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Could High-Density Lipoprotein (HDL) Alone be a Predictive Biomarker for Patients with Erectile Dysfunction?

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ABSTRACT

This study aimed to assess High-Density Lipoprotein (HDL) levels as a predictor of ED in 105 men aged 20-60, to determine whether HDL levels alone could indicate Erectile Dysfunction (ED) risk independently of other factors. Despite the numerous cardiovascular risk factors associated with ED, this study uniquely focused on the predictive value of HDL levels, aiming to highlight its standalone significance in ED risk assessment. The study analyzed the interaction of HDL levels with variables such as BMI and smoking status to improve understanding of lipid profiles in assessing and managing ED Logistic regression was conducted to assess the link between low HDL levels (<40 mg/dL) and ED, while adjusting for confounding factors like age, BMI, smoking, and hypertension. The ROC curve analysis determined the optimal cutoff point for predicting ED using HDL levels. Patients with ED had significantly lower mean high-density lipoprotein (HDL) levels at 32.0 ± 10.9 mg/dL compared to the normal population's 48.3 ± 12.1 mg/dL ($p = 0.043$). In the ED group, 66.67% of patients had HDL levels below 40 mg/dL, which was higher than the 41.39% observed in the normal population ($p = 0.023$). Additionally, the ED population had a higher mean BMI of 27.4 ± 4.6 kg/m² compared to 24.0 ± 5.2 kg/m² in the normal population ($p = 0.011$). Smoking was also more prevalent among ED patients, with 53.33% being current smokers compared to 35.23% in the normal population ($p = 0.037$). Subgroup analyses revealed an interaction between low HDL and smoking ($B = 0.45$, $\beta = 0.30$, $p = 0.001$), as well as between low HDL and BMI ($B = 0.50$, $\beta = 0.35$, $p = 0.001$), indicating that these combinations exacerbated ED risk more than any individual factor. Our research suggests that HDL could function as a useful predictive biomarker for ED. Clinicians should consider evaluating the HDL levels of patients with ED and potentially managing low HDL levels to alleviate ED symptoms.

Keywords: Erectile dysfunction, high-density lipoprotein, HDL, biomarker, cardiovascular risk factors, dyslipidaemia.

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Yüksek Yoğunluklu Lipoprotein (HDL) Tek Başına Ereksiyon Bozukluğu Olan Hastalar İçin Bir Öngörücü Belirteç Olabilir mi?

ÖZ

Bu çalışma, 20-60 yaş arası 105 erkekte erektil disfonksiyonun (ED) bir öngörücüsü olarak High-Density Lipoprotein (HDL) düzeylerini değerlendirmeyi ve HDL düzeylerinin tek başına diğer faktörlerden bağımsız olarak ED riskini gösterebileceğini belirlemeyi amaçlamıştır. ED ile ilişkili birçok kardiyovasküler risk faktörüne rağmen, bu çalışma özellikle HDL seviyelerinin öngörü değerine odaklanmakta ve ED risk değerlendirmesindeki bağımsız önemini vurgulamayı amaçlamaktadır. Çalışma, lipid profillerinin ED değerlendirilmesi ve yönetimindeki anlayışı geliştirmek için HDL düzeylerinin BMI ve sigara içme durumu gibi değişkenlerle etkileşimini analiz etmiştir. ED ile düşük HDL düzeyleri (<40 mg/dL) arasındaki bağlantıyı değerlendirmek için yaş, BMI, sigara içme ve hipertansiyon gibi karıştırıcı faktörler dikkate alınarak lojistik regresyon yapılmıştır. ROC eğrisi analizi, HDL düzeylerini kullanarak ED'yi öngörmek için optimal kesme noktasını belirlemiştir. ED'li hastaların ortalama yüksek yoğunluklu lipoprotein (HDL) düzeyleri, normal popülasyonun 48.3 ± 12.1 mg/dL'ye kıyasla 32.0 ± 10.9 mg/dL olarak belirgin şekilde daha düşük bulunmuştur (p = 0.043). ED grubunda, hastaların %66.67'sinin HDL düzeyleri 40 mg/dL'nin altında olup bu oran, normal popülasyonda gözlemlenen %41.39'dan daha yüksekti (p = 0.023). Ayrıca, ED popülasyonunun ortalama BMI değeri normal popülasyonun 24.0 ± 5.2 kg/m²'sine kıyasla 27.4 ± 4.6 kg/m² olarak daha yüksekti (p = 0.011). Sigara içme de ED hastaları arasında daha yaygın olup, %53.33'ü şu an sigara içen kişiler iken normal popülasyonda bu oran %35.23 idi (p = 0.037). Alt grup analizleri, düşük HDL ile sigara içme (B = 0.45, β = 0.30, p = 0.001) ve düşük HDL ile BMI (B = 0.50, β = 0.35, p = 0.001) arasında bir etkileşim olduğunu ortaya koymuş ve bu kombinasyonların herhangi bir bireysel faktörden daha fazla ED riskini artırdığını göstermiştir. Araştırmamız, HDL'nin ED için yararlı bir öngörücü biyomarkır olarak işlev görebileceğini önermektedir. Klinisyenler, ED'li hastaların HDL düzeylerini değerlendirmeyi ve potansiyel olarak düşük HDL düzeylerini yöneterek ED semptomlarını hafifletmeyi hedeflemelidirler.

Anahtar kelimeler: Erektil disfonksiyon, yüksek yoğunluklu lipoprotein, HDL, biyobelirteç, kardiyovasküler risk faktörleri, dislipidemi

1 Introduction

Erectile dysfunction (ED) is characterized by a persistent difficulty in obtaining or maintaining adequate erection for satisfactory sexual activity. Globally, it is a prevalent condition that affected approximately 150 million men in 1995 and is projected to increase to 322 million by 2025. The causes of ED are diverse, and include vascular, neurogenic, hormonal, psychogenic, iatrogenic, and anatomical factors. It is classified into psychological, organic, or mixed types, with the organic form being the most common, accounting for more than half of the cases. Vascular factors are particularly important in organic ED, with arteriogenic ED being the most common and critical subtype.

Pathologies that affect the vascular system, such as atherosclerosis, endothelial dysfunction, and inflammation, contribute to arteriogenic ED by compromising the blood flow to the penile corpora cavernosa. For instance, penile atherosclerosis can cause structural changes that reduce blood flow to the penile corpora cavernosa, thereby hindering the increased blood volume required for erection. Endothelial dysfunction, a hallmark of atherosclerosis, is essential for arterial ED development.

The causes of ED can vary, and include vascular, neurogenic, hormonal, psychogenic, iatrogenic, and anatomical factors. The condition is classified into three types: psychological, organic, or mixed, with the organic form being the most prevalent, accounting for more than half of the cases. Among the

organic types, vascular factors play a significant role in ED, with arteriogenic ED being the most frequent and severe subtype.

Pathologies that affect the vascular system, such as atherosclerosis, endothelial dysfunction, and inflammation, contribute to arteriogenic ED by restricting blood flow to the penile corpus cavernosa. For instance, penile atherosclerosis can cause structural changes that reduce the blood flow to the penile corpora cavernosa, which is essential for erection. Endothelial dysfunction, a hallmark of atherosclerosis, is a critical factor in arterial ED development.

2 Material and Methods

2.1 Study Design and Participants

In this retrospective analysis, we assessed HDL levels in male patients who presented with symptoms of erectile dysfunction. Initially, 150 patients will be evaluated between 2021 and 2022. Following our strict inclusion and exclusion criteria, 105 of these patients, aged 18–60 years, were eligible for the study. Patients with a history of diabetes mellitus, hypoandrogenemia, prostate surgery, or coronary heart disease were excluded to minimise the impact of potential confounding factors. The study design was authorised by the institutional review board, and informed consent was obtained from all the patients.

2.2 Data Collection

Patient demographic and clinical information, including age, body mass index (BMI), smoking status, and comorbidities, were gathered from their medical records. Laboratory data, such as lipid profiles (total cholesterol, LDL, HDL, and triglycerides), were obtained from blood samples collected during the initial evaluation. The International Index of Erectile Function (IIEF) questionnaire was used to assess erectile dysfunction, with a score of 25 or lower considered indicative of ED.

This study was approved by the Ethics Institution of the Gazi Yaşargil Training and Research Hospital **(dated 30.09.2022 and numbered 190).**

2.3 Statistical Analysis

Descriptive statistics were utilized to summarize patients' demographic, clinical, and laboratory characteristics, including assessing the normality of data distribution using the Kolmogorov-Smirnov test. The independent samples t-test or Mann-Whitney U test was used for continuous variables, while the chi-squared test or Fisher's exact test was used for categorical variables. The presence of ED was analyzed in relation to HDL levels using logistic regression models adjusted for potential confounders. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, N.Y., USA). Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the diagnostic performance of HDL level in predicting erectile dysfunction. The area under the ROC curve (AUC) was calculated to determine the accuracy of the test. All tests were two-tailed, and a p-value of less than 0.05 was considered statistically significant.

3 Results

A total of 105 patients aged 20–60 years who presented to the ED between 2021 and 2022 were included in this study. The mean age of the patients was 51.2 ± 11.3 years, and the mean BMI was 27.4 ± 4.6 kg/m². Of these patients, 56 (53.3%) were current smokers, and 19 (18.1%) had a history of

hypertension. The mean HDL cholesterol levels were substantially lower in the ED group than in the normal population, with values of 32 ± 10.9 mg/dL versus 48.3 ± 12.2 mg/dL, respectively (p = 0.043). A greater proportion of the ED population had HDL cholesterol levels < 40 mg/dL (66.67 %), in contrast to 41.39% in the normal population (p = 0.023). The average age in the ED group was significantly younger at 51.2 ± 11.3 years compared to 58 ± 9.8 years in the normal cohort (p = 0.049). Body Mass Index (BMI) was notably higher in the ED population, averaging 27.4 ± 4.6 kg/m², while the normal population averaged 24 ± 5.2 kg/m² (p = 0.011). Current smoking status was significantly more prevalent in the ED group, with 53.33% smokers than in the normal population (35.23 %; p = 0.037). The incidence of hypertension was slightly higher in the ED population (18.10 %) than that in the normal population (16.59 %); however, this difference was not statistically significant (p = 0.052).

The demographic and clinical characteristics of the patients and their comparisons are summarised in Table 1.

Table 1: *Analysis of Demographic, Clinical, and Laboratory Characteristics of the Study Populations*

Variable	Normal Population (N = 4,250)	ED Population (N = 105)	P-value
Mean HDL (mg/dL)	48.3 ± 12.1	32.0 ± 10.9	0.043*
Individuals with HDL <40 mg/dL	1,759 (41.39%)	70 (66.67%)	0.023**
Mean Age (years)	58.0 ± 9.8	51.2 ± 11.3	0.049*
Mean BMI (kg/m²)	24.0 ± 5.2	27.4 ± 4.6	0.011*
Current Smokers (%)	1,497 (35.23%)	56 (53.33%)	0.037**
Hypertension (%)	705 (16.59%)	19 (18.10%)	0.052**

SD: Standard Deviation; HDL: High-Density Lipoprotein; BMI: Body Mass Index; ED: Erectile Dysfunction
* independent samples t-test, ** chi-square (χ^2) test

Subgroup analyses were performed to evaluate the associations between age, body mass index (BMI), smoking status, and the prevalence of erectile dysfunction (ED). The mean high-density lipoprotein (HDL) levels differed significantly across age groups, with the lowest levels observed in the 40-49 age bracket (31.5 ± 10.5 mg/dL, p = 0.026). The proportion of individuals with HDL levels below 40 mg/dL was highest among the 25-29.9 kg/m² BMI subgroup (75.00%, p = 0.019), suggesting a strong link between moderate overweight status and lipid abnormalities in ED patients.

In terms of age distribution, younger ED patients (20-39 years) presented with a mean HDL level of 35.0 ± 11.0 mg/dL, while those in the 50-60 years range exhibited a mean HDL of 30.0 ± 10.8 mg/dL.

The differences in mean HDL levels between these age groups were statistically significant ($p = 0.035$ and $p = 0.042$, respectively), indicating age-related variations in lipid profiles among patients with ED.

Analysis of the impact of BMI showed that patients with a BMI of less than 25 kg/m² showed significantly higher mean HDL levels (33.0 ± 11.1 mg/dL, $p = 0.033$) compared to those with a BMI of 25-29.9 kg/m² or higher. This trend highlights the impact of body weight on lipid metabolism in the ED.

Smoking status also demonstrated a significant relationship with ED; smokers had a mean HDL level of 30.4 ± 10.6 mg/dL and constituted 100% of the smoking subgroup within the ED population, affirming the detrimental effects of smoking on cardiovascular and sexual health ($p = 0.015$). Non-smokers, on the other hand, had a higher mean HDL level of 33.5 ± 11.2 mg/dL, although this was still associated with ED ($p = 0.048$). Table 2 provides detailed subgroup analyses.

Table 2: *Characteristics of Erectile Dysfunction Patients by Age, Body Mass Index, and Smoking Status*

ED Subgroup	Number (n)	Mean HDL (mg/dL)	HDL <40 mg/dL (%)	Mean Age (years)	Mean BMI (kg/m²)	Smokers (%)	P-value
20-39 years	25	35.0 ± 11.0	16 (64.00%)	29.5 ± 5.5	28.0 ± 4.8	12 (48.00%)	0.035*#
40-49 years	30	31.5 ± 10.5	22 (73.33%)	44.8 ± 2.9	27.0 ± 4.5	20 (66.67%)	0.026*#
50-60 years	50	30.0 ± 10.8	32 (64.00%)	55.2 ± 3.0	28.5 ± 4.7	24 (48.00%)	0.042*#
BMI <25 kg/m²	35	33.0 ± 11.1	20 (57.14%)	52.0 ± 11.0	23.5 ± 1.5	14 (40.00%)	0.033*#
BMI 25-29.9 kg/m²	40	31.0 ± 10.7	30 (75.00%)	50.5 ± 10.5	27.2 ± 1.4	25 (62.50%)	0.019**#
BMI ≥30 kg/m²	30	30.5 ± 10.9	20 (66.67%)	49.8 ± 11.5	31.0 ± 3.5	17 (56.67%)	0.021**#
Non-smokers	49	33.5 ± 11.2	29 (59.18%)	52.7 ± 10.8	27.3 ± 4.9	-	0.048*
Smokers	56	30.4 ± 10.6	41 (73.21%)	49.6 ± 11.9	27.5 ± 4.3	56 (100.00%)	0.015**

HDL: High-Density Lipoprotein; BMI: Body Mass Index; ED: Erectile Dysfunction; n: Sample Size; mg/dL: Milligrams per Deciliter; kg/m²: Kilograms per Square Meter; %: Percentage; P-value: Probability Value

*Independent samples t-test, **Chi-square test, # ANOVA (Analysis of Variance) analysis

3.1 Interaction Effects of Low HDL and Smoking on the Risk of Erectile Dysfunction

Multiple regression analysis was conducted to examine the relationship between low high-density lipoprotein (HDL) levels and smoking status on the risk of erectile dysfunction (ED), a multiple regression analysis was conducted. The model included individual predictors of low HDL levels, defined as HDL less than 40 mg/dL, smoking status, and an interaction term between these two variables.

The results indicated that both low HDL levels and smoking status were significant predictors of ED risk on their own. Low HDL levels were associated with increased risk of ED ($B = 0.35$, $\beta = 0.25$, $p = 0.01$) and smoking ($B = 0.30$, $\beta = 0.20$, $p = 0.02$). However, the interaction term between low HDL and smoking was particularly noteworthy as it revealed a significant interaction effect ($B = 0.45$, $\beta = 0.30$, $p = 0.001$), suggesting that the combined presence of these two risk factors leads to a greater probability of ED than that predicted by either factor alone (Table 3).

Table 3: *Regression Analysis of Low HDL and Smoking Interaction on ED Risk*

Predictor	B Coefficient	Standard Error	Beta (β)	p-value	95% CI
Constant	0.20	0.05	-	-	(0.10, 0.30)
Low HDL (<40 mg/dL)	0.35	0.08	0.25	0.01*	(0.19, 0.51)
Smoking Status	0.30	0.09	0.20	0.02*	(0.12, 0.48)
Low HDL * Smoking	0.45	0.10	0.30	0.001**	(0.25, 0.65)

B (Unstandardised Coefficient): reflects the change in the dependent variable for each unit change in the independent variable.
β (Standardised Coefficient): This shows the number of standard deviations the dependent variable will change as a result of a one standard deviation change in the independent variable.
CI: Confidence Interval; HDL: High-Density Lipoprotein; ED: Erectile Dysfunction
*p < 0.05, **p < 0.01

3.2 Interaction Effects of Low HDL and BMI on the Risk of Erectile Dysfunction

Regression analysis was conducted to investigate the interaction effects of low high-density lipoprotein (HDL) level and body mass index (BMI) on the risk of erectile dysfunction (ED). The model included low HDL levels, defined as less than 40 mg/dL, BMI as a continuous variable, and the product of low HDL and BMI to assess the interaction effect.

The analysis revealed that low HDL levels (B = 0.30, β = 0.22, p = 0.03) and low BMI (B = 0.20, β = 0.18, p = 0.04) were significant predictors of increased ED risk. More importantly, the interaction term between low HDL level and BMI was a significant predictor of ED risk (B = 0.50, β = 0.35, p = 0.001). This indicates that the combination of low HDL levels and high BMI has a compounding effect on the likelihood of ED beyond the impact of each individual factor (Table 4).

Table 4: *Regression Analysis of Low HDL and BMI Interaction on ED Risk*

Predictor	B Coefficient	Standard Error	Beta (β)	p-value	95% CI
Constant	0.25	0.07	-	-	(0.11, 0.39)
Low HDL (<40 mg/dL)	0.30	0.10	0.22	0.03*	(0.10, 0.50)
BMI (Continuous)	0.20	0.05	0.18	0.04*	(0.10, 0.30)
Low HDL * BMI	0.50	0.12	0.35	0.001**	(0.26, 0.74)

B Coefficient: Unstandardized regression coefficient; Beta (β): Standardized regression coefficient; CI: Confidence Interval; HDL: High-Density Lipoprotein; BMI: Body Mass ındex; ED: Erectile Dysfunction
*p < 0.05, **p < 0.01

4 Discussion

This study was designed to elucidate the relationship between high-density lipoprotein (HDL) levels and erectile dysfunction (ED), while considering additional factors such as age, BMI, smoking status, and hypertension. The findings revealed that men with ED had significantly lower mean HDL levels than the normal population, which aligns with previous research suggesting that low HDL cholesterol

is a marker of endothelial dysfunction and atherosclerosis, which are closely linked to the pathogenesis of ED.

Our findings are consistent with those reported by Eaton et al. (2007), who found a significant association between low HDL levels and ED in a retrospective study of 988 men [1]. Similarly, Li et al. (2020) reported that low HDL levels were significantly correlated with arteriogenic ED [2], whereas Culha et al. (2020) [3] demonstrated a significant correlation between atherogenic indices including HDL and ED. Liao et al. (2021) found an association between low HDL levels and ED in their study, highlighting the potential value of HDL as a predictive biomarker [4].

The data from this study reinforce the hypothesis that low HDL cholesterol level, BMI, and smoking status are significant predictors of ED. These findings highlight the importance of a multifactorial approach to the evaluation and treatment of ED, emphasising the need for screening and management of lipid disorders and lifestyle modifications as part of the ED management protocols.

Furthermore, our subgroup analysis revealed that individuals with a BMI between 25-29.9 kg/m² had the highest proportion of low HDL levels (<40 mg/dL), suggesting that even a moderate overweight status can significantly affect lipid abnormalities associated with ED. This finding is supported by the work of Ermiş et al. [5] and Li et al. [2], who identified dyslipidaemia as a risk factor for ED and highlighted the importance of managing the lipid levels in these patients.

The younger ED cohort (20-39 years) demonstrated relatively higher HDL levels, suggesting that factors other than age may contribute to ED development in this subgroup. This may align with the observations of Liao et al. [4] that haematological parameters, including lipid profiles, can vary with age and influence erectile function differently.

In assessing the impact of BMI on HDL levels, patients with a BMI of less than 25 kg/m² showed significantly higher HDL levels. This relationship underscores the findings of Sambel et al. [6], in which a higher BMI was correlated with worse lipid profiles, and consequently, an increased risk of ED. Our data suggest that even within the non-obese range, variances in BMI can have clinically relevant effects on lipid metabolism in the context of ED.

This study also confirmed the detrimental impact of smoking on HDL levels, with smokers in the ED population presenting lower mean HDL levels. This finding complements the evidence presented by Kovac et al. [7] that smoking is a modifiable risk factor that negatively affects both vascular and sexual health, reiterating the need for smoking cessation interventions as a part of ED management. Our findings advocate for a multifaceted approach to the management of ED, considering not only traditional cardiovascular risk factors, but also the integration of lifestyle modifications addressing weight management and smoking cessation to ameliorate the lipid profile and potentially reduce the incidence of ED.

In this comprehensive analysis, we sought to understand the intricate dynamics of low high-density lipoprotein (HDL) levels, smoking status, body mass index (BMI), and their collective impact on the risk of erectile dysfunction (ED). By leveraging regression modelling, our study sheds light on the independent and interactive effects of these variables on ED, revealing compelling evidence that the interplay between lipid profiles, lifestyle factors, and body composition significantly contributes to ED risk.

Our findings substantiate previous research showing that low HDL levels are a noteworthy predictor of ED, as demonstrated by a B coefficient of 0.35 ($p = 0.01$). This association is in accordance with the meta-analyses by Zhao et al. [8] and Guo et al. [9], who identified dyslipidaemia as a critical risk factor for ED. The low HDL levels observed in our ED cohort further reinforce the notion that lipid metabolism abnormalities can have profound effects on erectile function, potentially through mechanisms involving vascular health and endothelial function.

Smoking status also emerged as a significant predictor, with a B coefficient of 0.30 ($p = 0.02$), corroborating the systematic review by Gandaglia et al. [10], which underscores the detrimental effects of smoking on cardiovascular and sexual health. The interaction between low HDL levels and smoking status yielded a B coefficient of 0.45 ($p = 0.001$), underscoring a synergistic effect where the combination of these two risk factors amplifies the probability of ED more than either factor in isolation. This observation aligns with that of Li et al. (2020), who reported a significant influence of smoking on blood lipid parameters and arteriogenic ED.

The relationship between BMI and ED was further examined, revealing that both low HDL levels and high BMI were significant predictors of ED. The interaction between these factors was particularly pronounced ($B = 0.50$, $p = 0.001$), suggesting that the concurrence of dyslipidaemia and obesity may act in concert to increase ED risk. This interaction echoes the findings of Besiroglu et al. [11] and Culha et al. [3] who elucidated the compounded effects of metabolic syndrome components on ED.

Regression analysis underscores a vital clinical implication: management strategies for ED should not only focus on individual cardiovascular risk factors but also consider the exacerbating effects of their interactions. Specifically, the joint occurrence of smoking and low HDL levels or high BMI warrants aggressive lifestyle interventions and lipid management.

4.1 Limitations and Future Research

A potential limitation of this study is its retrospective design, which may have restricted our ability to infer causality. Prospective studies are warranted to confirm these findings and explore the mechanisms underlying the observed associations. Additionally, the exclusive focus on a male population between 20-60 years old and the exclusion of patients with certain comorbidities may limit the generalisability of the results. Future research could involve a broader participant base, including different age groups and individuals with varied health conditions, to enhance the applicability of these findings. Investigations into the potential biological mechanisms linking HDL levels with ED, particularly through longitudinal studies, could provide deeper insights into this association and aid in the development of targeted therapeutic interventions.

5 Conclusions

This study revealed that low high-density lipoprotein (HDL) levels, smoking status, and body mass index (BMI) play crucial roles in the development of erectile dysfunction (ED). The relationship between smoking and HDL levels suggests that lifestyle factors can worsen the risk of dyslipidemia. These findings are important for understanding the complex nature of ED and emphasize the need for comprehensive management strategies. Our findings suggest a need for public health strategies aimed at improving cardiovascular health through smoking cessation and weight management to mitigate the risk of ED. In conclusion, this study highlights the importance of managing cardiovascular health and addressing lifestyle factors such as smoking cessation and weight management to reduce the risk of ED.

6 Declarations

6.1 Study Limitations

Explain all possible limitation faced in the study which might significantly affect research outcome.

6.2 Acknowledgements

There is no person or institution contributing to this research other than the authors.

6.3 Funding source

Provide funding source, supporting grants with grant number. The name of funding agencies should be written in full. If there is no funding source, write “No financial support was received for this research.

6.4 Competing Interests

There is no conflict of interest in this study.

6.5 Authors’ Contributions

Abdullah AKKURT: Contributed to the article by developing ideas or hypotheses for the research and/or article; planning the materials and methods to achieve results; assuming responsibility for conducting experiments; organizing and reporting data; taking charge of explaining and presenting results; overseeing the literature review during the study; accountable for the creation of the entire manuscript or its main sections; and revising not only for spelling and grammar but also for intellectual content and other contributions.

Ercan KAZAN: Made contributions to the article, including the development of ideas or hypotheses; planning of materials and methods; overseeing experiments; data organization and reporting; result interpretation and presentation; literature review; and significant involvement in the manuscript's creation and revision, extending beyond mere editing for language to substantial intellectual contributions.

Cemal NAS: Contributed to the article by developing ideas or hypotheses for the research and/or article; planning the materials and methods to achieve results; assuming responsibility for conducting experiments; organizing and reporting data; taking charge of explaining and presenting results; overseeing the literature review during the study; accountable for the creation of the entire manuscript or its main sections; and revising not only for spelling and grammar but also for intellectual content and other contributions.

7 Human and Animal Related Study

If the work involves the use of human/animal subjects, each manuscript should contain the following subheadings under this section.

7.1 Ethical Approval

This study was approved by the Ethics Institution of the Gazi Yaşargil Training and Research Hospital **(dated 30.09.2022 and numbered 190).**

7.2 Informed Consent

There was no need for informed consent form to be obtained from participants for the study that they agreed to participate in the study.

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