Arch Rheumatol 2024;39(3):393-403
doi: 10.46497/ArchRheumatol.2024.10486

ORIGINAL ARTICLE

Gout and erectile dysfunction: Increased carotid intima-media thickness is independently associated with greater likelihood for erectile dysfunction

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Received: September 14, 2023
Accepted: July 01, 2024
Published online: August 24, 2024

Citation: Yigit E, Yasar S, Can M, Bayraktar Z. Gout and erectile dysfunction: Increased carotid intima-media thickness is independently associated with greater likelihood for erectile dysfunction. Arch Rheumatol 2024;39(3):393-403. doi: doi: 10.46497/ArchRheumatol.2024.10486.

ABSTRACT

Objectives: The study aimed to compare gout patients and healthy subjects in terms of erectile dysfunction, carotid intima-media thickness (CIMT), and other variables and to investigate the relationship between CIMT and erectile dysfunction.

Patients and methods: This cross-sectional study was conducted with 134 male gout patients (median age: 56 years; range, 48 to 62 years) and 104 healthy males (median age: 47 years; range, 40.5 to 54.5 years) between September 2022 and June 2023. Age, comorbidities, height, weight, laboratory results, gout treatment data, insulin resistance evaluated by the homeostatic model assessment for insulin resistance, presence and severity of erectile dysfunction evaluated by the six-item International Index of Erectile Function erectile function domain (IIEF-EF), and CIMT measured by ultrasound were assessed.

Results: Hypertension, hyperlipidemia, greater insulin resistance, erectile dysfunction, and bilaterally increased CIMT were significantly more common in the gout group. The mean IIEF-EF score of gout patients was significantly lower than that of controls. Multivariable logistic regression revealed increased CIMT as the sole parameter independently associated with erectile dysfunction ($p=0.010$). When both groups were categorized into CIMT-based subsets, erectile dysfunction was present in 97.9% of patients with coexistence of gout and increased CIMT (≥0.9 mm), a significantly higher proportion compared to the other three subsets ($p<0.001$).

Conclusion: Increased CIMT was the only factor independently associated with a greater likelihood of erectile dysfunction in patients with and without gout; however, coexistence of gout and increased CIMT appears to result in a significantly elevated risk for erectile dysfunction.

Keywords: Cardiovascular diseases, carotid intima-media thickness, dysfunction, erectile, gout, insulin resistance.

Gout is the most prevalent form of inflammatory arthritis globally[1] and is estimated to have an incidence ranging from 0.1 to 6.8% in different populations.[2] It is characterized by the accumulation of monosodium urate crystals in joints, tendons, and other tissues as a result of persistently elevated urate levels (hyperuricemia). Patients suffer from recurrent inflammatory attacks.[2]

Hyperuricemia is the triggering feature of the disease and is defined as having a serum uric acid concentration ≥6.8 mg/dL.[1] It increases the risk for rheumatological adverse outcomes and may lead to cardiovascular, renal/genitourinary, metabolic, and ophthalmological comorbidities.[1-3] One of the most common genitourinary comorbidities is erectile dysfunction, as demonstrated by many studies.[3-6] There is no paucity of evidence concerning possible factors that are associated with erectile dysfunction in gout, including hyperuricemia,[7-10] endothelial injury,[11] comorbidities,[2,6,12] inflammation,[3,11] vitamin D deficiency,[11] metabolic syndrome,[11] depression,[11] insulin resistance,[13] gout treatment,[14] and increased lipoprotein(a) levels.[15] However, the exact cause for the frequency of erectile dysfunction in gout

patients is unknown. This is largely due to the underlying characteristics of patients and the multifaceted relationships between gout, erectile dysfunction, and comorbid conditions; therefore, a precise causal relationship has not been documented.[3,4,7,11] One of the most common comorbidities in gout patients is cardiovascular disease (CVD),[5,6] and CVD has been strongly associated with erectile dysfunction and other comorbidities.[4,16] The bidirectional relationships between gout and CVD[17] and between CVD and erectile dysfunction[16,18] complicate our understanding of direct relationships. It is also interesting to note that erectile dysfunction has been presented as a predictor for CVD in some studies.[16,18] Carotid intima-media thickness (CIMT) is a well-established surrogate marker for cardiovascular conditions,[19,20] and there have been attempts to assess potential relationships between erectile dysfunction and CIMT.[20,21] However, there is no data regarding the relationship between CIMT and the risk for erectile dysfunction in gout patients. We postulated that the higher risk of erectile dysfunction in patients with gout may be related to increased CIMT. Therefore, we aimed to compare healthy subjects and gout patients in terms of erectile dysfunction, CIMT, and other variables and to investigate the relationships between CIMT and erectile dysfunction.

PATIENTS AND METHODS

This cross-sectional study was carried out by the urology, internal medicine, and rheumatology departments of the İstanbul Medipol University Faculty of Medicine between September 2022 and June 2023. The study included 134 male patients (median age: 56 years; range, 48 to 62 years) with gout (gout group) and 104 male participants (median age: 47 years; range, 40.5 to 54.5 years) in the control group. The control group consisted of subjects who applied to the internal medicine outpatient clinic for any reason other than gout or for routine controls and met the inclusion criteria. The exclusion criteria for both groups were as follows: being younger than 35 years of age, presence of diabetes, cerebrovascular disease, coronary artery disease, congestive heart failure, thyroid dysfunction, chronic obstructive pulmonary disease, chronic kidney failure, chronic liver disease, neurological or psychiatric disease, using medication for insulin resistance or hyperlipidemia, the presence of uncontrolled hypertension, and missing data on any of the variables included in the study. Furthermore, for the gout group, gout patients older than 65 years were excluded since the incidence of erectile dysfunction may increase due to different reasons in older individuals. Finally, gout patients who experienced a gout attack within the last three months were excluded due to the established variations in laboratory values during and after a severe gout attack. In the control group, patients older than 75 years and those with a suspicion for gout or other diseases causing chronic inflammation were excluded.

Age and comorbidities were questioned, and measurements were performed to determine height and weight. Body mass index (BMI) was calculated by dividing the weight by the square of the height (kg/m^2). Laboratory results, including blood fasting glucose, uric acid, blood urea nitrogen, creatinine, total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and testosterone levels, were recorded from measurements performed closest to the index application (all within a week prior or after). All laboratory analyses were carried out by the university hospital via the use of standard calibrated devices and according to the manufacturer's recommendations.

Gout diagnosis was made with the demonstration of monosodium urate crystals from aspirates of an affected joint or tophus or when clinical features met the preliminary criteria for the classification of gouty arthritis.[5,22] Last attack dates (for exclusion) and treatment data of gout patients were recorded.

Insulin resistance was evaluated using the homeostatic model assessment for insulin resistance (HOMA-IR) by the following formula: HOMA-IR = fasting glucose (mg/dL) × fasting insulin (uIU/mL)/405. Insulin resistance was defined as a HOMA-IR ≥2.7.[23]

Erectile dysfunction was evaluated using the 6-item International Index of Erectile Function (IIEF) erectile function domain (IIEF-EF). This scoring system yields a score ranging from 1 to 30 points, which reflects the erectile

dysfunction severity as follows: 0-10, severe erectile dysfunction; 11-16, moderate; 17-21, mild-moderate; 22-25, mild; 26-30, no erectile dysfunction.[24,25] Any patient with a score <26 points was considered to have some degree of erectile dysfunction. The Turkish version of the IIEF was validated for the Turkish population.[26]

Carotid intima-media thickness was evaluated using a high-resolution, B-mode ultrasound device (Toshiba Aplio XG; Toshiba Corp., Tokyo, Japan) equipped with a high-frequency linear array ultrasound probe (5-12 MHz; color Doppler flow imaging, GE Vivid 7; GE Vingmed, Horten, Norway) according to routine methods by a specialist radiologist. Measurements were made with the patient lying in the supine position and the head turned approximately 20° to the opposite side. Visualization was performed in the longitudinal view of the common carotid artery from a point located approximately 1 cm to the carotid bifurcation. The CIMT of the far wall was evaluated as the distance between the lumen-intima interface and the media-adventitia interface. The average of three measurements from both common carotid arteries was recorded as CIMT, and CIMT values ≥0.9 mm were considered to show increased CIMT.[27,28]

Hyperlipidemia was defined as the presence of any of the following: fasting total cholesterol level of 200≥ mg/dL, triglycerides ≥150 mg/dL, LDL ≥130 mg/dL, or HDL ≤40 mg/dL.[29]

The primary outcome of the study was to investigate whether increased CIMT was associated with erectile dysfunction. The secondary outcome of the study was to detect differences between gout patients and healthy controls in terms of CIMT values, erectile dysfunction frequency and severity, and some other variables.

Statistical analysis

All analyses were performed on IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). The distribution of continuous data was checked by employing histogram and Q-Q plot analyses. For normally distributed data, mean ± standard deviation (SD) was used to summarize, whereas median (first quartile-third quartile) was used for data with nonnormal distribution. Student's t-test was employed in the comparison of normally distributed data, while the Mann-Whitney U test was used for those with nonnormal distribution. Categorical data were summarized with absolute (n) and relative frequencies (%) according to analyzed groups and dependent variables. The analysis of these parameters was performed with chi-square tests (Pearson or Yate's correction) or the Fisher-Freeman-Halton test, depending on assumptions and group counts in relevant comparisons. Logistic regression was used to identify factors independently associated with erectile dysfunction. For the creation of the multivariable model, variables were first analyzed with univariate regression, and those with significance were included in multivariable analysis. For routine analyses, a p-value <0.05 was considered statistically significant, whereas the Bonferroni correction was employed for multiple comparisons.

RESULTS

Additionally, mean BMI (27.39±1.44 *vs.* 24.78±1.20) values were significantly higher in patients with gout compared to controls (p<0.001). Hypertension (p=0.015), hyperlipidemia, (p<0.001) and insulin resistance (p<0.001) were significantly more frequent in the gout group. Laboratory analyses showed that the fasting blood glucose, uric acid, blood urea nitrogen, creatinine, fasting total cholesterol, and triglyceride levels of gout patients were significantly higher compared to controls, whereas HDL and testosterone levels were significantly lower in the gout group (p<0.001 for all).

The mean IIEF-EF score of gout patients (21.16±2.87) was significantly lower than that of healthy subjects (23.75±2.43; p<0.001). The percentage of patients categorized as having mild-moderate erectile dysfunction was significantly higher in the gout group (p<0.001). Both right and left CIMT values were higher in patients with gout, and these patients also had a higher frequency of bilaterally increased CIMT (p<0.001 for all; Table 1).

In a subgroup of patients with both gout and increased CIMT, erectile dysfunction frequency

Table 1. Summary of variables with regard to groups

	Gout group (n=134)					Control group (n=104)					
	n	%	Mean±SD	Median	1st-3rd quartile	n	%	Mean±SD	Median	1st-3rd quartile	*p*
Age (year)				56	48-62				47	40.5-54.5	<0.001*
Body mass index (kg/m^2)			27.39±1.44					24.78±1.20			<0.001†
Hypertension	43	32.1				18	17.3				0.015‡
Hyperlipidemia	133	99.3				65	62.5				<0.001¶
HOMA-IR				4.1	2.9-5.4				1.8	1.5-2.05	<0.001*
Insulin resistance (≥2.7)	106	79.1				4	3.8				<0.001¶
Fasting blood glucose (mg/dL)				112	104-117				96	89-103	<0.001*
Uric acid (mg/dL)			6.43±0.94					5.50±0.76			<0.001†
BUN (mg/dL)			15.69±1.24					13.43±1.32			<0.001†
Creatinine (mg/dL)			1.02±0.09					0.89±0.10			<0.001†
Total cholesterol (mg/dL)			194.68±15.48					180.01±13.04			<0.001†
Triglyceride (mg/dL)				226	189-284				155.5	145.5-171.5	<0.001*
HDL (mg/dL)				45	42-47				46	43.5-49	<0.001*
LDL (mg/dL)				97	93-108				98	89-105.5	0.347*
Testosterone (ng/mL)			3.95±0.31					5.33±0.38			<0.001†
IIEF-EF score			21.16±2.87					23.75±2.43			<0.001†
Erectile dysfunction											<0.001‡
No (26-30)	8	6.0				29	27.9				
Mild (22-25)	50	37.3				61	58.7				
Mild to moderate (17-21)	74	55.2				13	12.5				
Moderate (11-16)	2	1.5				1	1.0				
Severe (0-10)	0	0.0				0	0.0				
CIMT (mm)											
Right				1.03	0.89-1.11				0.82	0.74-0.89	<0.001*
Left				1.03	0.89-1.10				0.82	0.75-0.90	<0.001*
Increased CIMT ≥0.9 (total)											<0.001‡
None	38	28.4				80	76.9				
Unilateral	1	0.7				2	1.9				
Bilateral	95	70.9				22	21.2				

SD: Standard deviation; HOMA-IR: The homeostatic model assessment-Insulin resistance; BUN: Blood urea nitrogen; HDL: High density lipoprotein; LDL: Low density lipoprotein; IIEF-EF: International Index of Erectile Function-Erectile Function; CIMT: Carotid intima-media thickness; * Mann Whitney U test; † Student's t test; ‡ Chi-square tests; ¶ Fisher-Freeman-Halton test.

Table 2. Comparison of erectile dysfunction positivity (IIEF-EF score <26) in CIMT-based subsets of the gout and control groups

	Gout group				Control group				
	Increased CIMT (n=96)		Non-increased CIMT (n=38)		Increased CIMT (n=24)		Non-increased CIMT (n=80)		
	n	%	n	%	n	%	n	%	*p*
ED positivity	94a	97.9	32b	84.2	20b	83.3	55b	68.8	<0.001

IIEF-EF: International Index of Erectile Function-Erectile Function; CIMT: Carotid intima-media thickness; ED: Erectile dysfunction; a,b: Same letters in different columns indicate that those groups did not have significant differences from each other, while different letters indicate that the groups had significant differences after Bonferroni correction. The analyses were performed with chi-square tests.

was 97.9%. Compared to the remaining three groups (gout patients without elevated CIMT, controls with elevated CIMT, and controls without elevated CIMT), this frequency was found to be significantly higher (p<0.001). Notably, Bonferroni-corrected results showed that erectile dysfunction frequencies were similar in all of these three groups (Table 2).

In multiple-group comparisons, the superscripted letters refer to pairwise comparison results. Same letters in different columns indicate that those groups did not have significant differences, while different letters indicate that the groups had significant differences after Bonferroni correction. For example, "a," "a, b," and "b" in three different columns indicate that there is a significant difference between the first and third groups, and that the second group is similar to both the first and third groups.

Univariate regression showed that age (p=0.022), hypertension (p=0.032), hyperlipidemia (p=0.002), having received treatment (p=0.017), insulin resistance (p=0.002), creatinine (p=0.007), testosterone (p<0.001), increased CIMT (p<0.001), and gout disease (p<0.001) were associated with erectile dysfunction. Multivariable logistic regression revealed that increased CIMT was the only factor independently associated with erectile dysfunction (odds ratio=3.723, 95% confidence interval: 1.363-10.172, p=0.010; Table 3, Figure 1).

Table 3. Odds ratios for erectile dysfunction (IIEF-EF score <26) and logistic regression analysis results

	Univariate			Multivariable		
	OR	95% CI	*p*	OR	95% CI	*p*
Age	1.048	1.007-1.092	0.022	0.990	0.936-1.047	0.722
Body mass index	1.215	0.994-1.485	0.058			
Hypertension	3.266	1.107-9.636	0.032	2.545	0.656-9.883	0.177
Hyperlipidemia	3.491	1.588-7.671	0.002	1.698	0.685-4.211	0.253
Treatment	3.075	1.226-7.715	0.017	0.495	0.092-2.661	0.412
Insulin resistance (HOMA-IR ≥2.7)	3.735	1.628-8.566	0.002	0.722	0.160-3.272	0.673
Creatinine	61.117	3.041-1228.263	0.007	0.597	0.013-27.486	0.792
Testosterone	0.343	0.208-0.566	<0.001	0.582	0.208-1.628	0.302
Increased CIMT (≥0.9)	6.770	2.704-16.948	<0.001	3.723	1.363-10.172	0.010
Gout disease	6.090	2.647-14.012	<0.001	3.003	0.263-34.268	0.376
Nagelkerke R2	-	-	0.238	-	-	-

IIEF-EF: International Index of Erectile Function erectile function domain; OR: Odds ratio; CI: Confidence interval; HOMA-IR: Homeostatic model assessment for insulin resistance; CIMT: Carotid intima-media thickness.

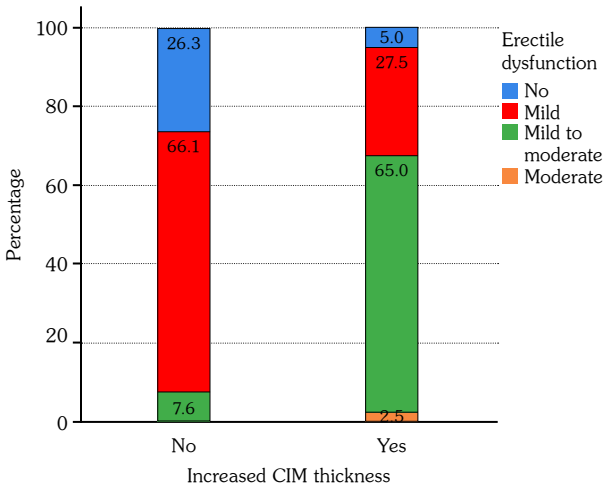

Figure 1. Erectile dysfunction with regard to CIMT.
CIMT: Carotid intima-media thickness.

DISCUSSION

While the literature undoubtedly shows potential relationships between gout and erectile dysfunction, the findings do not exclude the potential confounding effects of heart disease and other comorbidities.[3,4] Therefore, the present study was planned to assess the degree of relationship between increased CIMT, a known risk factor for cardiovascular events, and the increased risk of erectile dysfunction in gout patients. Although insulin resistance, hyperlipidemia, increased frequency and severity of erectile dysfunction, and increased CIMT risk were higher in gout patients, multivariable analyses showed that increased CIMT was the only independent risk factor for erectile dysfunction in our population. Therefore, a feasible interpretation of our results is that gout may indirectly contribute to the strong relationship between erectile dysfunction and CIMT.

Gout is often accompanied by not only rheumatological disorders but also CVD and renal/genitourinary, metabolic, and ophthalmological comorbidities in various combinations and severity.[1,2] One of the most common genitourinary comorbidities is erectile dysfunction, and many studies have reported data that suggest an association between gout and erectile dysfunction.[4-6] The prevalence of erectile dysfunction in hyperuricemic men was estimated at 33% in a meta-analysis,[30] with prevalence rates ranging from 1 to 76% in different studies.[5,12] From a comparative aspect, this rate is around 2% in men under 40 years of age, while a steep rise is evident after middle age, reaching up to 86% in those older than 80 years of age.[31] In the present study, the rate of erectile dysfunction was 94% in gout patients and 72% in control patients. However, since the exclusion criteria were broad, it must be noted that these rates do not indicate a general prevalence of erectile dysfunction for either group. Furthermore, the following three factors may have caused high erectile dysfunction rates. First, the inclusion of patients with relatively older age. Second, the frequencies of hypertension, hyperlipidemia, and insulin resistance were high, and testosterone levels were low. Third, we evaluated erectile dysfunction with a questionnaire and the responses were subjective, which may have caused higher rates due to the sensitivity of the survey.

Schlesinger et al.[5] reported the prevalence of erectile dysfunction in patients with gout to be 76% compared to 51% in those without gout and found this difference to be significant. Additionally, they identified severe erectile dysfunction in 26% of patients with gout compared to 15% of those without gout, which also demonstrated statistical significance. In another study, men with gout were found to have a 1.21-fold higher risk of erectile dysfunction compared to those without gout.[12] The likelihood of developing organic erectile dysfunction was 1.52 times higher in patients with gout, while the likelihood of developing psychogenic erectile dysfunction was 1.18 times higher.[12] In a population-based cohort study from England, the rate of erectile dysfunction after gout diagnosis was calculated to be 193 per 10,000 person-years.[32] This corresponded to a 31% increased risk of erectile dysfunction compared to those without gout. The risk of erectile dysfunction in the first year after gout diagnosis was found to be higher compared to the one-year period prior to gout diagnosis.[32]

There are various potential reasons for the greater likelihood of erectile dysfunction in patients with gout. First, the two conditions may have common underlying/triggering factors. Second, gout may be a primary cause of erectile dysfunction. Third, comorbidities among gout

patients or their effects may directly cause or lead to erectile dysfunction. As such, gout may be an indirect factor that increases the likelihood of erectile dysfunction, given that the patient has underlying conditions that strongly elevate the likelihood of erectile dysfunction. In the general population, various risk factors, including environmental risks, alcohol use, diet, obesity, medications, chronic diseases, menopause, undergoing surgery, and genetic risk factors,[1,2] are established to be associated with a higher risk of gout due to development of hyperuricemia. Many of these factors are also associated with erectile dysfunction.[4,33] Moreover, it has been reported that many parameters associated with gout may contribute to erectile dysfunction, such as hyperuricemia, increased reactive oxygen species, decreased nitric oxide synthesis,[7,9,10,34] endothelial damage,[11] comorbid conditions,[2,6,12] inflammation,[3,11,35] vitamin D deficiency,[11] metabolic syndrome,[11] depression,[11] insulin resistance,[13] gout treatment,[14] and increased lipoprotein(a) level.[15] In the present study, we investigated whether elevated CIMT was associated with erectile dysfunction in patients with gout. Previous studies have reported significant relationships between uric acid levels and CIMT[36,37] and between erectile dysfunction and CIMT.[20,21] Despite conflicting findings from other research,[38,39] to our knowledge, there are no studies investigating this particular relationship in gout patients. We showed that increased CIMT was the only independent risk factor for erectile dysfunction in our patient population. Age, BMI, presence and treatment of gout, hyperlipidemia, insulin resistance, hypertension, creatinine, and testosterone levels were not identified as independent variables associated with erectile dysfunction. We also observed that erectile dysfunction was significantly more common among patients with coexistence of gout and elevated CIMT. It is crucial to note that the small number of patients without erectile dysfunction in the gout group would have obscured advanced analyses in smaller subsets of the gout population. This is a potential limitation; however, since the primary multivariable analysis revealed only increased CIMT as an independent factor for erectile dysfunction, the present findings are crucial for the planning of future studies that can include more stratified patient groups.

Carotid intima-media thickness is a useful noninvasive surrogate marker of subclinical atherosclerosis. The measurement of CIMT allows early evaluation and risk assessment of structural vascular abnormalities.[19,20] It is also known that high urate concentrations can cause endothelial dysfunction by blocking nitric oxide-mediated vasodilator mechanisms, induce oxidative stress in vascular smooth-muscle cells, and activate the renin-angiotensin system, causing hypertension.[3,40] Moreover, there may be a relationship between inflammation caused by monosodium urate crystals in the vascular tissue and the formation of vascular calcifications in coronary arteries and thoracic aorta.[41] We found that patients with gout had significantly increased CIMT values bilaterally, and a higher percentage of patients in this group were detected to have increased CIMT. In one study, CIMT was found to be somewhat higher in gout patients compared to the group without gout, but the difference was not significant. The same authors also reported that the duration of gout was positively correlated with CIMT.[19] In other studies, CIMT is suggested to be correlated with serum uric acid level,[36,37] but this is a disputed issue.[38,39] Various risk factors for increased CIMT have been established, including age,[42-44] sex,[43] smoking,[42,45] hypertension,[42,43,45] fasting glucose,[44,45] cholesterols,[43] family history,[45] leptin-to-adiponectin ratio,[44] and IIEF score.[20,21] A similar relationship to the one between gout and erectile dysfunction also exists between gout and CIMT. Some studies have described correlations between CIMT and erectile dysfunction.[20,21,46] Zhang et al.[46] found that both patients with moderate and severe erectile dysfunction had significantly higher CIMT values compared to controls. Furthermore, the CIMT value of the severe erectile dysfunction group was significantly higher compared to those with mild erectile dysfunction. CIMT values also demonstrated a negative correlation with the 5-item version of IIEF (IIEF-5) scores. In another study, Chen et al.[20] investigated CIMT in young patients with erectile dysfunction who had insulin resistance. They found significantly higher CIMT among these patients compared to healthy controls, and detected a significant correlation between CIMT and IIEF-5 scores. Multivariate regression revealed that IIEF-5 score was independently associated with CIMT.

Yao et al.[21] demonstrated that patients with erectile dysfunction had increased CIMT relative to controls, with logistic regression identifying CIMT as a risk factor for erectile dysfunction. They showed that young men with CIMT values >0.623 mm had a 4.16-fold higher risk of erectile dysfunction.

In a recent review, cigarette smoking, use of opioids, diabetes, depression, obstructive sleep apnea, ankylosing spondylitis, chronic prostatitis/pelvic pain syndrome, psoriasis, chronic periodontitis, gout, human immunodeficiency virus infection, platelet volume, and CVD were all reported as factors associated with an increased risk of erectile dysfunction.[47] There appears to be an incompletely understood relationship between erectile dysfunction, CVD, and gout, illustrated by the shared comorbidities between the conditions.[4,16] Furthermore, it has been shown that erectile dysfunction is an independent predictor of cardiovascular events,[16,18] indicating an interesting resemblance with CIMT.[19,20] However, it is unknown whether the significant association between increased CIMT and erectile dysfunction is a direct effect or if it is related to the fact that both are predictors of CVD. Recent studies provide supportive evidence for direct associations between gout, CVD, and cardiovascular mortality.[48,49]

Despite the many factors and complex associations mentioned above, the actual contribution of increased CIMT on erectile dysfunction in gout is unclear. There appears to be a mutual cause-and-effect relationship between CIMT, erectile dysfunction, and gout, in which the primary cause or trigger is ambiguous. Increased CIMT is a well-evidenced predictor of CVD-related events; however, its potential role as an index sign of gout or erectile dysfunction in gout cannot be excluded. The findings of this study and available data are insufficient to reach a definitive answer, but the results and the limitations are crucial for the planning of future studies.

To the best of our knowledge, this is the first study to investigate the relationship between erectile dysfunction and CIMT in patients with gout. However, the study has several limitations. The single-center study design with a relatively small sample size limits the ability to generalize the results. The small number of gout patients without some degree of erectile dysfunction prevented multivariable analyses in the relevant subsets of gout patients. Some important variables such as smoking data, detailed lifestyle information, obstructive sleep apnea, and gout severity and duration were not included in the study. To avoid possible biases, the control group was randomly selected, which led to differences in age and BMI. Although we attempted to eliminate this limitation by regression analysis adjusted for age, which ultimately revealed no significant impact of age on erectile dysfunction in this patient group, the fact that the patients in the control group were younger, had lower BMI, and had fewer comorbidities may have had an impact on low erectile dysfunction frequency. Additionally, the differences in testosterone levels may have caused variations in erectile dysfunction prevalence, potentially introducing bias. In the context of erectile dysfunction, the diagnosis and severity were ascertained through self-reported questionnaires, and no distinction was made between vasculogenic and psychogenic erectile dysfunction, which is important to consider since CIMT is also a vascular parameter. Finally, although receiving treatment was assessed as a whole, medication details were not included, and potential differences may have influenced uric acid levels, and thus, the severity or frequency of erectile dysfunction.[30]

In conclusion, hyperlipidemia, insulin resistance, erectile dysfunction, and increased CIMT risk were found to be higher in gout patients than in the normal population. Increased CIMT was identified as the only variable independently related to erectile dysfunction. It appears that gout may have an indirect role in the significant relationship between CIMT and erectile dysfunction. Increased CIMT appears to contribute to a greater risk of erectile dysfunction in patients with gout and healthy people, but the coexistence of both conditions significantly increases the likelihood of erectile dysfunction. More extensive studies that take into account the limitations of the present research are needed to understand the causal relationships between gout, CIMT, and erectile dysfunction.

Ethics Committee Approval: The study protocol was approved by the İstanbul Medipol University Ethics Committee (date: 13.09.2022, no: 790). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept: E.Y., S.Y., M.C., Z.B.; Data collection: E.Y., M.C., Z.B.; Analysis: S.Y.; Literature review: E.Y.; Writing the article: E.Y., S.Y.; Critical review: M.C., Z.B.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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