High Uric Acid Decreases the Number of Nocturnal Erections: A Propensity Score-Matched Analysis

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Purpose: Metabolic syndrome is considered a risk predictor for erectile dysfunction (ED). However, the effect of serum uric acid (UA) on the development of ED is not well understood.

Materials and Methods: We used propensity score matching (PSM) to adjust for numerous confounding factors such as age, metabolic syndrome, sex hormones, and several blood measurements. Participants in the normal UA and high UA groups were matched at a 1:1 ratio by propensity score. We used two diagnostic methods, the International Index of Erectile Function-5 (IIEF-5) and nocturnal penile tumescence and rigidity (NPTR), to assess and diagnose ED.

Results: Before PSM, a total of 120 participants were included. Compared with participants with normal serum UA (n = 61), those with high serum UA (n=59) had statistically significant differences in some baseline characteristics (BMI 27.8 ± 7.4 vs 24.4 ± 5.1 kg/m², $p = 0.004$; TG 2.1 ± 1.8 vs 1.5 ± 0.9 mmol/L, $p = 0.015$; creatinine 70.5 ± 9.9 vs 66.3 ± 10.7 μmol/L, $p = 0.03$; T 450.9 ± 181.0 vs 598.2 ± 186.3 ng/dL, $p < 0.001$). After PSM, a total of 82 participants were included, with 41 in the high serum UA group (Group A) and 41 in the normal serum UA group (Group B). Based on the IIEF-5, 40 of 41 participants (97.6%) with high UA were diagnosed with ED, whereas 39 of 41 participants (95.1%) with normal UA were diagnosed with ED; the incidence was not statistically significant between the two groups ($p > 0.999$). Based on NPTR results, the mean number of erections in Group A was 4.1 ± 2.0, which was significantly less than in Group B (5.3 ± 1.9, $p = 0.004$). Nine of 41 participants (22.0%) with high UA developed ED, whereas 14 of 41 participants (34.1%) with normal UA developed ED; this difference in incidence was not statistically significant ($p = 0.326$).

Conclusion: Our study revealed that high UA decreased the number of nocturnal erections as diagnosed by NPTR. High uric acid may be a potential risk factor for ED, and larger studies are needed.

Keywords: Erectile Dysfunction; IIEF-5; NPTR; Propensity Score Matching; Uric Acid

INTRODUCTION

The Fourth International Consultation on Sexual Medicine defined erectile dysfunction (ED) as the persistent inability to attain or maintain a penile erection sufficient to permit satisfactory sexual performance.[1] ED is a significant public health burden, with a prevalence of 10%-20% in the overall male population.[2,3] With prevalence rates gradually increasing, the number of affected men is estimated to reach 322 million by 2025.[4] The etiology of ED is complex, and its mechanism has not been clearly elucidated. It is widely accepted that the interplay between physiological factors, psychological factors, and metabolic disorders plays a vital role in the development of ED.[5,6]

There is mounting evidence indicating that metabolic syndrome components such as obesity, dyslipidemia, hypertension, and diabetes may significantly increase the risk of ED.[5-7] The mechanisms by which obesity may contribute to erectile dysfunction include hormonal disorders, insulin resistance, and psychological factors.[8] Penile erection is maintained by a balance of blood inflow and outflow. Hypertension and hyperlipidemia may cause endothelial dysfunction, leading to an increase in vascular smooth muscle contraction, which alters penile blood flow and is related to ED.[9-11] Diabetes might impair erectile function by increasing levels of oxygen-free radicals and impairing nitric oxide synthesis, and insulin resistance has been linked with the severity of ED.[12-15] Hormones such as testosterone can increase the expression of enzymes that play an essential role in the erectile process, so a deficiency may be associated with ED.[16] The etiology of ED is multifactorial and complicated, and its pathogenesis, involving several physiological systems, is still not clear.

A growing body of literature has been published concerning the association between uric acid (UA) and ED risk.[17-19] High serum UA is recognized as a risk marker for inducing oxidative stress and stimulating arginase, which eliminates endothelial NO.[20-24] However, other research indicates that high serum UA is not a predictor of ED.[25] The conclusions of these studies are inconsistent, and many confounders exist in the relationship between UA and ED. Therefore, we performed this study to investigate the relevance of UA and ED by using propensity score matching (PSM) to eliminate con-

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Table 1. Basic characteristics of participants before and after PSM

Variables	Before PSM		*P*	After PSM		*P*
	High UA (n=59)	Normal UA (n=61)		Group A (n=41)	Group B (n=41)	
Age (years)	31.51 ± 6.25	33.75 ± 8.10	0.092	31.54 ± 6.84	33.10 ± 8.11	0.349
BMI (kg/m²)	27.82 ± 7.40	24.40 ± 5.11	0.004	27.72 ± 7.28	25.05 ± 5.92	0.072
Duration of disease (months)	30.48 ± 46.59	28.29 ± 28.07	0.554	25.66 ± 24.49	30.17 ± 44.47	0.571
Education			0.131			0.412
High school or below	27 (45.8%)	39 (63.9%)		19 (46.3%)	25 (61.0%)	
Bachelor	27 (45.8%)	18 (29.5%)	19 (46.3%)	14 (34.1%)		
Graduate or higher	5 (8.4%)	4 (6.6%)	3 (7.3%)	2 (4.9%)		
Monthly income (CNY)		0.267		0.256		
≤6000	33 (56.0%)	33 (54.1%)		23 (56.1%)	21 (51.2%)	
6000-10000	13 (22.0%)	20 (32.8%)		8 (19.5%)	14 (34.1%)	
≥10000	13 (22.0%)	8 (13.1%)		10 (24.4%)	6 (14.6%)	
Morning erection			0.451			> 0.999
No	19 (32.2%)	24 (39.3%)		14 (34.1%)	15 (36.6%)	
Yes	40 (67.8%)	37 (60.7%)		27 (65.8%)	26 (63.4%)	
Hypertension			> 0.999			> 0.999
No	55 (93.2%)	56 (91.8%)		38 (92.7%)	37 (90.2%)	
Yes	4 (6.8%)	5 (8.2%)		3 (7.3%)	4 (9.8%)	
Diabetes	0.619		1.000			
No	58 (98.3%)	58 (95.1%)		40 (97.6%)	40 (97.6%)	
Yes	1 (1.7%)	3 (4.9%)		1 (2.4%)	1 (2.4%)	
Smoking			0.353			0.645
No	32 (54.2%)	39 (63.9%)		28 (68.3%)	25 (61.0%)	
Yes	27 (45.8%)	22 (36.1%)		13 (31.7%)	16 (39.0%)	
Drinking			0.583			> 0.999
No	30 (50.8%)	35 (57.4%)		23 (56.1%)	24 (58.5%)	
Yes	29 (49.2%)	26 (42.6%)		18 (43.9%)	17 (41.5%)	
TC (mmol/L)	5.10 ± 1.09	5.03 ± 0.83	0.664	4.91 ± 1.10	4.97 ± 0.83	0.778
TG (mmol/L)	2.09 ± 1.77	1.45 ± 0.92	0.015	1.96 ± 1.90	1.56 ± 1.05	0.240
HDL (mmol/L)	1.21 ± 0.24	1.28 ± 0.30	0.119	1.21 ± 0.23	1.29 ± 0.33	0.211
LDL (mmol/L)	3.15 ± 0.96	3.08 ± 0.71	0.649	3.02 ± 0.89	3.05 ± 0.75	0.869
Creatinine (μmol/L)	70.46 ± 9.88	66.33 ± 10.72	0.030	70.44 ± 10.65	67.39 ± 10.60	0.198
Glu (mmol/L)	5.20 ± 1.35	5.31 ± 1.05	0.622	5.37 ± 1.56	5.25 ± 0.86	0.651
FSH (IU/L)	3.60 ± 1.94	4.27 ± 5.46	0.375	3.61 ± 1.67	3.38 ± 1.81	0.540
LH (IU/L)	3.29 ± 1.43	3.40 ± 1.96	0.721	3.37 ± 1.46	3.23 ± 1.79	0.691
PRL (ng/mL)	16.51 ± 10.35	15.95 ± 8.99	0.751	17.66 ± 12.01	17.39 ± 9.50	0.911
E2 (pg/mL)	26.16 ± 8.68	26.36 ± 11.94	0.913	27.32 ± 8.74	26.54 ± 11.17	0.725
P (ng/mL)	0.21 ± 0.10	0.22 ± 0.10	0.752	0.21 ± 0.10	0.22 ± 0.09	0.944
T (ng/dL)	450.90 ± 181.00	598.20 ± 186.30	< 0.001	504.60 ± 177.40	578.50 ± 187.50	0.071

Abbreviations: CNY, China Yuan; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Glu, blood glucose; FSH, follicle-stimulating hormone; LH, luteinizing hormone; PRL, prolactin; E2, estradiol; P, progesterone; T, testosterone.

founding factors.

MATERIALS AND METHODS

Study Design and Population

From October 2018 to October 2021, 191 participants from our medical center were recruited. The exclusion criteria were as follows: (1) any history of drug use or disease which may affect sexual function; (2) incomplete baseline information (age, height, weight, education, income, smoking, drinking, blood measurements, and sex hormone levels); (3) incomplete International Index of Erectile Function-5 (IIEF-5) questionnaires; and (4) incomplete nocturnal penile tumescence and rigidity (NPTR) records. A total of 120 participants met the criteria for the analysis. All participants signed informed consent forms. A serum UA concentration greater than 414 μmol/L was defined as high, while a concentration less than or equal to 414 μmol/L was considered normal.

Data Collection and Erectile Function Assessment

Baseline information was extracted from our database, including: (1) age, height, weight, education, income, morning erection status, and duration of disease; (2) history of hypertension, diabetes, smoking, and drinking; (3) blood measurements: total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), creatinine, and blood glucose (Glu); and (4) sex hormones: follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), estradiol (E2), progesterone (P), and testosterone (T).

All participants underwent a detailed physical examination to check the penis and testicles. We used the IIEF-5 questionnaire to assess and diagnose ED. A score of 22-25 was considered normal (no ED), and a score of 21 or less indicated ED. The severity of ED was classified based on the score: 12-21 was mild, 8-11 was moderate, and 5-7 was severe.

NPTR monitoring was performed by trained physicians using the RigiScan Plus device (GOTOP Inc.). The principle of NPTR measurement involves placing two string loops, one at the tip and one at the base of the penis, to record rigidity and tumescence data during the patient's sleep. To avoid interference from other factors, participants were instructed to abstain from alcohol, caffeine, and sleeping medications that might affect night sleep. In our study, the primary outcome was the duration of tip rigidity greater than 60%. If this duration lasted more than 10 minutes for an event, the patient's function was defined as normal for that event. Otherwise, it was recognized as ED.[26] Data collected included the number of effective erectile events (EEEs), which were defined as events with tip rigidity greater

Table 2. Prevalence and incidence of ED in participants after PSM

Variables IIEF-5	Group A (n=41)	Group B (n=41)	*P*
≥ 22	1 (2.4%)	2 (4.9%)	> 0.999
< 22	40 (97.6%)	39 (95.1%)	
Mild	22 (55.0%)	23 (59.0%)	0.821
Moderate	11 (27.5%)	9 (23.1%)	0.797
Severe	7 (17.5%)	7 (17.9%)	1.000
The EEEs of NPTR			
≥ 1	32 (78.0%)	27 (65.9%)	0.326
0	9 (22.0%)	14 (34.1%)	

*To determine the significance of the difference between IIEF-5 scores of independent group, The Kruskal-Wallis test was used. *P* values < 0.05 were regarded as significance

than 60% lasting more than 10 minutes. We also recorded many other parameters, such as tumescence activity units (TAUs), rigidity activity units (RAUs), and total erection time (TET).

Statistical Analysis

PSM was performed to reduce the effect of confounding baseline characteristics and balance the high UA and normal UA cohorts. A logistic regression model was constructed with five confounding factors—patient age, BMI, T, TG, and creatinine—as independent variables. PSM was utilized to minimize the influence of biases and confounding variables, using a caliper value of 0.02 and a 1:1 matching ratio. Continuous variables were reported as mean ± standard deviation (SD) and compared using the independent samples t-test. Categorical variables were expressed as frequency and percentage and compared using the chi-square test or Fisher's exact test. Statistical analysis was performed using SPSS v.26.0.

RESULTS

Baseline Data

According to the criteria, 120 participants were included: 59 in the high serum UA group and 61 in the normal serum UA group. Before PSM, compared with participants with normal serum UA, those with high serum UA had statistically significant differences in some baseline characteristics (BMI 27.8 ± 7.4 vs 24.4 ± 5.1 kg/m², $p = 0.004$; TG 2.1 ± 1.8 vs 1.5 ± 0.9 mmol/L, $p = 0.015$; creatinine 70.5 ± 9.9 vs 66.3 ± 10.7 μmol/L, $p = 0.03$; T 450.9 ± 181.0 vs 598.2 ± 186.3 ng/dL, $p < 0.001$). Our subjects were matched at a 1:1 ratio using propensity scores, resulting in 41 participants with high serum UA (Group A) and 41 with normal serum UA (Group B) (**Figure 1**). After PSM, these differences were no longer significant between the two groups. The baseline data before and after propensity score matching for participants with high and normal serum UA are presented in (**Table 1**).

Prevalence and Incidence of ED

We also studied the incidence rate of ED according to the IIEF-5 questionnaire and NPTR monitoring. Based on the IIEF-5 results, the mean total score in Group A was 12.9 ± 4.7, which was not significantly different from the mean total score in Group B (13.4 ± 5.3, $p = 0.644$). Forty of 41 participants (97.6%) with high UA developed ED, whereas 39 of 41 participants (95.1%) with normal UA developed ED; the incidence had no statistical significance between the two groups ($p > 0.999$). In Group A, 22 of 41 participants (53.7%) developed mild ED vs 23 (56.1%) in Group B ($p = 0.821$); 11 of 41 participants (26.8%) developed moderate ED vs 9 (22.0%) in Group B ($p = 0.797$); and 7 of 41 participants (17.1%) developed severe ED vs 7 (17.1%) in Group B ($p = 1.000$). There was no significant difference in severity between the two groups. Based on the NPTR results, 9 of 41 participants (22.0%) with high UA developed ED, whereas 14 of 41 participants (34.1%) with normal UA developed ED; the incidence was not statistically significant between Group A and Group B ($p = 0.326$). These results are detailed in (Table 2) and (**Figure 2**).

Parameters of NPTR

The primary NPTR indicator for diagnosing organic ED is a penile tip rigidity of ≥ 60% maintained for ≥10 minutes. The mean number of such events (EEEs) in Group A was 1.3 ± 1.0, and in Group B was 1.5 ± 1.4; this difference was not statistically significant ($p = 0.519$). However, the mean total number of erections in Group A was 4.1 ± 2.0, which was significantly less

Table 3. The parameters of NPTR and result of IIEF-5

Variables	Group A (n=41)	Group B (n=41)	*P*
NPTR			
Number of erections	4.07 ± 1.99	5.34 ± 1.92	0.004
EEEs	1.29 ± 1.00	1.44 ± 1.36	0.519
Tip AER (%)	55.85 ± 14.59	54.39 ± 10.21	0.600
Base AER (%)	48.98 ± 13.68	47.88 ± 10.20	0.682
Tip RAU	42.34 ± 38.82	43.88 ± 26.13	0.834
Base RAU	36.61 ± 37.32	38.61 ± 22.35	0.769
Tip TAU	29.10 ± 24.82	30.41 ± 20.74	0.795
Base TAU	30.63 ± 30.00	30.54 ± 18.09	0.986
Tip MT (%)	86.93 ± 10.89	89.66 ± 10.85	0.259
Base MT (%)	82.13 ± 11.23	82.44 ± 12.84	0.910
TET (min)	70.46 ± 57.33	77.65 ± 43.28	0.523
Tip D60% (min)	47.55 ± 64.16	37.68 ± 28.06	0.370
Base D60% (min)	27.91 ± 47.22	23.06 ± 24.29	0.560
Tip MT (cm)	8.71 ± 1.16	8.85 ± 1.03	0.561
Base MT (cm)	9.18 ± 0.89	9.07 ± 0.87	0.583
Average Tip tumescence (cm)	8.30 ± 1.02	8.32 ± 0.92	0.910
Average base tumescence (cm)	8.87 ± 0.81	8.72 ± 0.81	0.401
Number of base D60% and lasting >10 min	0.88 ± 1.08	0.80 ± 1.05	0.757
Total score of IIEF-5	12.85 ± 4.72	13.37 ± 5.27	0.644

Abbreviations: IIEF-5, International Index of Erectile Function-5; NPTR, nocturnal penile tumescence and rigidity; EEEs, effective erectile events; AER, average event rigidity; RAUs, rigidity activity units; TAUs, tumescence activity units; MT, maximal tumescence; TET, total erection time; D60%, duration of erectile episodes with rigidity ≥ 60%.

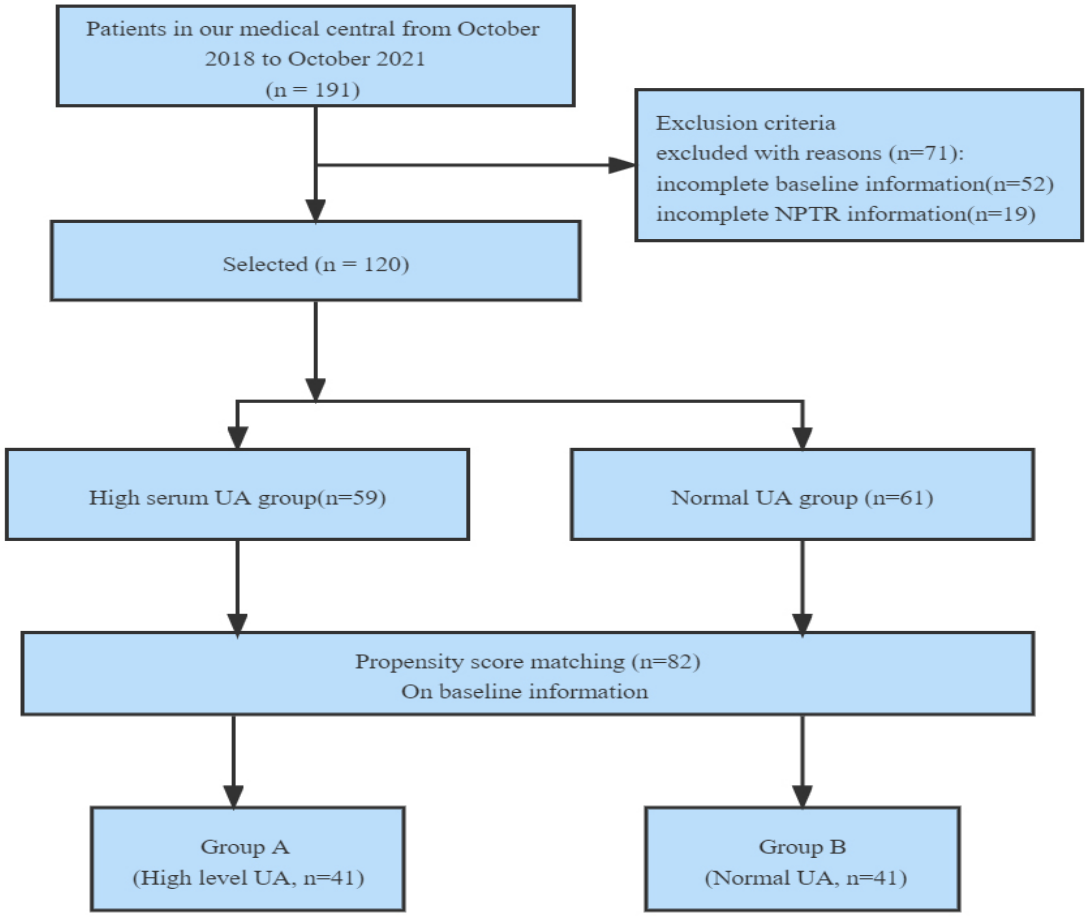

Figure 1. Flowchart of inclusion criteria of the PSM analysis in participants with normal UA or high UA.

than in Group B (5.3 ± 1.9, $p = 0.004$). There were no statistically significant differences in other NPTR monitoring parameters between the two groups. These results are shown in (**Table 3** & **Figure 2**).

DISCUSSION

ED is characterized by inadequate penile erection and has been identified as a primary health burden in the aging male population.[27] ED can impair intimacy between men and their partners and even damage relationships.[28] Lizza et al.[29] classified ED by its cause as either organic or psychogenic. Distinguishing the etiology of ED is significant. For example, for a man with primary psychogenic ED, the best treatment is psychosexual therapy to restore confidence, rather than medication for organic ED.

ED is multidimensional, related to multiple systems of the body, and studies have verified that it is strongly associated with metabolic diseases.[30-33] Meanwhile, expanding research has demonstrated that treating metabolic diseases can improve erections, and lifestyle alterations are regarded as the first step in improving and treating ED.[34-39] Hyperuricemia can increase reactive oxygen species and lead to endothelial dysfunction. Numerous studies have shown that lowering UA is beneficial for improving endothelial function.[36,38,39] The relationship between hyperuricemia and ED remains controversial. Therefore, it is crucial to define the relationship between UA and ED, as treating high UA might be a method to cure ED.

To study the effect of a single factor on a disease, the most rigorous design is a randomized trial, which can minimize systematic bias.[40] However, it is difficult to conduct randomized controlled trials because they require more time, money, and energy. Conclusions can also be drawn from observational studies. However, the weakness of observational research is that its outcomes can be influenced by various confounders, not just the treatment.[41] PSM can minimize the effect of confounding factors by matching subjects in treatment and control groups with comparable baseline characteristics in observational studies.[42] PSM can avoid the shortcomings of traditional statistical methods such as multifactorial regression[43] and is increasingly applied in medical studies.[44]

Several experimental and clinical investigations have explored the relationship between UA and ED, but there were shortcomings in those studies, and their conclusions were inconsistent. Salem et al.[45] conducted a large study including 251 patients with ED and 252 age-matched men without ED to explore this relationship, and their results showed that UA concentration was a

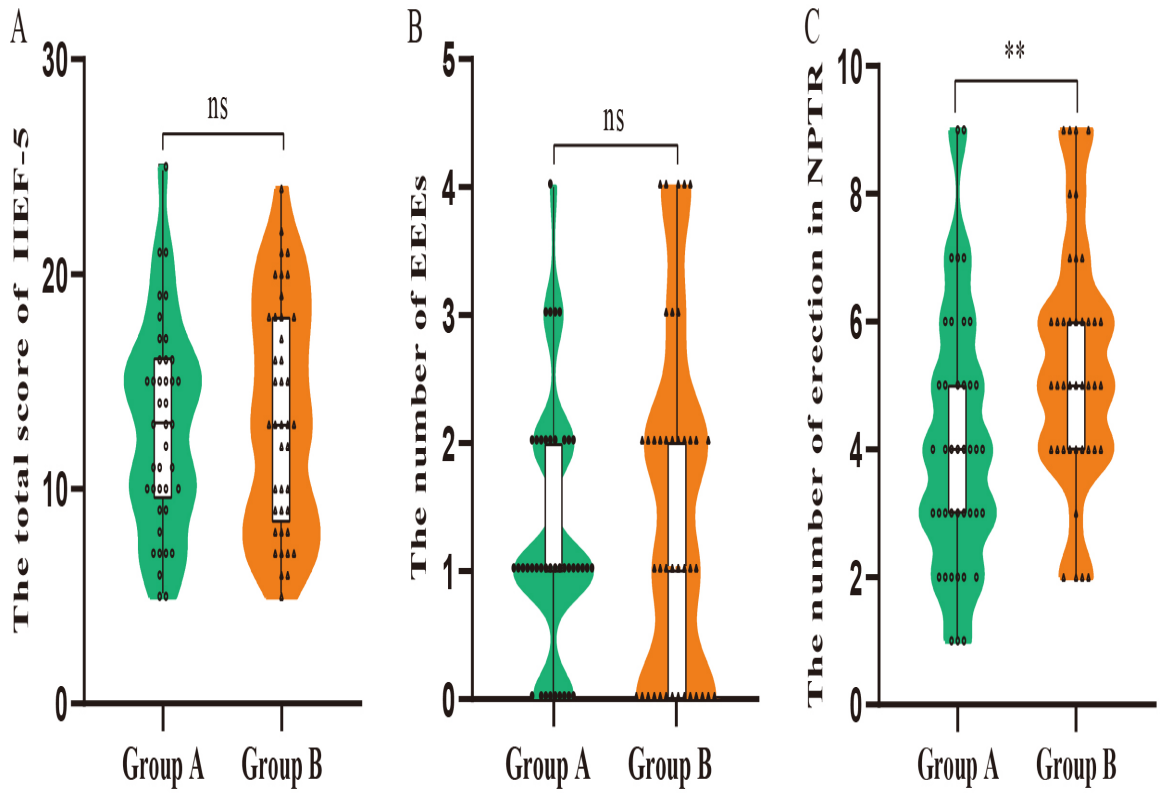

Figure 2. Violin plot analysis of three parameters between Group A and Group B. (A: the violin plot of the total score of IIEF-5 between two groups; B: the violin plot of the number of EEEs between two groups; C: the violin plot of the number of erections in NPTR between two groups)

risk factor for ED in a logistic regression model. However, this research is limited because it used a logistic regression model to adjust for metabolic syndrome factors but lacked other factors, such as certain sex hormones, which might interfere with the conclusion. Gao et al.[46] conducted a population-based cross-sectional study on a larger sample of 1365 men, and the results indicated that UA might be a protective factor in the development of ED. This research adjusted for some sex hormones, but those confounding factors were eliminated using logistic regression, which has limitations in adjusting for numerous factors. Our study adopted the statistical method of PSM to eliminate confounding factors. We adjusted for numerous confounding factors, such as age, education, income, metabolic syndrome, blood measurements, and sex hormones, which previous studies have proven to be closely related to ED.

Another limitation of previous research[25,47] investigating the link between UA and ED is the sole reliance on the IIEF-5 questionnaire to diagnose ED. The IIEF-5 is extensively used in the diagnosis of ED because it is a simple diagnostic tool for patients to self-administer or for physicians to use in clinical settings.[48] The IIEF-5 has a certain degree of specificity and sensitivity for evaluating treatment-related effects in patients with ED.[49] In our study, the incidence of ED between the high UA group and the normal UA group was not statistically significant when using the IIEF-5 method. Furthermore, there was no statistical significance in the severity of ED between the two groups. Our results demonstrated that high UA is not an etiological factor for psychogenic ED. However, the IIEF-5 is primarily a valid and reliable instrument for detecting patients with psychogenic ED.[50] The etiology of ED is complex and multifactorial, involving not only psychogenic but also organic lesions, and the etiology is closely related to treatment. Therefore, a supplementary method is needed to assess and diagnose organic ED.

A healthy man has 3-5 nocturnal penile tumescence episodes during sleep.[51] Bradley et al.[52] first introduced NPTR as an assessment to distinguish the etiologies of ED in 1985. NPTR can minimize the effect of psychological factors such as anxiety and stress to evaluate the impact of organic factors on ED. It is widely recognized that normal NPTR records may suggest psychogenic ED, while abnormal records indicate organic ED.[53] In our study, there was a significant difference in the total number of erections between the two groups, but the primary diagnostic indicator, EEEs, showed no statistical significance. Therefore, the incidence of ED between the high UA and normal UA groups was not statistically significant when using the NPTR method, which might mean high UA is not an etiology of organic ED.

To the best of our knowledge, this is the first study to adopt PSM to adjust for the most confounding factors to date in evaluating the relationship between UA and ED. In our study, we used two methods to diagnose and distinguish the cause of ED. Therefore, we believe our study adopted superior statistical and diagnostic methods to demonstrate the relevance between UA and ED. Both diagnostic methods have shown that high UA was

not a risk factor for ED. This result was confirmed in research by Barassi et al.[54] and Tuokko et al.[25] The reason for this negative result may be that UA could promote small-vessel disease, which is closely related to other metabolic diseases such as hypertension, diabetes, and obesity. When adjusting for these factors, the true relationship between UA and ED might be concealed. Therefore, more research is needed to elaborate on the mechanism of metabolic diseases in the process of ED. There are limited studies utilizing NPTR to assess the relationship between uric acid levels and erectile dysfunction. Our findings indicate that elevated uric acid levels significantly reduce the frequency of nocturnal erections. This information could assist clinicians, particularly those specializing in andrology, in drawing more accurate, evidence-supported conclusions. For cases of idiopathic erectile dysfunction, we recommend testing for uric acid level and conducting NPTR.

There are several limitations in our study. Firstly, our sample size after matching was small. Even so, we still believe our conclusion is reliable, as the dataset was the result of PSM analysis. Secondly, the mean age of participants in Group A was 31.5 ± 6.8 years and in Group B was 33.1 ± 8.1 years; these results cannot be generalized to all patients suffering from ED. Therefore, larger studies including different age groups are needed to evaluate the association between UA and ED. Furthermore, although we adjusted for major confounding factors of ED, some unidentified factors might remain.

CONCLUSIONS

In conclusion, based on the results of our PSM analysis, high UA decreased the number of erections during the night, as diagnosed by NPTR. High uric acid may be a potential risk factor for ED, and more large studies are needed to confirm this association.

SUMMARY

This study found that men with high uric acid levels had fewer erections during sleep. This suggests that high uric acid could be a risk factor for erectile dysfunction, but more research is needed to confirm this connection.

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Author Contributions

Conceptualization: AQZ, SRW, and XQL. Writing—original draft: all authors. Writing—review & editing: all authors.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

REFERENCES

1. McCabe MP, Sharlip ID, Atalla E, Balon R, Fisher AD, Laumann E, et al. Definitions of Sexual Dysfunctions in Women and Men: A Consensus Statement From the Fourth International Consultation on Sexual Medicine 2015. J Sex Med. 2016;13:135-143.
2. Nicolosi A, Moreira ED, Shirai M, Bin MTM, Glasser DB. Epidemiology of erectile dysfunction in four countries: cross-national study of the prevalence and correlates of erectile dysfunction. Urology. 2003;61:201-206.
3. Saigal CS, Wessells H, Pace J, Schonlau M, Wilt TJ. Predictors and prevalence of erectile dysfunction in a racially diverse population. Arch Intern Med. 2006;166:207-212.
4. McKinlay JB. The worldwide prevalence and epidemiology of erectile dysfunction. Int J Impot Res. 2000;12 Suppl 4:S6-S11.
5. Inman BA, Sauver JL, Jacobson DJ, McGree ME, Nehra A, Lieber MM, et al. A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. Mayo Clin Proc. 2009;84:108-113.
6. Shiri R, Koskimäki J, Hakama M, Häkkinen J, Huhtala H, Tammela TL. Effect of life-style factors on incidence of erectile dysfunction. Int J Impot Res. 2004;16:389-394.
7. Batty GD, Li Q, Czernichow S, Neal B, Zoungas S, Huxley R, et al. Erectile dysfunction and later cardiovascular disease in men with type 2 diabetes: prospective cohort study based on the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) trial. J Am Coll Cardiol. 2010;56:1908-1913.
8. Skrypnik D, Bogdański P, Musialik K. [Obesity--significant risk factor for erectile dysfunction in men]. Pol Merkur Lekarski. 2014;36:137-141.
9. Najari BB, Kashanian JA. Erectile Dysfunction. JAMA. 2016;316:1838.
10. Koroglu G, Kaya-Sezginer E, Yilmaz-Oral D, Gur S. Management of Erectile Dysfunction: An Under-Recognition of Hypertension. Curr Pharm Des. 2018;24:3506-3519.
11. Miner M, Billups KL. Erectile dysfunction and dyslipidemia: relevance and role of phosphodiesterase type-5 inhibitors and statins. J Sex Med. 2008;5:1066-1078.
12. Kouidrat Y, Pizzol D, Cosco T, Thompson T, Carnaghi M, Bertoldo A, et al. High prevalence of erectile dysfunction in diabetes: a systematic review and meta-analysis of 145 studies. Diabet Med. 2017;34:1185-1192.
13. Wu YX, Yang CT, Li N, Zheng X, Li X, Zhang H, et al. How Does Diabetes Impair Penile Tissues during Erectile Dysfunction? Endocr Metab Immune Disord Drug Targets. 2020;20:1535-1542.
14. Thorve VS, Kshirsagar AD, Vyawahare NS, Joshi VS, Ingale KG, Mohite RJ. Diabetes-induced erectile dysfunction: epidemiology, pathophysiology and management. J Diabetes Complications. 2011;25:129-136.
15. Chitaley K, Kupelian V, Subak L, Wessells H. Diabetes, obesity and erectile dysfunction: field overview and research priorities. J Urol. 2009;182 Suppl 6:S45-S50.
16. Blute M, Hakimian P, Kashanian J, Shteynshluyger A, Lee M, Shabsigh R. Erectile dysfunction and testosterone deficiency. Front Horm Res. 2009;37:108-122.
17. Khosla UM, Zharikov S, Finch JL, Nakagawa

T, Roncal C, Mu W, et al. Hyperuricemia induces endothelial dysfunction. Kidney Int. 2005;67:1739-1742.
18. Park JH, Jin YM, Hwang S, Cho DH, Kang DH, Jo I. Uric acid attenuates nitric oxide production by decreasing the interaction between endothelial nitric oxide synthase and calmodulin in human umbilical vein endothelial cells: a mechanism for uric acid-induced cardiovascular disease development. Nitric Oxide. 2013;32:36-42.
19. Matheus AS, Tibiriçá E, Da SP, de Fátima BDMM, Gomes MB. Uric acid levels are associated with microvascular endothelial dysfunction in patients with Type 1 diabetes. Diabet Med. 2011;28:1188-1193.
20. Totaro M, Dimarakis S, Castellini C, D'Andrea S, Parisi A, D'Amato F, et al. Erectile dysfunction in hyperuricemia: A prevalence meta-analysis and meta-regression study. Andrology. 2022;10:72-81.
21. Wu X, Liu G, Zhang Y, Zhang W, Dai Y, Jiang H, et al. The association between uric acid and erectile dysfunction: A systematic review and Meta-analysis. Andrologia. 2022;54:e14319.
22. Zharikov S, Krotova K, Hu H, Baylis C, Johnson RJ, Block ER, et al. Uric acid decreases NO production and increases arginase activity in cultured pulmonary artery endothelial cells. Am J Physiol Cell Physiol. 2008;295:C1183-C1190.
23. Gersch C, Palii SP, Kim KM, Angerhofer A, Johnson RJ, Henderson GN. Inactivation of nitric oxide by uric acid. Nucleosides Nucleotides Nucleic Acids. 2008;27:967-978.
24. Kang DH, Han L, Ouyang X, Kahn AM, Kanellis J, Li P, et al. Uric acid causes vascular smooth muscle cell proliferation by entering cells via a functional urate transporter. Am J Nephrol. 2005;25:425-433.
25. Tuokko AT, Murtola T, Korhonen P, Kaipia A. Hyperuricemia Is Not an Independent Predictor of Erectile Dysfunction. Sex Med. 2021;9:100319.
26. Hatzimouratidis K, Amar E, Eardley I, Giuliano F, Hatzichristou D, Montorsi F, et al. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. Eur Urol. 2010;57:804-814.
27. Shamloul R, Ghanem H. Erectile dysfunction. Lancet. 2013;381:153-165.
28. Muneer A, Kalsi J, Nazareth I, Arya M. Erectile dysfunction. BMJ. 2014;348:g129.
29. Lizza EF, Rosen RC. Definition and classification of erectile dysfunction: report of the Nomenclature Committee of the International Society of Impotence Research. Int J Impot Res. 1999;11:141-143.
30. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, et al. Erectile dysfunction. Nat Rev Dis Primers. 2016;2:16003.
31. Matsui H, Sopko NA, Hannan JL, Bivalacqua TJ. Pathophysiology of erectile dysfunction. Curr Drug Targets. 2015;16:411-419.
32. Clark NG, Fox KM, Grandy S. Symptoms of diabetes and their association with the risk and presence of diabetes: findings from the Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD). Diabetes Care. 2007;30:2868-2873.
33. Quek KF, Sallam AA, Ng CH, Chua CB. Prevalence of sexual problems and its association with social, psychological and physical factors among men in a Malaysian population: a cross-sectional study. J Sex Med. 2008;5:70-76.
34. Schulster ML, Liang SE, Najari BB. Metabolic syndrome and sexual dysfunction. Curr Opin Urol. 2017;27:435-440.
35. Pernow J, Jung C. The Emerging Role of Arginase in Endothelial Dysfunction in Diabetes. Curr Vasc Pharmacol. 2016;14:155-162.
36. Ding F, Shan C, Li H, Zhang Y, Guo C, Zhou Z, et al. Simvastatin alleviated diabetes mellitus-induced erectile dysfunction in rats by enhancing AMPK pathway-induced autophagy. Andrology. 2020;8:780-792.
37. Julian TH, Syeed R, Glascow N, Zis P. Alcohol-induced autonomic dysfunction: a systematic review. Clin Auton Res. 2020;30:29-41.
38. Lee AC, Ho LM, Yip AW, Fan S, Lam TH. The effect of alcohol drinking on erectile dysfunction in Chinese men. Int J Impot Res. 2010;22:272-278.
39. Maiorino MI, Bellastella G, Esposito K. Lifestyle modifications and erectile dysfunction: what can be expected? Asian J Androl. 2015;17:5-10.
40. Schulz KF. Randomized controlled trials. Clin Obstet Gynecol. 1998;41:245-256.
41. Ranstam J. Bias in observational studies. Acta Radiol. 2008;49:644-645.
42. Benedetto U, Head SJ, Angelini GD, Blackstone EH. Statistical primer: propensity score matching and its alternatives. Eur J Cardiothorac Surg. 2018;53:1112-1117.
43. Rubin DB. The design versus the analysis of observational studies for causal effects: parallels with the design of randomized trials. Stat Med. 2007;26:20-36.
44. Austin PC. A critical appraisal of propensity-score matching in the medical literature between 1996 and 2003. Stat Med. 2008;27:2037-2049.
45. Salem S, Mehrsai A, Heydari R, Pourmand G. Serum uric acid as a risk predictor for erectile dysfunction. J Sex Med. 2014;11:1118-1124.
46. Gao F, Jiang B, Cang Z, Wang N, Han B, Li Q, et al. Serum Uric Acid Is Associated with Erectile Dysfunction: A Population-Based Cross-Sectional Study in Chinese Men. Sci Rep. 2017;7:2087.
47. Aribas A, Kayrak M, Ulucan S, Keser A, Demir K, Alibasic H, et al. The relationship between uric acid and erectile dysfunction in hypertensive subjects. Blood Press. 2014;23:370-376.
48. NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence.

JAMA. 1993;270:83-90.
49. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology. 1997;49:822-830.
50. Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Peña BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999;11:319-326.
51. Wasserman MD, Pollak CP, Spielman AJ, Weitzman ED. The differential diagnosis of impotence. The measurement of nocturnal penile tumescence. JAMA. 1980;243:2038-2042.
52. Bradley WE, Timm GW, Gallagher JM, Johnson BK. New method for continuous measurement of nocturnal penile tumescence and rigidity. Urology. 1985;26:4-9.
53. Zou Z, Lin H, Zhang Y, Wang R. The Role of Nocturnal Penile Tumescence and Rigidity (NPTR) Monitoring in the Diagnosis of Psychogenic Erectile Dysfunction: A Review. Sex Med Rev. 2019;7:442-454.
54. Barassi A, Corsi RM, Pezzilli R, Dozio E, Damele C, Vaccalluzzo L, et al. Levels of uric acid in erectile dysfunction of different aetiology. Aging Male. 2018;21:200-205.