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Metabolic and hormonal biomarkers of erectile dysfunction: the role of atherogenic index and testosterone-to-estradiol ratio

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Abstract

Background: We aimed to investigate the relationship between erectile dysfunction (ED), the atherogenic index of plasma (AIP) and the testosterone-to-estradiol (T/E2) ratio. Given the role of metabolic and hormonal imbalances in ED, we sought to determine whether these parameters could serve as potential biomarkers for ED risk assessment. **Methods**: A retrospective included 117 ED patients and 115 controls. Participants' demographic, clinical and biochemical data were collected, including body mass index (BMI), lipid profile and hormone levels. The AIP was calculated as log10 (triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C)) and the T/E2 ratio was determined. Univariate and multivariate logistic regression analyses were conducted to assess the associations between these factors and ED. **Results**: ED patients had significantly higher AIP levels (0.639 ± 3.02) compared to controls (0.131 ± 0.15, $p < 0.001$). Additionally, the T/E2 ratio was significantly lower in ED patients (10.96 ± 5.97) than in controls (17.31 ± 8.12, $p < 0.001$). Obesity, as indicated by a higher BMI, was also strongly associated with ED ($p < 0.001$). Multivariate analysis identified BMI Odds Ratio (OR: 1.354, $p < 0.001$), E2 levels (OR: 1.080, $p < 0.001$) and AIP (OR: 2.31, $p < 0.001$) as independent predictors of ED. **Conclusions**: We suggest that both metabolic and hormonal imbalances contribute to ED pathophysiology. The increased AIP levels observed in ED patients highlight the potential role of lipid metabolism dysfunction and atherosclerosis in erectile function impairment. The reduced T/E2 ratio indicates the influence of hormonal imbalance, particularly the detrimental effects of increased aromatization of testosterone into estradiol. Given that AIP and T/E2 are associated with cardiovascular and endocrine health, they may serve as valuable biomarkers for early ED risk assessment. These results emphasize the importance of lifestyle interventions, weight management and metabolic optimization in preventing and managing ED.

Keywords

Erectile dysfunction (ED); Atherogenic index of plasma (AIP); Testosterone-to-estradiol ratio (T/E2)

Biomarcadores metabólicos y hormonales de la disfunción eréctil: el papel del índice aterogénico y de la relación testosterona/estradiol

Resumen

Antecedentes: Nuestro objetivo fue investigar la relación entre la disfunción eréctil (DE), el índice aterogénico del plasma (IAP) y la relación testosterona/estradiol (T/E2). Dado el papel de los desequilibrios metabólicos y hormonales en la fisiopatología de la DE, se evaluó si estos parámetros pueden servir como biomarcadores potenciales para la evaluación del riesgo de DE. **Métodos**: Se realizó un estudio retrospectivo con 117 pacientes con DE y 115 controles. Se recopilaron datos demográficos, clínicos y bioquímicos, incluidos el índice de masa corporal (IMC), el perfil lipídico y los niveles hormonales. El IAP se calculó como log10 (triglicéridos/colesterol HDL), y se determinó la relación T/E2. Se aplicaron análisis de regresión logística univariada y multivariada para evaluar las asociaciones entre estos factores y la DE. **Resultados**: Los pacientes con DE presentaron niveles significativamente más altos de IAP (0.639 ± 3.02) en comparación con los controles (0.131 ± 0.15, $p < 0.001$). Además, la relación T/E2 fue significativamente menor en los pacientes con DE (10.96 ± 5.97) que en los controles (17.31 ± 8.12, $p < 0.001$). La obesidad, reflejada en un mayor IMC, también se asoció fuertemente con la DE ($p < 0.001$). El análisis multivariado identificó al IMC (razón de probabilidades (OR): 1.354, $p < 0.001$), los niveles de E2 (OR: 1.080, $p < 0.001$) y el IAP (OR: 2.31, $p < 0.001$) como predictores independientes de la DE. **Conclusiones**: Nuestros hallazgos sugieren que los desequilibrios metabólicos y hormonales contribuyen de manera significativa a la disfunción eréctil. El aumento del IAP observado en pacientes con DE resalta el posible papel de la disfunción del metabolismo lipídico y la aterosclerosis en la alteración de la función eréctil. La reducción de la relación T/E2 indica un impacto hormonal desfavorable, particularmente por el aumento de la aromatización de testosterona a estradiol. Dado que el IAP y la relación T/E2 están relacionados con la salud cardiovascular y endocrina, pueden constituir biomarcadores útiles para la evaluación temprana del riesgo de DE. Estos resultados subrayan la importancia de las intervenciones sobre el estilo de vida, el control del peso y la optimización metabólica en la prevención y manejo de la DE.

Palabras Clave

Disfunción eréctil; Índice aterogénico del plasma (IAP); Relación testosterona/estradiol (T/E2)

1. Introduction

Erectile dysfunction (ED) is recognized as a condition that can adversely affect the mental and physical health, as well as the life satisfaction, of both men and their partners. It is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual intercourse [1, 2]. Although traditionally regarded as a urological condition, ED is now increasingly recognized as a potential early marker of systemic vascular and endocrine dysfunction, particularly in the context of cardiovascular risk [3]. Research has established a strong pathophysiological link between ED and cardiovascular diseases (CVD), with both sharing common risk factors [4]. Atherosclerosis, endothelial dysfunction, and subclinical inflammation play a crucial role in the development of ED, as well as the deterioration of cardiovascular health [5]. Factors such as smoking, obesity, diabetes and dyslipidemia not only contribute to the development and progression of atherosclerosis but also damage the structure of penile blood vessels, thereby triggering ED [6]. Therefore, ED may be considered an early indicator, especially for CVD [7].

Although numerous biochemical markers have been identified for assessing atherosclerosis, the Atherogenic Plasma Index (AIP) has gained prominence recently due to its ease of measurement and high prognostic value [8, 9]. AIP, calculated as the logarithmic transformation of the triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) ratio, strongly correlates with the size of atherogenic and anti-atherogenic lipoprotein particles [10, 11]. This correlation makes AIP a highly reliable predictor of CVD. Studies have demonstrated that elevated AIP levels are associated with the progression of atherosclerotic processes, making it a more precise risk indicator than traditional lipid profile parameters [12].

In addition to these metabolic and vascular factors, hormonal balance, especially the testosterone-to-estradiol (T/E2) ratio, plays a critical role in erectile function [13]. Testosterone is a key regulator of male sexual function and has an impact on libido, erectile mechanisms and overall penile tissue integrity [14]. Low testosterone levels may contribute to the development of ED by causing endothelial dysfunction and apoptosis of smooth muscle cells in penile arteries [15]. Although E2 is present in lower concentrations in men, it plays a regulatory role in vascular health [16]. However, an imbalance in the T/E2 ratio—characterized by significantly increased aromatization of testosterone to E2 due to obesity or metabolic disorders—increases the risk of ED. High E2 levels may worsen ED by promoting inflammatory responses and causing vascular dysfunction [9, 10]. Therefore, the T/E2 ratio stands out as an important biomarker for assessing the impact of hormonal balance on ED.

While AIP is widely recognized as an important biomarker for cardiovascular risk assessment, its potential relationship with ED remains largely unexplored. Given AIP's impact on cardiovascular health, investigating its association with penile vascular function holds significant clinical interest. In contrast, the T/E2 ratio plays a critical role in determining the impact of hormonal balance on erectile function. This study aims to evaluate the relationship between the AIP and the T/E2 ratio in the context of ED.

2. Materials and methods

Our study is a hospital-based case-control study conducted through a retrospective review of patients who presented to the Izmir Katip Celebi University Ataturk Training and Research Hospital. The study included 117 patients diagnosed with ED in 2024 and a control group of 115 individuals without ED. All participants were consecutively enrolled from the outpatient urology clinic between January and December 2024. The ED group included men who presented with complaints of erectile dysfunction during routine consultations. At the same time, the control group consisted of age-matched, sexually active men attending the urology clinic for unrelated, non-sexual complaints such as mild benign prostatic hyperplasia (BPH), or lower urinary tract symptoms (LUTS) including frequency, urgency or nocturia. None of these individuals had a history or symptoms of erectile dysfunction, and all had International Index of Erectile Function-5 (IIEF-5) scores above 22, confirming normal erectile function. We acknowledge that metabolic and hormonal alterations may also be present in patients with BPH/LUTS; however, due to the retrospective nature of the study, recruitment of completely asymptomatic men was not feasible. Therefore, this real-world control group was selected based on the absence of ED-related complaints and preserved sexual function, which was deemed appropriate for comparative purposes. No patients were specifically referred from other specialties or selected through public recruitment.

The study was approved by the Institutional Ethics Committee of Izmir Katip Celebi University (Approval No: 2025-SAEK-0353, Date: 14 April 2025), and informed consent was obtained from all participants.

The inclusion criteria consisted of being between the ages of 40 and 75, experiencing ED symptoms for at least six months (for the case group), and the absence of ED symptoms in the control group. Both groups comprised sexually active individuals who had maintained a regular sexual life for at least six months.

Patients with severe cardiovascular disease, neurological disorders (such as multiple sclerosis, spinal cord injury or lumbar disc herniation), as well as those with a history of major pelvic surgery, were excluded from the study. Additionally, individuals diagnosed with hypogonadism, those receiving hormone replacement therapy, patients who had undergone ED treatment within the past three months, and those with a history of acute systemic illness were not included.

To avoid the inclusion of psychogenic ED cases, patients with normal nocturnal erections and those who experienced erections during masturbation were excluded. Further subclassification of organic ED into vascular, neurogenic, or endocrine categories was not performed due to the retrospective nature of the study and the limitations of available diagnostic data (*e.g.*, absence of penile Doppler ultrasound, nocturnal penile tumescence testing or neurophysiological evaluations). Moreover, individuals with a sudden onset of ED were assessed for psychogenic causes and excluded if necessary.

ED was diagnosed based on the International IIEF-5 criteria. Patients with an IIEF-5 score below 22 were classified into the ED group, whereas those with a score above 22 were included in the control group.

Demographic, clinical and biochemical data were obtained from hospital records and patient history forms. The study variables included age, BMI, smoking and alcohol consumption, presence of hypertension, diabetes and coronary artery disease, as well as laboratory parameters such as lipid profile high-density lipoprotein cholesterol (HDL), triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL) and hormone profile (total testosterone, estradiol). Additionally, the T/E2 ratio and the AIP, calculated using the log-transformed triglyceride-to-HDL ratio, were analyzed. Total testosterone (T) was measured in ng/dL and estradiol (E2) in pg/mL. The T/E2 ratio was calculated by dividing testosterone (ng/dL) by estradiol (pg/mL), in accordance with established methods. Statistical analysis was performed using SPSS 22.0 (IBM Corp., Armonk, NY, USA) software. Continuous variables were presented as mean $\pm$ standard deviation, while categorical variables were reported as frequencies and percentages. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Comparisons between groups were made using the Student's *t*-test for normally distributed variables, the Mann-Whitney U test for non-normally distributed variables, and the Chi-square (χ^2) test for categorical variables.

Univariate analyses were initially performed to identify independent risk factors for ED, followed by multivariate logistic regression analysis for significant variables. AIP was rescaled by a factor of 10 to improve clinical interpretability, and odds ratios were reported per 0.1-unit increase in the logistic regression model. The goodness-of-fit for the regression model was assessed using the Hosmer-Lemeshow test, and a *p*-value of less than 0.05 was considered statistically significant.

3. Results

The study included a total of 232 participants, comprising 117 patients diagnosed with ED and 115 control subjects without ED. The mean IIEF-5 score among patients in the ED group was 13.2 $\pm$ 4.6, reflecting predominantly moderate to severe erectile dysfunction. In contrast, the mean IIEF-5 score in the control group was 24.6 $\pm$ 1.1, consistent with normal erectile function ($p < 0.001$). Mean age of all participants was 52.4 $\pm$ 11.87 years, with a statistically significant difference between cases (50.39 $\pm$ 11.22 years) and controls (54.43 $\pm$ 12.22 years, $p = 0.007$). The prevalence of hypertension (36.8% in ED group *vs.* 33% in controls, $p = 0.554$), diabetes mellitus (28.2% in ED group *vs.* 22.6% in controls, $p = 0.328$), and history of coronary artery disease (31.6% in ED group *vs.* 20.9% in controls, $p = 0.063$) did not show statistically significant differences between groups.

Lifestyle factors such as smoking and alcohol consumption were evaluated, revealing a significantly higher proportion of current smokers among ED patients (65% *vs.* 47.8%, $p = 0.009$). In contrast, alcohol use did not differ significantly between groups (24.8% in ED group *vs.* 20% in controls, $p = 0.382$).

Anthropometric and metabolic parameters were also analyzed. The mean BMI was significantly higher in ED patients (27.04 $\pm$ 3.51 kg/m^2) compared to controls (23.66 $\pm$ 2.97 kg/m^2, $p < 0.001$). Lipid profile assessment showed signif-

icantly lower HDL cholesterol levels in ED patients (38.74 ± 7.44 mg/dL) compared to controls (44.65 ± 7.93 mg/dL, $p < 0.001$). In contrast, triglyceride levels were significantly increased in the ED group (221.63 ± 86.39 mg/dL) relative to controls (141.77 ± 48.46 mg/dL, $p < 0.001$).

Hormonal analyses revealed that ED patients had significantly lower testosterone levels (387.03 ± 160.65 ng/dL) compared to controls (485.34 ± 190.97 ng/dL, $p < 0.001$), while E2 levels were significantly higher in the ED group (30.75 ± 10.19 pmol/L) than in controls (38.39 ± 9.88 pmol/L, $p < 0.001$). Consequently, the T/E2 ratio was significantly reduced in ED patients (10.96 ± 5.97) compared to controls (17.31 ± 8.12, $p < 0.001$).

AIP was significantly increased in the ED group (0.639 ± 3.02) compared to controls (0.131 ± 0.15, $p < 0.001$). Comparison of the Demographic and Clinical Characteristics of each group is presented in Table 1.

Univariate analysis identified several significant prognostic factors for ED, including age ($p = 0.010$), BMI ($p < 0.001$), HDL cholesterol ($p < 0.001$), triglycerides ($p < 0.001$), testosterone ($p < 0.001$), E2 ($p < 0.001$), T/E2 ratio ($p < 0.001$), AIP ($p < 0.001$) and smoking status ($p = 0.009$). In multivariate logistic regression, BMI (OR: 1.354, $p < 0.001$), E2 (OR: 1.080, $p < 0.001$), and AIP (per 0.1-unit increase) remained an independent predictor of ED with an odds ratio of 2.31 (95% (Confidence Interval) CI: 1.52–3.50, $p < 0.001$). Univariate analyses in ED patients are presented in Table 2.

In the multivariate logistic regression analysis, BMI, E2 levels and AIP were identified as independent prognostic factors for ED. The odds ratio (OR) for BMI was 1.354 (95% CI: 1.202–1.526, $p < 0.001$), indicating that an increase in BMI is associated with a higher risk of ED. Similarly, higher E2 levels were significantly correlated with ED risk, with an odds ratio of 1.080 (95% CI: 1.042–1.120, $p < 0.001$), calculated per 1 pg/mL increase in E2 concentration. Notably, AIP exhibited the strongest association with ED, with an OR of 2.31 (95% CI: 1.52–3.50, $p < 0.001$), suggesting a substantial impact of lipid-related metabolic alterations on erectile function. Clinical outcomes in ED patients based on multivariate analyses are presented in Table 3.

TABLE 1. Comparison of demographic and clinical characteristics of erectile dysfunction and control groups.

Patient Characteristics	ED Group	Control Group	*p* Value
Age (yr) (mean, SD)	50.39 ± 11.22	54.43 ± 12.22	0.007**
IIEF-5 (mean, SD)	13.2 ± 4.6	24.6 ± 1.1	<0.001**
Hypertension (n, %)			
Yes	43 (36.8)	38 (33.0)	0.554***
No	74 (63.2)	77 (67.0)	
Diabetes mellitus (n, %)			
Yes	33 (28.2)	26 (22.6)	0.328***
No	84 (71.8)	89 (77.4)	
CVD (n, %)			
Yes	37 (31.6)	24 (20.9)	0.063***
No	80 (68.4)	91 (79.1)	
Smoke (n, %)			
Yes	76 (65.0)	55 (47.8)	0.009***
No	41 (35.0)	60 (52.2)	
Alcohol (n, %)			
Yes	29 (24.8)	23 (20.0)	0.382***
No	88 (75.2)	92 (80.0)	
BMI (kg/m^2) (mean, SD)	27.04 ± 3.51	23.66 ± 2.97	<0.001*
HDL-Cholesterol (md/dL) (mean, SD)	38.74 ± 7.44	44.65 ± 7.93	<0.001**
Triglycerides (mg/dL) (mean, SD)	221.63 ± 86.39	141.77 ± 48.46	<0.001**
Testosterone (ng/dL) (mean, SD)	387.03 ± 160.65	485.34 ± 190.97	<0.001**
Estradiol (pmol/L) (mean, SD)	30.75 ± 10.19	38.39 ± 9.88	<0.001**
T/E2 Ratio (mean, SD)	10.96 ± 5.97	17.31 ± 8.12	<0.001**
AIP (mean, SD)	0.639 ± 3.02	0.131 ± 0.15	<0.001**

**Student's t test, **Mann-Whitney U test, ***Chi-square test.*
IIEF-5: International Index of Erectile Function-5; CVD: Cardiovascular diseases; BMI: Body mass index; T/E2 Ratio: Testosterone/Estradiol Ratio; AIP: Atherogenic Plasma Index; HDL: High-density lipoprotein; ED: Erectile dysfunction; SD: Standard Deviation.

TABLE 2. Odds ratios on univariate analyses in erectile dysfunction patients.

Parameters	Erectile Dysfunction (Univariate)		
	Odds ratio	95% CI	*p* Value
Age (yr)	0.971	0.949–0.993	0.010
Hypertension			
No	1.177	0.686–2.022	0.554
Yes		reference	
Diabetes mellitus			
No	1.345	0.742–2.436	0.328
Yes		reference	
CVD			
No	1.754	0.967–3.180	0.064
Yes		reference	
Smoke			
No	2.022	1.193–3.426	0.009
Yes		reference	
Alcohol			
No	1.318	0.709–2.451	0.383
Yes		reference	
BMI (kg/m^2)	1.376	1.247–1.519	<0.001
HDL-Cholesterol (md/dL)	0.900	0.865–0.937	<0.001
Triglycerides (mg/dL)	1.021	1.015–1.027	<0.001
Testosterone (ng/dL)	0.997	0.995–0.998	<0.001
Estradiol (pmol/L)	1.080	1.049–1.112	<0.001
T/E2 Ratio	0.877	0.838–0.917	<0.001
AIP	2.310	1.520–3.500	<0.001

CVD: Cardiovascular diseases; BMI: Body mass index; T/E2 Ratio: Testosterone/Estradiol Ratio; AIP: Atherogenic Plasma Index; HDL: high-density lipoprotein; CI: Confidence Interval.
Note: The inverse associations of age and smoking with ED observed in univariate analysis were not confirmed in multivariate analysis, likely due to confounding or sample-specific characteristics.

TABLE 3. Adjusted odds ratio and 95% confidence intervals for clinical outcomes in erectile dysfunction patients with multivariate analyses.

Parameters	Erectile Dysfunction	
	OR (95% CI)	*p* Value
BMI	1.354 (1.202–1.526)	<0.001
Estradiol	1.080 (1.042–1.120)	<0.001
AIP (per 0.1-unit increase)	2.31 (1.52–3.50)	<0.001

BMI: Body mass index; AIP: Atherogenic Plasma Index; OR: odds ratio; CI: Confidence Interval.

4. Discussion

We examined the relationship between anthropometric measurements and specific laboratory parameters that were considered predictive of ED. Our findings indicated that a high BMI, elevated E2 levels, an increased AIP, and a low T/E2 ratio were all associated with the presence of ED.

Age differed significantly between the ED and control groups ($p = 0.007$), with control participants being, on average, older. Although this may initially appear counterintuitive, it is important to note that age may not function as a direct biological determinant of erectile dysfunction. Instead, age may serve as a proxy variable that reflects the cumulative burden of metabolic and vascular changes, such as endothelial dysfunction, chronic inflammation, reduced testosterone production and increased aromatase activity over time. These age-related pathophysiological processes may contribute to the development of ED. Therefore, the observed age difference may be better interpreted as an indirect indicator of underlying mechanisms rather than an independent etiological

factor. Interestingly, in univariate analysis, age and smoking showed a negative association with ED. However, these findings are likely confounded by sample composition, as the control group included older men with preserved erectile function and differing smoking histories. These variables were not significant in the multivariate model, reinforcing the interpretation that the observed associations were confounded rather than indicative of a true protective effect.

The relationship between ED and the T/E2 ratio is important for understanding the effects of hormonal balance on sexual function. Testosterone plays a critical role in male sexual health, influencing functions such as sexual desire, erection attainment and maintenance [17]. Testosterone, in particular, exerts influence on nitric oxide synthase (NOS) and the RhoA/Rho kinase pathway, both of which are integral to erectile health [18]. Low testosterone levels can lead to symptoms such as reduced sexual drive and ED [19]. Furthermore, testosterone undergoes a process known as aromatization, converting into E2 [20]. E2, while present at lower levels in men, must be maintained within a precise balance [21]. Any disruption to this balance—particularly an increase in E2 levels accompanied by a decline in the T/E2 ratio—can significantly impact hormonal equilibrium. This conversion has implications for the hypothalamic-pituitary-gonadal axis, resulting in reduced gonadotropin secretion and lower circulating testosterone levels [22]. The presence of estrogen can negatively impact male sexual behavior by diminishing pressure within the cavernous cavity and impairing nitric oxide-mediated relaxation of spongiform smooth muscle [18, 23].

In Pan *et al.*'s [24] study, nocturnal penile tumescence tests were conducted on all participants to examine the relationship between endocrine differences. The study demonstrated a negative correlation between the E2/T ratio and penile erection, particularly at the penile base. In their study, El-Sakka *et al.* [23] emphasized that low testosterone levels have a primary impact on ED; however, they also found that concurrently increased E2 levels exert an additional detrimental effect.

We observed significantly higher E2 levels and lower T/E2 ratio in patients with ED. These findings suggest that this hormonal imbalance may negatively impact vascular health, thereby contributing to the development of ED.

Our findings are consistent with previous studies that evaluated the metabolic and hormonal contributors to ED. For instance, El-Sakka *et al.* [23] emphasized that high estradiol levels exert an additional negative impact beyond testosterone deficiency. Pan *et al.* [24] demonstrated that a reduced T/E2 ratio negatively correlates with nocturnal penile tumescence. Similarly, Ermiş *et al.* [8] and Guo *et al.* [25] identified significantly elevated AIP values in men with ED, supporting the role of dyslipidemia in ED pathophysiology [13, 23, 25]. While most previous studies have supported the association between metabolic/hormonal imbalance and ED, some authors have reported inconsistencies in the predictive value of individual parameters such as estradiol or HDL levels, possibly due to population heterogeneity or methodological differences [26]. These discrepancies highlight the need for standardized protocols in future research to delineate subtype-specific biomarker profiles in ED.

Compared to these previous reports, our study provides a combined evaluation of both metabolic (AIP) and hormonal (T/E2) indicators in a single multivariate model, allowing a more integrated risk stratification for ED.

AIP is recognized as a significant indicator of lipid metabolism and cardiovascular health, as it reflects the balance between atherogenic and anti-atherogenic lipids [27]. Relevant literature indicates that abnormalities in AIP may be associated with imbalances in the endocrine system, which can result in decreased levels of androgens such as testosterone [28]. This decrease may indirectly contribute to ED. Furthermore, atherosclerosis, a vascular condition, can impede blood flow to the genital organs, thereby diminishing the ability to achieve an erection. Given that AIP serves as a marker for assessing the risk of atherosclerosis, its potential role as a biomarker for ED warrants careful consideration.

Ermis *et al.* [8] reported significantly higher AIP values in the ED group compared to the control group within a population identified as having vasculogenic erectile dysfunction. Specifically, the mean AIP value in patients with ED was reported as 0.51 ± 0.15, whereas it was 0.29 ± 0.11 in the control group. This finding is consistent with our results, where we observed significantly elevated AIP levels in the ED group (0.639 ± 3.02) compared to controls (0.131 ± 0.15, $p < 0.001$). Additionally, Ermis *et al.* [8] identified a positive correlation between AIP levels and ED severity, further supporting the role of lipid-related metabolic alterations in erectile dysfunction.

Similarly, Guo *et al.* [25] emphasized the importance of early identification of individuals with elevated AIP values. In their analysis of a large U.S. population cohort, men in the highest AIP tertile had 49% higher odds of ED compared to those in the lowest tertile (OR: 1.49, 95% CI: 1.15–1.91), and each one-unit increase in AIP was associated with a 65% increase in ED risk (adjusted OR: 1.65, 95% CI: 1.03–2.64). These findings reinforce the predictive utility of AIP and are consistent with our observation of a robust independent association between AIP and ED. Minor differences in effect size across studies may reflect variations in study design, population characteristics, or AIP measurement scales.

Our study revealed significantly elevated AIP levels in the ED group, which aligns with these findings. These results suggest that AIP may serve not only as a marker of cardiovascular disease risk but also as a potential early indicator of ED.

The connection between obesity and erectile function is both significant and concerning. An increase in BMI can profoundly disrupt the delicate structure of penile blood vessels, fostering conditions such as endothelial dysfunction, inflammation and oxidative stress [29, 30]. Moreover, obesity plays a pivotal role in altering testosterone metabolism, resulting in heightened E2 levels as aromatase activity in adipose tissue ramps up [31]. This condition also lays the groundwork for insulin resistance, which often leads to troubling hyperglycemia. Elevated blood sugar levels not only damage nerves but also jeopardize the integrity of blood vessels, further diminishing erectile performance [32]. Compounding this issue, both insulin resistance and hyperglycemia intensify endothelial dysfunction, creating a troubling cycle that significantly raises the risk of ED [32].

Similarly, our study found that a high BMI was associated

with ED. This finding aligns with existing literature and reinforces the detrimental effects of obesity on erectile function. Factors such as obesity-induced endothelial dysfunction, hormonal imbalances and insulin resistance play a significant role in the pathophysiology of ED.

Maintaining a healthy weight and adopting lifestyle modifications are likely to be crucial in reducing ED risk and preserving sexual health.

This study has several limitations that should be considered when interpreting the results. First, this study has a relatively small sample size, which may restrict the generalizability of the findings to the broader population. In addition, its retrospective and hospital-based nature may limit the generalizability of the findings. We also note that the exclusion of patients with psychogenic ED—initially regarded as a limitation—should instead be viewed as a methodological strength. This approach enhanced the internal validity of the study by reducing heterogeneity and minimizing potential confounding from non-organic factors, allowing for a more straightforward interpretation of the associations between biological markers and organic erectile dysfunction. Another limitation is that hormonal and lipid parameters were assessed simultaneously, which may not fully capture dynamic fluctuations over time.

Lastly, the absence of etiological subclassification of ED into vascular, neurogenic or endocrine origins represents a methodological limitation. These subtypes may exhibit distinct biochemical profiles, and the inability to distinguish them could have introduced confounding. Future prospective studies incorporating objective vascular and neurological assessments are needed to explore these relationships more precisely. Furthermore, due to the lack of subclassification, it is possible that vasculogenic ED constituted the majority of our cohort, which may have exaggerated the strength of association with AIP. This potential overrepresentation should be considered when interpreting the findings.

5. Conclusions

High AIP levels and lower T/E2 ratios were strongly associated with ED, indicating their potential as biomarkers for evaluating vascular and endocrine factors contributing to ED. Moreover, obesity was identified as a significant factor influencing both metabolic and hormonal imbalances, further increasing the risk of ED. These findings highlight the importance of early metabolic and hormonal assessments in ED patients to inform preventive and therapeutic approaches. Lifestyle changes, such as weight management and cardiovascular risk reduction, may play a crucial role in mitigating ED and enhancing overall vascular health.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

AG and EMY—designed the research study; wrote the manuscript. EMY and KD—performed the research. SNG and YA—provided help and advice on methodology and interpretation. EMK—analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Institutional Ethics Committee of Izmir Katip Celebi University (Approval No: 2025-SAEK-0353, Date: 14 April 2025). Written informed consent was obtained from all participants prior to data collection, in accordance with the Declaration of Helsinki.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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