° Interquartile range, ** Independent sample t test, *** Mann Whitney U Test

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Table 2. Echocardiographic and biochemical findings of the study groups

Variables	Mean of study population	Dermatochalasis group (n=132)	Control group (n=77)	p
Hemoglobin (g/dL)	13.9±1.57	13.78±1.7	14.1±1.3	.16**
Serum creatinine (mg/dL)	0.79±0.17	0.78±0.19	0.8±0.14	.47**
Total cholesterol (mg/dL)	206.39±35.57	204.93±35.35	209.25±36.08	.42**
LDL (mg/dL)	128.03±30.74	125.88±32.65	132.82±25.57	.16**
Glucose (mg/dL)	89.30±110.35	89.38±12.84	89.17±2.77	.88**
EF (%)	62±20.70	65 (57-68)°	65 (59-69)°	.22***
LVeDD (mm)	44.25±4.20	44.41±4.38	44.02±3.92	.53**
LVsSD (mm)	34.31±4.05	33.84±4.08	35.02±3.92	.06**
IVS (mm)	9.77±1.08	9.72±1.19	9.87±0.84	.35**
LVPW (mm)	9.64±0.94	9.59±1.05	9.72±0.71	.31**
E wave (cm/s)	76.89±21.74	66.37.57±18.61	74.11±21.8	.02**
A wave (cm/s)	76.07±17.38	78.11±21.29	72.71±5.59	.056**
E/A	1.53±1.38	0.91 (0.74-1.38)°	1.07 (0.8-1.02)°	.04***
Septal E' wave (cm/s)	9.51±3.56	9.06±1.9	10.28±2.72	.01**
Septal A wave (cm/s)	10.61±2.53	10.88±2.82	10.14±1.84	.04**
Septal E/E'	9.54±1.95	12.78±0.98	11.18±1.57	.01**
Lateral E' wave (cm/s)	10.02±2.48	9.1±0.14	11.84±1.94	.03**
Lateral A wave (cm/s)	11.26±2.65	11.5±2.7	10.85±2.53	.09**
Lateral E/E'	9.59±2.67	11.51±3.18	7.33±1.59	.02**

LDL: low density lipoprotein, EF: ejection fraction, LVeDD: left ventricular end diastolic diameter, LVeSD: left ventricular end systolic diameter, IVS: interventricular septum thickness, LVPW: posterior wall thickness, E: early diastolic flow velocity, A: late diastolic flow velocity, E': early diastolic myocardial velocity
** Independent sample t test, *** Mann Whitney U Test

Discussion

Dermatochalasis is a common age-related eyelid disorder that causes visual and cosmetic problems. The histological examinations of excisional biopsy samples showed an increase in the number and width of dilated lymphatic vessels, an enhancement in the amount of macrophages, and concomitant interfibrillary edema in dermatochalasis [2-4]. Furthermore, the histopathological research discovered a reduction in elastin and collagen fibers as well as a degradation in their organization [2-5]. The fundamental cause of lymphangiectasia and dermatochalasis is assumed to be the deterioration in the structure of elastin and collagen fibers [4,6,7].

Collagen and elastin fibers are the most essential extracellular matrix components; collagen fibers provide tissue strength, while elastin fibers provide tissue flexibility and cohesion [8-10]. Elastin and collagen fibers are also abundant in the cardiovascular system, especially in the valvular structure and the heart tissue. These fibers have crucial roles in relaxation and the pumping functions of the heart. While the elastin fibers are responsible for carrying the whole load at low pressures in the heart, the collagen fibers are also activated to help carry the strain at diastolic pressure [15-17].

Left ventricular diastolic dysfunction means impairments in the relaxation and filling of the left ventricle during the diastole phase. The main reasons of left ventricular diastolic dysfunction are decreased left ventricular relaxation, decreased restoring forces, early diastolic suction, and increased stiffness of the left ventricular chambers [18]. As a result of these abnormalities, left ventricular diastolic filling pressure increases, which makes it difficult for blood to enter the ventricle. This can cause high pressures in the left atrium and, subsequently, in the pulmonary veins, resulting in symptoms including shortness of breath, pulmonary congestion, and, in severe cases, heart failure [19]. Left ventricular diastolic dysfunction is a common early finding, and as it worsens, it generates systolic dysfunction as well [20].

Left ventricular diastolic dysfunction is usually detected using echocardiography and graded according to the degree of diastolic function abnormalities. The E\E' ratio has been recommended as

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the best single Doppler parameter for detecting left ventricular filling pressure in many cardiac disorders, and it is recognized as an excellent indicator of cardiac mortality [21].

While the E/E' ratio rises modestly in the early stages of left ventricular diastolic dysfunction, it decreases as the disease progresses. This is due to the fact that E' velocity is more affected and lowered than E velocity at the early stage [18].

In this study, we hypothesized that connective tissue abnormalities may be seen in other systems and tissues that contain abundant collagen and elastin fibers, such as the cardiovascular system, in patients with dermatochalasis. When we assessed the echocardiographic measurements, we discovered an increase in A waves in dermatochalasis patients, and a reduction in E and E' waves. As a consequence, we noticed a reduction in the E\A ratio and an increase in the E\E' ratios which indicate a mild degree of impairment in the left ventricular diastolic function of the heart. The relaxation problem that produces this diastolic disfunction might be caused by a decrease in the amount of elastin and collagen fibers in the myocardial layer of the heart, as well as degradation in their structures. No substantial difference was found in EF, LVeDD, LVsDD, IVS, or LVPW between the two groups, which indicates the lack of advanced degrees of cardiac disorders.

Although dermatochalasis is most commonly seen in elderly individuals, it can also be observed in younger adults. The underlying reason for affecting younger adults may be the structural variances in the elastin and collagen fibers caused by genetic polymorphisms [22,23]. We included relatively younger adults in our study in order to avoid age-related cardiac abnormalities. Despite the lack of any symptoms of heart disease, we discovered a deterioration in left ventricular diastolic functions in adults with dermatochalasis compared to age- and gender-matched adults in our research. These findings imply that people who acquire dermatochalasis at a younger age have degeneration of connective tissue fibers not only in their eyelids but also in their hearts.

There are several studies in the literature that indicate cardiac involvement, particularly diastolic dysfunction, in a variety of disorders characterized by connective tissue degeneration. Yazici et al. [24] stated that diastolic dysfunction was more common in patients with rheumatoid arthritis (RA) compared to healthy people over a 5-year period of time. Arslan et al. [25] also performed cardiac examinations in patients with active RA by both conventional Doppler and TDI in their research. According to this research, patients with RA had higher A wave and deceleration time (DT) values than the control group. Additionally, the E/A ratio and E wave were noted to be decreased in patients with RA compared to the control group. Furthermore, he claimed that there was a link between the period of time with the illness and the level of cardiac involvement. Leung et al. [26] reported that patients with systemic lupus erythematosus (SLE) had abnormal left ventricular diastolic filling parameters. He discovered a significant decrease in the E wave and E/A ratio, but an increase in the A wave and isovolumic relaxation time in patients with SLE. Bayram et al. [27] stated that people with Sjogren's syndrome have reduced systolic and diastolic functions of the left ventricle. While she found a reduction in myocardial performance index, systolic myocardial wave, E/A ratio, and E and A waves, she discovered an increase in isovolumic relaxation time in patients with Sjogren's syndrome.

Our study showed that patients with dermatochalasis exhibited a significant increase in A waves, and E\E' ratios, along with a decrease in E, E' waves, and E/A ratio. These findings indicate that connective tissue changes are not confined to the eyelids; but also affect the heart in dermatochalasis. Further comprehensive studies investigating other cardiac functions beyond left ventricular diastolic function in patients with dermatochalasis are needed. Moreover, investigations of other tissues and systems with abundant elastin and collagen fibers in patients with dermatochalasis may be beneficial. The major limitation of our study is that we did not perform a correlation analysis between the stage of dermatochalasis and the left ventricular functions. It would be beneficial for future research to include comparison and correlation analyses based on dermatochalasis stage.

Conclusion

In the current study, despite the lack of any clinical symptoms of heart disease, we discovered signs of left ventricular diastolic dysfunction in patients with dermatochalasis. Connective tissue dysfunction affects the heart as well as the eyelids in patients with dermatochalasis. The systemic and cardiac implications of dermatochalasis should be thoroughly researched for the early detection and treatment of potential illnesses. A cardiology follow-up every six months using PW Doppler and TDI echocardiography in patients with dermatochalasis may be beneficial for the early management of left ventricular diastolic dysfunction. As far as we know, this is the first study to look at the systemic consequences of dermatochalasis, and it may provide a starting point for future research.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
This study was approved by the Sancaktepe Sehit Prof. Dr. Ilhan Varank Training and Research Hospital's ethics committee (approval number:2020\86) in compliance with the Declaration of Helsinki's principles.

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