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ORIGINAL RESEARCH

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Relationship between diagonal earlobe crease (Frank's sign) and international index of erectile dysfunction score (IIEF-5)

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Abstract

The objective of this study is to examine the association between erectile dysfunction (ED) and the presence of diagonal earlobe crease (DELC), a physical sign commonly associated with atherosclerosis. A total of 96 male patients, aged between 50 and 65 years, were referred to our institute between December 2020 and March 2021 for various urological conditions. These patients were included in the study. Erectile performance was assessed using the IIEF-5 score, and DELC was visually identified by a urologist. The patients were administered the IIEF-5 questionnaire, and the results were categorized into two groups: the DELC group included patients with an earlobe crease, while non-DELC group consisted of patients with normal earlobes. In total, 96 patients participated in the study. We observed a decrease in IIEF-5 scores among patients in the DELC group compared to those in the non-DELC group. A statistically significant difference was found between the DELC group and the non-DELC group ($p < 0.01$). This study demonstrates that the presence of an earlobe crease may serve as a predictive sign of atherogenic erectile dysfunction in male patients aged 50–65 years. Further investigations should be conducted to explore the utility of DELC as a standard indicator during the physical examination of erectile dysfunction.

Keywords

Diagonal ear lobe crease; Erectile dysfunction; Atherosclerosis

1. Introduction

The Frank's sign is a diagonal skin fold between the tragus and the edge of the auricle, forming a 45° angle. It was first described by Sanders T. Frank in 1973 as a risk factor for atherosclerosis [1]. In a prospective study, Frank's sign demonstrated 90% sensitivity and 32% specificity in predicting significant coronary artery disease [2].

DELC has been identified in the medical literature as a surrogate marker for identifying high-risk patients with occult atherosclerosis [3–5]. It has been found to be more prevalent in males, and a statistically significant positive association was observed between DELC and conditions such as diabetes mellitus, hypertension, myocardial infarction and coronary artery disease in both sexes [6]. Given the close association between DELC and atherosclerosis, we aim to demonstrate that the presence of DELC could serve as a predictive sign of atherogenic erectile dysfunction [7].

Previous studies have consistently found a significant association between coronary artery disease (CAD) and DELC [8, 9]. This article aims to establish a unified connection between DELC and ED based on the well-established correlation between CAD and DELC.

Erectile dysfunction (ED) is a frequently encountered disorder, with its incidence rising notably between the ages of 50 and 75. Among individuals within this age bracket, atherosclerosis (AS) is recognized as a primary causative factor for atherogenic ED. The two conditions, atherosclerosis and ED, share overlapping risk factors, and ED itself has been acknowledged as an independent cardiovascular risk factor. In a rat model, Kim *et al.* [10] successfully induced atherogenic ED through chronic pelvic ischemia, which was validated through molecular and histologic evidence. Predictors of vascular risk, including obesity, hyperlipidemia, metabolic syndrome, diabetes mellitus and hypertension, are associated with the presence of ED and vascular endothelial dysfunction [11]. The relationship between arteriosclerosis and erectile dysfunction has been previously reported [12, 13].

Although the role of atherosclerosis as a significant underlying cause of erectile dysfunction (ED) is widely recognized, there is currently a lack of studies that have directly compared the existence of diagonal earlobe creases (DELC) with scores indicative of erectile function.

2. Materials and methods

Between December 2020 and March 2021, all male patients aged 50 to 65 years who were referred to our Department of

Urology outpatient clinic with various urological conditions were included in the study. The study population consists of male patients presenting to the urology outpatient clinic. The urology outpatient clinic where the study will be conducted receives an average of 25 male patients daily. Patients with neurological disease or mental illness were excluded. Patients with diabetes mellitus, hypertension, heart disease or cerebrovascular disease were grouped as the chronic disease group. Erectile performance was measured using the IIEF-5 score [14], and the bilateral presence of DELC was visually identified by a urologist. The IIEF-5 questionnaire was administered to the patients, and the results were divided into two groups. The DELC group included patients with an earlobe crease, while the non-DELC group consisted of patients with normal earlobes. In total, 96 patients participated in the study.

Due to its noninvasiveness and simplicity, the IIEF-5 score was chosen as a practical method for diagnosing ED. The IIEF-5 instrument is a validated, multidimensional, self-administered questionnaire that serves as a sensitive indicator of erectile function [14].

Statistical analysis: Statistical analysis was performed using the open-source statistical software Jamovi Software (v 1.6.23). Values were expressed as means ± standard deviation (SD). The statistical difference between the normal and DELC groups, smokers/ex-smokers and non-smokers, and patients with or without chronic disease was analyzed using independent sample *t*-tests. A Chi-square test is used to study the relationship between DELC and subgroups. The limit of statistical significance was set at $p < 0.01$. Pearson's analysis was employed for the correlation analysis between patients' ages, patients' body mass index (BMI) and IIEF-5 scores.

The sample size calculation was based on the mean IIEF-5 score levels from a previous similar study [15]. The mean IIEF-5 score levels were reported as 20.97 ± 7.26 in the low coronary group and 25.26 ± 5.17 in the control group. Calculations performed with G*Power 3.1 (http://www.gpower.hhu.de) indicate a power of 95% with alpha = 0.05 when comparing the two means using a student *t*-test, requiring a sample size of 48 for each group and a total sample size of 96 individuals.

Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as positive/negative.

3. Results

The mean age of the participants was 57.5 ± 4.93 years (57.1 ± 4.56 years in non-DELC group, 57.9 ± 5.30 years in DELC group). In DELC group, the mean IIEF-5 score was 9.83 ± 6.34, while in non-DELC group, it was 17.2 ± 7.43. Out of the total participants, 38 were smokers/ex-smokers and 33 had chronic diseases. The IIEF-5 score was 12.3 ± 7.77 in patients with chronic diseases, compared to 14.1 ± 7.79 in patients without chronic diseases. The IIEF-5 scores according to the incidence of DELC are demonstrated in Fig. 1.

The normality of the distribution was assessed using the Shapiro-Wilk test and Kolmogorov-Smirnov test, which indicated a parametric distribution. A statistically significant difference was observed between the DELC group and the non-DELC group ($p < 0.01$), indicating that the presence of an earlobe crease was associated with a higher incidence of erectile dysfunction. The presence of an earlobe crease was identified as an autonomous prognostic determinant for the occurrence of erectile dysfunction.

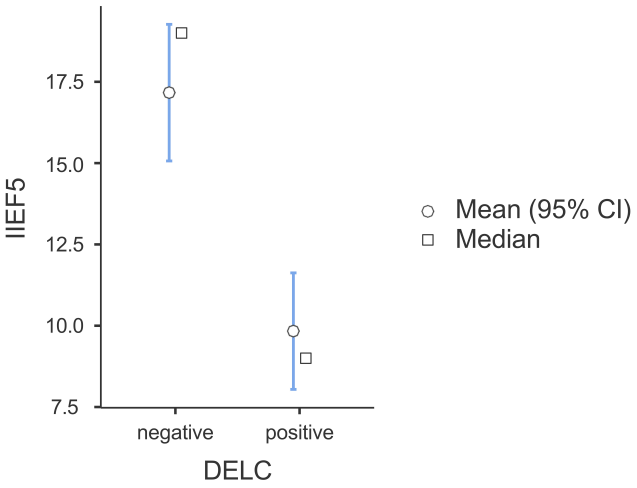

FIGURE 1. Incidence of DELC and IIEF-5 scores. DELC: diagonal earlobe crease; IIEF5: international index of erectile dysfunction 5; CI: confidence interval.

Earlobe crease was found to be an independent prognostic factor for erectile dysfunction.

The analysis of the study population according to smokers/ex-smokers and nonsmoker patients showed no significant difference ($p = 0.541$), suggesting that smoking status did not have a significant impact on erectile dysfunction in this study. Additionally, the presence of chronic diseases (such as diabetes, hypertension, heart disease and cerebrovascular disease) did not increase the incidence of erectile dysfunction ($p = 0.266$).

Correlation analysis indicated that patient age had no negative effect on IIEF-5 scores ($r = -0.074$, $p = 0.466$), suggesting that there was no significant relationship between age and erectile function in this study.

The analysis of the study population, including the comparisons between groups, smokers/ex-smokers, nonsmokers and the impact of chronic diseases with subgroups, is presented in Tables 1,2,3.

TABLE 1. Analysis of the study population.

Group descriptives						
	Group	N	Mean	Median	SD	SE
IIEF5 Score	DELC negative	48	17.20	19.0	7.43	1.070
IIEF5 Score	DELC positive	48	9.83	9.0	6.34	0.914

DELC: diagonal earlobe crease; IIEF5: international index of erectile dysfunction 5; SD: standart derivation ; SE: systematic error.

TABLE 2. Independent samples *t*-test.

		Statistic	Df	*p*
IIEF5 and DELC	Student's *t*-test	5.20	94.0	<0.001

DELC: diagonal earlobe crease; IIEF5: international index of erectile dysfunction 5; Df: degrees of freedom.

TABLE 3. Analysis of subgroups.

Chronic disease			
DELC	Positive	Negative	Total
Negative	13	35	48
Positive	20	28	48
Total	33	63	96
χ^2 tests			
	Value	Df	*p*
χ^2	2.26	1	0.133
N	96		
Smoking			
DELC	Negative	Positive	Total
Negative	26	22	48
Positive	32	16	48
Total	58	38	96
χ^2 tests			
	Value	Df	*p*
χ^2	1.57	1	0.210
N	96		
Diabetes mellitus			
DELC	Negative	Positive	Total
Negative	44	4	48
Positive	42	6	48
Total	86	10	96
χ^2 Tests			
	Value	Df	*p*
χ^2	0.447	1	0.504
N	96		
Hypertensıon			
DELC	Positive	Negative	Total
Negative	12	36	48
Positive	18	30	48
Total	30	66	96
χ^2 Tests			
	Value	Df	
χ^2	1.75	1	0.186
N	96		
Cerebrovascular disease			
DELC	Negative	Positive	Total
Negative	45	3	48
Positive	45	3	48
Total	90	6	96

TABLE 3. Continued.

χ^2 Tests						
		Value		Df		p
χ^2		0.00		1		1.000
N		96				
Heart disease						
DELC		Negative		Positive		Total
Negative		44		4		48
Positive		41		7		48
Total		85		11		96
χ^2 Tests						
		Value		Df		p
χ^2		0.924		1		0.336
N		96				
Independent samples t-test						
		Statistic		Df		p
BMI	Student's t-test	0.942		94.0		0.349
Group Descriptives						
	Group	N	Mean	Median	SD	SE
BMI	Negative	48	26.4	26.1	4.88	0.705
	Positive	48	25.5	24.3	4.65	0.671
Independent Samples t-Test						
		Statistic		Df		p
Age	Student's t-test	−0.702		94.0		0.485
Group Descriptives						
	Group	N	Mean	Median	SD	SE
Age	Negative	48	57.1	57.0	4.56	0.658
	Positive	48	57.9	58.5	5.30	0.765

DELC: diagonal earlobe crease; BMI: body mass index; Df: degrees of freedom; SD: standart derivation; SE: systemic error.

4. Discussion

Endothelial dysfunction is a crucial factor in the pathogenesis of atherosclerosis, contributing to the development and progression of the disease. Nitric oxide (NO), released by the endothelium, is widely recognized as the primary neurotransmitter responsible for penile erection. NO is synthesized by the enzyme NO synthase, which is primarily secreted by vascular endothelial cells. The incapacity to expand the minor arterioles within the penile tissue arises from a diminished synthesis of nitric oxide (NO) synthase, a phenomenon interrelated with both endothelial dysfunction and the presence of atherosclerotic pathology [12]. This reduction in NO availability, caused by impaired endothelial NO synthase activity, leads to increased vasoconstriction, resulting in decreased blood flow and oxygen supply. Consequently, there is an increased production of free oxygen radicals due to the imbalance in oxygen supply and demand. The inflammatory milieu in this context contributes to the fibrotic changes within the corpora cavernosa, subsequently leading to a gradual decline in erectile function. Erectile dysfunction (ED) has been correlated with endothelial dysfunction in conduit vessels, heightened calcification of coronary arteries and asymptomatic angina, irrespective of conventional cardiovascular risk factors [16]. Erectile dysfunction is a complex medical condition with multiple contributing factors. Extensive evidence supports the notion that endothelial dysfunction plays a pivotal role in the development of this ailment. Moreover, Vitamin D deficiency has been postulated to contribute to the manifestation of endothelial impairment [17]. The studies have demonstrated that reduced levels of testosterone (hypogonadism), in addition to effects such as decreased sexual desire, loss of morning erections and erectile dysfunction, also represent an established risk factor for atherosclerosis [18].

Several studies have demonstrated an association between DELC, cardiovascular disease and non-lacunar ischemic stroke, providing support for the notion that DELC could serve as an indicator of long-standing atherosclerosis [19].

The earlobe exhibits an end-artery pattern of microcirculation, lacking collaterals. When these end-arteries become

obstructed due to reduced blood flow, it results in radical oxidative stress and an increase in intimal blood vessel thickness. It is hypothesized that Frank's sign is the consequence of the loss of elastic fibers caused by this low blood oxygenation [20].

The penis receives its blood supply from the internal pudendal artery, a branch of the anterior division of the internal iliac artery. As an end-artery organ, the penis is highly susceptible to peripheral vascular disease. Additionally, erectile dysfunction is considered a clinical indicator of coronary heart disease. In a systemic review, 13 cross-sectional studies were analyzed to evaluate the use of DELC for the diagnosis of CAD. The sensitivity of DELC ranged from 26% to 90%, while the specificity ranged from 32% to 96%. This study suggests that the presence of DELC should not significantly impact clinical management. However, due to its feasibility, DELC could be considered as a supplementary component of the physical examination for patients with CAD [21].

5. Conclusions

This study provides evidence that the presence of a diagonal earlobe crease can function as a predictive indicator for the occurrence of erectile dysfunction among individuals within the age range of 50 to 65 years. The diagnosis of erectile dysfunction (ED) is contingent upon the utilization of questionnaire forms, physical inspection of the penis and testicles, blood assessments encompassing low testosterone levels, diabetes and elevated cholesterol, along with the application of penile Doppler ultrasound imaging. The current study introduces a novel physical examination indicator aimed at identifying atherogenic erectile dysfunction.

According to our findings, this study is the first to demonstrate a significant positive correlation between the diagonal earlobe crease and erectile dysfunction within a substantial participant cohort.

In conclusion, the presence of the diagonal earlobe crease may indicate atherosclerosis-originated atherogenic erectile dysfunction. This well-characterized study provides strong evidence supporting the association between the diagonal earlobe crease and erectile dysfunction. Due to its easy observability, the visual inspection of the auricles could be integrated into the routine clinical examination of patients with erectile dysfunction. Furthermore, there is a requirement for an adequate number of scientific investigations to validate the inclusion of physical examination findings among patients presenting with erectile dysfunction.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author UTB.

AUTHOR CONTRIBUTIONS

UTB—writing review, data analyzing and editing. The author contributed to editorial changes in the manuscript. The author read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was reviewed and approved by the local ethical committee of Mugla Sitki Kocman University (protocol 200253). The objectives and methodologies of the study were elucidated to the participants through both verbal communication and written documentation. Personal information and data were kept confidential and anonymous. The participants provided informed consent and expressed their agreement for the publication of this research.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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