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REVIEW

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The relationship between hyperuricemia and erectile dysfunction: a scoping review

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Abstract

Recent studies suggest an association between hyperuricemia (HUA) and erectile dysfunction (ED), yet controversy remains regarding whether HUA is an independent risk factor. The proposed mechanisms include HUA-induced oxidative stress, inflammation, and metabolic syndrome, leading to pathophysiological changes. To explore this, we conducted a scoping review following PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews) guidelines. We performed literature searches in PubMed, Web of Science, and other databases, using the Newcastle-Ottawa Scale (NOS) and Appraisal tool for Cross-Sectional Studies (AXIS) for quality assessment. We included 16 clinical studies (n = 295,705) published between 2014 and 2025, comprising 13 cross-sectional and 3 cohort studies. A positive correlation between HUA and ED was supported by 15 of the 16 studies (93.8%). Among these, five demonstrated the association persisted after adjusting for confounding factors, while two identified HUA as an independent factor. The three cohort studies were all rated as high quality (NOS score 9/9). An exploratory pooled analysis of these high-quality studies revealed that patients with gout had a 16% increased risk of developing ED (HR (Hazard Ratio) = 1.16, 95% CI (confidence interval) 1.104–1.219, $p < 0.001$). This estimate should be interpreted cautiously due to the limited number of studies and heterogeneity. In conclusion, a significant association exists between HUA and erectile function, though the relationship remains complex. The pathophysiology may involve an "oxidative stress-inflammation-metabolism" triad. While controlling uric acid levels shows potential for the prevention and treatment of ED, further research is required before this approach can be supported for routine clinical application.

Keywords

Hyperuricemia; Erectile dysfunction; Oxidative stress; Nitric oxide; Endothelial dysfunction; Scoping review

1. Research background

The occurrence of Erectile Dysfunction (ED) is usually the result of multiple factors working together. Improving lifestyle, actively managing chronic diseases, and paying attention to mental health and hormone levels are key to preventing and treating ED [1]. Its incidence increases significantly with age and is closely related to complications such as cardiovascular disease, diabetes, and metabolic syndrome [2]. Vascular endothelial dysfunction is the core and common pathological mechanism of ED, and most ED cases are closely related to vascular damage [3]. Hyperuricemia (HUA) is defined as fasting serum uric acid levels exceeding 420 μmol/L (7.0 mg/dL) (in males) on two non-consecutive days under normal purine diet conditions [4]; gout is caused by the formation and deposition of monosodium urate crystals within joints, leading to acute, severe pain and aseptic inflammation [5]. Research indicates that HUA has a potential association with ED, and the mechanism may involve HUA-induced oxidative stress, inflammatory activation, and metabolic syndrome, which subsequently damage vascular endothelial function, disrupt endocrine homeostasis, and exacerbate psychological stress [6].

Current research has found that uric acid can impair endothelial function by inhibiting nitric oxide (NO) production, while NO is a key molecule for maintaining vascular dilation and penile erection [7, 8]. Furthermore, the association between HUA and ED is particularly significant in populations with comorbid hypertension, diabetes, and other metabolic diseases, suggesting that uric acid levels synergistically promote ED progression with age, blood pressure, and metabolic disorders [9].

Although HUA is closely related to endothelial damage, microvascular lesions, and hypertension, whether it is an independent risk factor for ED remains controversial. Some studies

believe that HUA directly promotes ED occurrence [10, 11], while other viewpoints suggest that HUA merely reflects a biomarker of underlying vascular pathological states [12]. This controversy has important clinical significance: if there is a causal relationship between HUA and ED, uric acid-lowering therapy may become a new strategy for ED prevention and intervention; conversely, if the association is primarily driven by coexisting cardiovascular risk factors, clinical management should focus on comprehensive metabolic-cardiovascular risk management.

2. Research objectives

This scoping review aims to systematically examine the existing literature on the relationship between hyperuricemia and erectile dysfunction, analyze the quality of existing evidence, explore potential pathological mechanisms, and provide references for clinical practice and future research directions.

3. Research methods

3.1 Study design and framework

This study is a scoping review conducted according to the methodological framework proposed by Arksey and O'Malley [13]. We chose the scoping review method because our primary objective is to examine the existing literature on the relationship between hyperuricemia and erectile dysfunction, identify key concepts and knowledge gaps, and examine the scope and nature of research activity in this field. Scoping reviews are suitable for exploring emerging topics because the literature on these topics may vary in study design, populations, and outcomes [14]. This scoping review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines [15].

3.2 Research questions

The research questions include primary and secondary questions. The primary research question is: what evidence currently exists indicating an association between hyperuricemia and erectile dysfunction, and what are the potential mechanisms of this relationship? Secondary questions include: (1) What study designs have been used to investigate this association? (2) Which populations have been studied? (3) What are the characteristics of this association in different patient groups? (4) What biological mechanisms have been proposed?

3.3 Search strategy and data sources

We searched literature from database inception to the present, with data sources including PubMed/MEDLINE, Web of Science Core Collection, Scopus, and Google Scholar. The search strategy was reviewed by a medical librarian and integrated Medical Subject Headings (Mesh) and free-text terms. Core search concepts were: (1) Population: males ("male", "men", "adult"); (2) Exposure: hyperuricemia ("hyperuricemia", "hyperuricaemia"), uric acid ("uric acid", "serum uric acid", "SUA"), gout ("gout"); (3) Outcome: erectile dysfunction ("erectile dysfunction", "ED", "impotence"), sexual dysfunction ("sexual dysfunction", "sexual function").

The PubMed search strategy example is as follows: (hyperuricemia [Mesh Terms] OR hyperuricemia [Title/Abstract] OR hyperuricaemia [Title/Abstract] OR "uric acid" [Mesh Terms] OR "uric acid" [Title/Abstract] OR "serum uric acid" [Title/Abstract] OR gout [Mesh Terms] OR gout [Title/Abstract]) AND (erectile dysfunction [Mesh Terms] OR "erectile dysfunction" [Title/Abstract] OR impotence [Mesh Terms] OR impotence [Title/Abstract] OR "sexual dysfunction" [Title/Abstract] OR "sexual function" [Title/Abstract]) AND (male [Mesh Terms] OR male [Title/Abstract] OR men [Title/Abstract]). The search was not limited by publication time or language, but non-English literature for which English versions could not be obtained was excluded during the full-text screening stage.

3.4 Study selection

3.4.1 Inclusion criteria

Studies meeting the following criteria were included: (1) Study design: clinical studies, including cross-sectional, case-control, cohort (prospective or retrospective), and randomized controlled trials; (2) Study population: adult males ($\geq$18 years old); (3) Exposure: measurement of serum uric acid levels or diagnosis of hyperuricemia or gout; (4) Outcome: assessment of erectile dysfunction using validated tools or clinical diagnosis; (5) Data availability: sufficient data to evaluate the relationship between hyperuricemia and erectile dysfunction.

3.4.2 Exclusion criteria

The following studies were excluded: (1) Reviews, editorials, commentaries, case reports, or conference abstracts; (2) Animal or *in vitro* studies; (3) Studies not providing original data on the relationship between hyperuricemia and erectile dysfunction; (4) Insufficient analytical data; (5) Duplicate publications.

3.4.3 Screening process

Two reviewers (reviewer initials were anonymized) independently screened titles and abstracts according to pre-established inclusion and exclusion criteria. Full texts of all potentially relevant studies were then obtained. The same two reviewers independently assessed the full texts to determine final inclusion. Disagreements were resolved through discussion; if consensus could not be reached, a third reviewer was consulted. The screening process was documented using a PRISMA flow diagram (Fig. 1).

3.5 Data extraction

Data extraction was completed independently by two reviewers, extracting the following information from each included study: (1) Study characteristics: first author, publication year, country, study design, sample size; (2) Population characteristics: age, comorbidities, study setting (clinical studies *vs.* population studies); (3) Hyperuricemia assessment: defini-

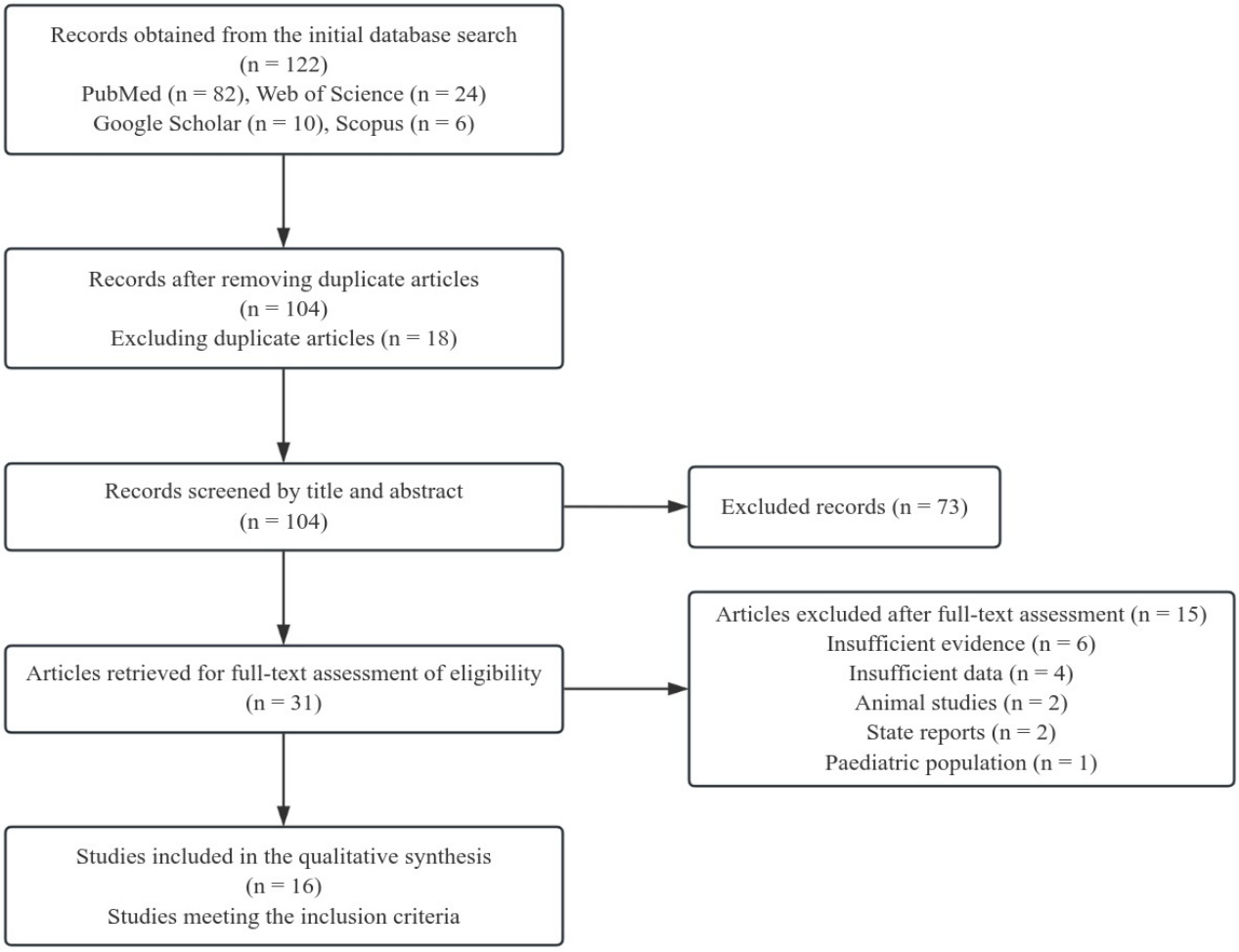


FIGURE 1. Literature selection flowchart (based on PRISMA statement).

tions used, measurement methods, cutoff values; (4) Erectile dysfunction assessment: assessment tools, definitions, severity classification; (5) Statistical analysis: analytical methods, confounding variable adjustment, effect measures; (6) Main conclusions: primary results on the relationship between hyperuricemia and erectile dysfunction; (7) Study quality indicators: response rates, loss to follow-up, potential sources of bias.

3.6 Quality assessment

The methodological quality of included studies was assessed using standardized tools with categorical evaluation, including two types: cohort studies/case-control studies and cross-sectional studies. Cohort studies/case-control studies used the NOS scale (Newcastle-Ottawa Scale) [16], scoring detailed criteria across three dimensions, with a total score of 9 points, $\geq$7 points indicating high quality, 4–6 points moderate quality, and $\leq$3 points low quality. Cross-sectional studies: The AXIS tool (Appraisal tool for Cross-Sectional Studies) [17, 18] was used, covering 11 dimensions of bias risk (such as sample representativeness, measurement standards, *etc.*).

3.7 Data synthesis and analysis

Given the heterogeneity in study design, study populations, and outcome measurements, the study employed a narrative synthesis approach rather than quantitative meta-analysis. Studies were categorized into three groups based on their main conclusions regarding the relationship: (1) studies showing a positive correlation between the two; (2) studies showing no significant correlation between the two; (3) studies showing that uric acid has a protective effect. For each category, we examined study characteristics, population characteristics, methodological approaches, and potential sources of heterogeneity. We also analyzed the biological mechanisms proposed by authors and summarized and calculated the risk coefficients for hyperuricemia leading to ED.

4. Research results

4.1 Study selection and characteristics

The initial database search yielded a total of 122 articles (PubMed = 82 articles; Web of Science = 24 articles; Google Scholar = 10 articles; Scopus = 6 articles). After excluding duplicate articles (n = 18), 104 articles underwent title and abstract screening. Of these, 31 articles were selected for full-text review. After full-text evaluation, 15 articles were excluded for the following reasons: review articles (n = 6), insufficient data on the relationship between hyperuricemia and erectile dysfunction (n = 4), animal studies (n = 2), case reports (n = 2), and pediatric population (n = 1). Finally, 16

studies met the inclusion criteria and were included in this scoping review.

4.2 Study characteristics and quality assessment

The 16 included studies involved a total of 295,705 participants and were published between 2014 and 2024, indicating growing research interest in this field. Twelve studies (n = 13, 75%) used cross-sectional design, and 4 studies used cohort design. Specifically, cross-sectional studies using the AXIS tool scored between 7–9 points (moderate-high), while cohort studies using the NOS scale all achieved full scores of 9 points (high quality). Methodological rigor was high (81% scored AXIS ≥8 points or NOS = 9 points) (as shown in Table 1, Ref. [19–34]).

4.3 Population characteristics

The studies primarily focused on middle-aged and elderly Asian males, with a large total sample size but extremely uneven distribution, showing a "bimodal distribution"—4 ultra-large cohort studies (totaling 295,705 people) coexisting with 12 small-to-medium cross-sectional studies (median sample of 200 people); 62.5% focused on specific disease populations (cardiovascular/metabolic disease patients), with only 37.5% covering general populations; geographic distribution was significantly skewed toward Asia (62.5%), with relatively weak evidence from Europe and America; although covering the 20–83 age range, the core focus was on the 45–70 age group. High-quality evidence mainly came from national cohorts (NOS = 9 points), while more than half of the cross-sectional studies had hospital-centric bias (single-center studies accounting for 25%).

4.4 Definitions of hyperuricemia and erectile dysfunction

The definition of hyperuricemia was highly heterogeneous across the 16 studies: only 1 US study (6.3%) used the international standard (>7.0 mg/dL), while the remaining 93.7% used non-standardized definitions, including relative grouping methods (18.8%, such as grouping by quartiles/median, with generally low cutoff points), disease proxy methods (18.8%, indirectly defined by gout diagnosis or medication treatment), and undefined definitions (56.3%, only reporting values without thresholds). Future studies are recommended to uniformly use the >7.0 mg/dL standard and supplement with sensitivity analyses to improve conclusion reliability. Unlike the high heterogeneity in hyperuricemia definitions, ED assessment methods have been largely standardized internationally, mainly evaluated through the International Index of Erectile Function-5 (IIEF-5) questionnaire, with the cutoff score for diagnosing ED typically set at ≤21 [18].

4.5 Relationship between hyperuricemia and erectile dysfunction

4.5.1 Studies showing positive correlation

Large sample evidence shows: Chen *et al.*'s [19] Taiwan cohort study (19,368 gout patients *vs.* 77,472 controls) showed that gout patients had a 1.21-fold increased risk of erectile dysfunction (95% CI 1.03–1.44); in cardiovascular disease populations, Salavati *et al.*'s [26] study showed that ED patients with comorbid coronary heart disease had higher serum uric acid levels than those with normal coronary arteries (6.5 ± 0.8 mg/dL *vs.* 5.6 ± 0.7 mg/dL, $p = 0.034$) [20]; in hypertensive comorbidity populations, Ticoalu *et al.*'s [21] study found that hyperuricemia increased erectile dysfunction risk (OR (Odds Ratio) = 3.89; 95% CI 1.08–15.70; $p = 0.017$). Therefore, most studies (approximately 93.8%) indicate that hyperuricemia is positively correlated with erectile dysfunction, with some studies showing this is independent of confounding factors such as age, BMI (Body Mass Index), diabetes, hypertension, and cardiovascular disease.

4.5.2 Studies showing no independent association

Two high-quality studies showed that after adjusting for cardiovascular risk factors, hyperuricemia had no independent association with erectile dysfunction: Tuokko *et al.*'s [22] Finnish study (n = 254): after multivariate adjustment OR = 1.14 (95% CI 0.59–2.19, $p = 0.7$). Wang *et al.*'s [23] study based on NHANES (National Health and Nutrition Examination Survey) data (n = 3810): fully adjusted model OR = 1.02 (95% CI 0.84–1.24, $p = 0.5$), with consistent sensitivity analysis results (OR = 0.85, 95% CI 0.60–1.19).

4.5.3 Studies showing opposite results

One cross-sectional study based on the Chinese general population (Gao *et al.* [24], n = 1365) reached the opposite conclusion: serum uric acid levels were independently positively correlated with erectile function (protective effect) (OR = 0.998). This contradictory result may stem from: Population differences: the study subjects were from the Chinese general population, while other studies were mostly based on clinical patients with comorbidities (such as coronary heart disease, hypertension, gout, *etc.*); Analytical method differences: different confounding factor adjustments or statistical methods; Non-linear relationships: there may be a U-shaped or inverted U-shaped relationship between uric acid and erectile function. Unmeasured confounding factors: such as specific genetic background, dietary or environmental factors.

Table 1 displays important data information from 16 studies on the association between hyperuricemia and erectile dysfunction (ED), covering cross-sectional (13 studies) and cohort studies (3 studies), with sample sources including single center (11 studies), regional (3 studies), and national databases (2 studies). Study quality was highest for cohort studies (NOS score 9/9), while cross-sectional studies were mostly of moderate quality (AXIS score 7–9/11). There was significant heterogeneity in conclusions, which may stem from study design (cross-sectional studies cannot establish causality), population differences (metabolic disease patients *vs.* general population), and insufficient control of confounding factors.

TABLE 1. Summary of literature on the association between uric acid and erectile dysfunction.

No.	Study Title (Publication Year)	Study Type	Risk Coefficient (HR/OR)	Assessment Tool	Quality Grade (Score/Total)	Bias Risk	Conclusion
1	A nationwide cohort study in Taiwan: association between gout and increased risk of erectile dysfunction in men aged 64 and below (2015) [19]	Cohort study	HR = 1.21	NOS	High (9/9)	Low	Gout patients have significantly higher risk of ED than non-gout population with dose-response relationship
2	Uric acid levels and erectile dysfunction in patients with coronary heart disease (2014) [20]	Cross-sectional study	OR = 1.36	AXIS	Moderate (7/11)	Moderate	Uric acid levels are associated with ED but not independent in multivariate analysis
3	Association between hyperuricemia and erectile dysfunction in hypertensive patients (2019) [21]	Cross-sectional study	OR = 3.89	AXIS	Moderate (8/11)	Moderate	Hyperuricemia is significantly associated with ED in hypertensive patients and is an independent risk factor
4	Hyperuricemia is not an independent predictor of erectile dysfunction (2021) [22]	Cross-sectional study	OR = 1.14	AXIS	High (9/11)	Low	Hyperuricemia is not an independent risk factor for ED; age education level and depression are significant predictors of ED
5	Serum uric acid is associated with erectile dysfunction: a cross-sectional study based on Chinese men (2017) [24]	Cross-sectional study	OR = 0.998	AXIS	High (9/11)	Low	Serum uric acid has independent protective effects on ED; age and uric acid are independent factors affecting ED
6	Serum uric acid as a predictor of erectile dysfunction (2014) [25]	Cross-sectional study	OR = 2.07	AXIS	Moderate (8/11)	Moderate	Serum uric acid can serve as a risk predictor for ED; hyperuricemia is an independent risk factor for ED
7	Are serum uric acid levels associated with erectile dysfunction in patients with coronary artery disease? (2016) [26]	Cross-sectional study	OR = 2.80	AXIS	Moderate (8/11)	Moderate	Risk of ED in coronary heart disease patients is 2.8 times higher than normal coronary artery patients, but statistical significance is marginal
8	Insulin resistance is an independent predictor of erectile dysfunction in gout patients (2019) [27]	Cross-sectional study	OR = 1.62	AXIS	Moderate (8/11)	Moderate	Insulin resistance is an independent predictor of ED in gout patients; ED prevalence in gout patients is significantly higher than controls
9	Uric acid levels in erectile dysfunction of different etiologies (2018) [28]	Cross-sectional study	Continuous variable comparison ($p < 0.001$)	AXIS	Moderate (7/11)	Moderate	Uric acid levels in arterial ED patients (5.8 mg/dL) significantly higher than non-arterial ED patients (4.4 mg/dL) and controls (4.6 mg/dL)

TABLE 1. Continued.

No.	Study Title (Publication Year)	Study Type	Risk Coefficient (HR/OR)	Assessment Tool	Quality Grade (Score/Total)	Bias Risk	Conclusion
10	Gout and risk of erectile dysfunction: a BMI-matched population-based study (2018) [29]	Cohort study	HR = 1.15	NOS	High (9/9)	Low	Gout is independently associated with increased risk of ED supporting hyperuricemia and inflammation as independent risk factors for ED
11	Correlation between serum uric acid levels and erectile dysfunction and vascular endothelial injury in male hypertensive patients (2020) [30]	Cross-sectional study	OR = 1.034	AXIS	Moderate (8/11)	Moderate	Serum uric acid is an independent factor for ED in hypertensive patients and is associated with vascular endothelial injury
12	Erectile dysfunction in type 2 diabetes patients: Predictive factors for early detection and treatment (2021) [31]	Cross-sectional study	OR = 1.021	AXIS	Moderate (8/11)	Moderate	Uric acid is an independent predictor of diabetic ED; risk increases by 2.1% per 1 μmol/L increase with optimal cutoff $\geq$392.5 μmol/L
13	Application value of serum 25(OH)D_3 uric acid triglycerides and homeostatic model assessment of insulin resistance in male patients with hyperuricemia (2021) [32]	Cross-sectional study	Multi-indicator assessment (combined prediction model)	AXIS	Moderate (7/11)	Moderate	Combined multi-indicator assessment has application value in male patients with hyperuricemia mainly focusing on hypogonadism
14	Risk of erectile dysfunction in male gout patients treated with Febuxostat or Allopurinol: a propensity score-matched cohort study (2022) [33]	Cohort study	HR = 1.354	NOS	High (9/9)	Low	Compared to allopurinol febuxostat may be associated with higher risk of ED
15	Association between uric acid and erectile dysfunction among US adults: NHANES 2001–2004 (2024) [23]	Cross-sectional study	OR = 1.02	AXIS	High (11/11)	Low	No significant association found between uric acid levels and ED; larger sample size studies needed for verification
16	Association between metabolic parameters and erectile function in patients with hyperuricemic erectile dysfunction (2025) [34]	Cross-sectional study	B = −0.552 ($p <$ 0.001)	AXIS	Moderate (8/11)	Moderate	Uric acid levels show significant negative correlation with erectile function; multiple linear regression model R^2 = 0.239

ED: Erectile Dysfunction; NOS: Newcastle-Ottawa Scale; HR: Hazard Ratio; OR: Odds Ratio; B: Beta (regression coefficient); AXIS: Appraisal tool for Cross-Sectional Studies; BMI: Body Mass Index; NHANES: National Health and Nutrition Examination Survey.

It is worth noting that the subgroup analysis focused on 3 high-quality cohort studies (Taiwan China, UK, and US databases), and pooled analysis using a fixed-effects model showed: the hazard ratio (HR) for gout patients developing ED was 1.16 (95% CI: 1.104–1.219, $p < 0.001$), with no heterogeneity ($I^2 = 0.0\%$). This result indicates that gout increases ED risk by 16%, with high-quality evidence level (GRADE (Grading of Recommendations Assessment, Development and Evaluation) system), supporting the causal association between hyperuricemia and ED and the necessity for clinical intervention.

5. Discussion

5.1 Main findings

This scoping review included 16 studies (295,705 participants) and systematically evaluated the association between hyperuricemia and erectile dysfunction. Results showed that 93.8% of studies (15/16) supported a positive correlation between the two, with one study reporting a protective association and no studies reporting null associations after proper adjustment, but only 31.3% of studies (5/16) confirmed an independent association. Exploratory pooled analysis of high-quality cohort studies indicated that gout patients had a 16% increased risk of developing ED (HR = 1.160, 95% CI 1.104–1.219, $p < 0.001$), with no heterogeneity ($I^2 = 0.0\%$). This exploratory estimate should be interpreted with high caution given the limited number of studies and heterogeneity in populations and definitions.

5.2 Evidence quality of association strength

Cohort studies provided the most reliable evidence support. Chen *et al.*'s [19] large cohort study based on Taiwan's National Health Insurance Database (19,368 gout patients *vs.* 77,472 controls) showed that gout patients had a 21% increased risk of ED (HR = 1.21, 95% CI 1.03–1.44). Similarly, a UK cohort study based on national electronic medical records confirmed this association (HR = 1.15) [29]. These large-sample, long-term follow-up cohort studies overcame the temporal limitations of cross-sectional designs and provided stronger evidence support for causal inference.

However, the independence of the association remains controversial. Two high-quality studies found no independent association after fully adjusting for cardiovascular risk factors: a Finnish community study (OR = 1.14, 95% CI 0.59–2.19, $p = 0.7$) [22] and a US study based on NHANES data (OR = 1.02, 95% CI 0.84–1.24, $p = 0.5$) [23]. This suggests that the association between hyperuricemia and ED may be partially mediated by coexisting metabolic-cardiovascular risk factors.

5.3 Comprehensive model of pathophysiological mechanisms

Based on the biological pathways summarized from included studies (Figs. 2,3,4), we synthesize previous mechanistic links into an integrated conceptual triad that HUA may lead to ED through the "oxidative stress-inflammation-metabolism" triad axis:

Evidence supporting the triad mechanism is organized by evidence level: (1) *In vitro* studies demonstrate uric acid crystal activation of inflammatory pathways; (2) Animal models show HUA-induced endothelial dysfunction; (3) Clinical observations include Salavati *et al.* [26] in coronary heart disease patients, Ticoalu *et al.* [21] in hypertensive cohorts, and Kim *et al.* [27] in insulin resistance/gut microbiome studies; (4) Limited intervention data from uric acid-lowering therapy studies. Each element of the triad is supported by oxidative stress (ROS (reactive oxygen species) generation, NADPH (Nicotinamide Adenine Dinucleotide Phosphate, reduced form) oxidase activation), inflammation (NF-κB (Nuclear Factor kappa-B) pathway, cytokine release), and metabolism (insulin resistance, endothelial dysfunction).

5.3.1 HUA inhibition of no synthesis mechanism

Hyperuricemia (HUA) activates the RAS (Renin Angiotensin System) system, xanthine oxidase (XO), and NADPH oxidase (NOX), increasing reactive oxygen species (ROS) and asymmetric dimethylarginine (ADMA), inhibiting endothelial nitric oxide synthase (eNOS) activity and nitric oxide (NO) synthesis, while damaging testicular interstitial cell structure and androgen synthesis, ultimately leading to erectile dysfunction (ED) [35].

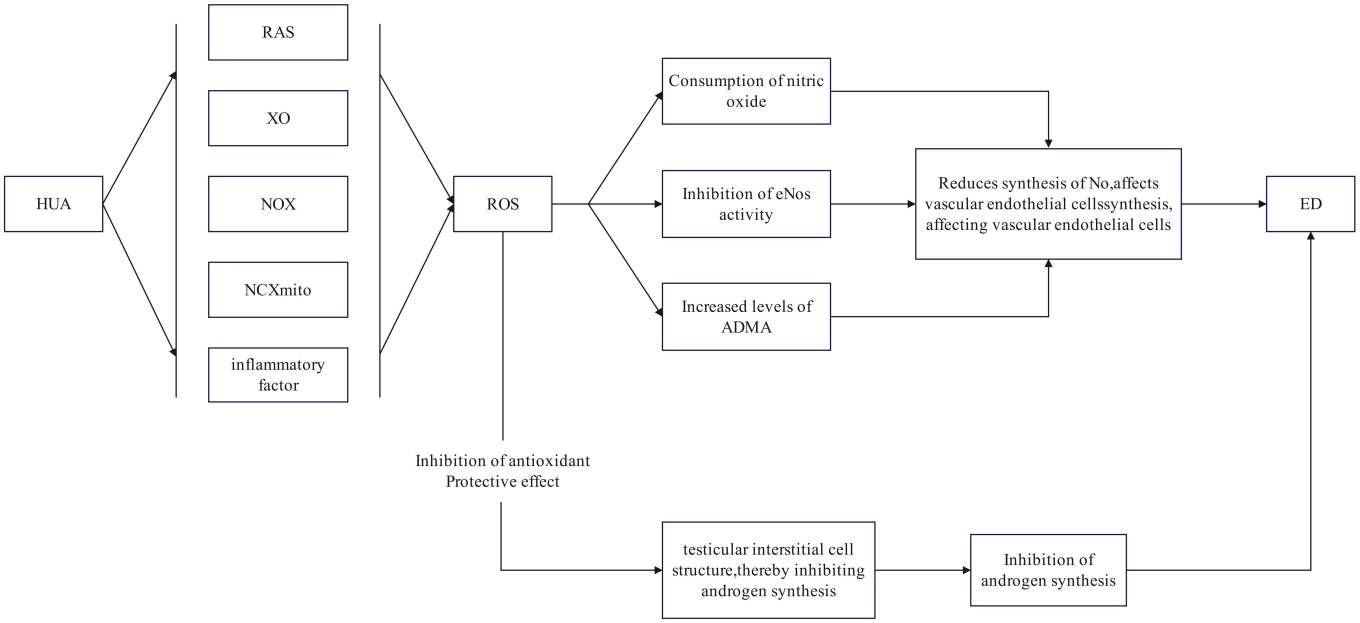
5.3.2 Uric acid crystal activation of inflammatory factor mechanism

Soluble uric acid and uric acid crystals activate the nuclear factor κB (NF-κB) signaling pathway, promoting the release of inflammatory cytokines (CRP (C-Reactive Protein), TNF-α (Tumor Necrosis Factor-alpha), IL-1β (Interleukin-1 beta)), increasing reactive oxygen species (ROS) generation, and reducing nicotinamide adenine dinucleotide (NAD+) levels, thereby decreasing nitric oxide (NO) bioavailability [36]. Persistent pain stimulation and chronic psychological stress further exacerbate erectile dysfunction (ED) [37].

5.3.3 HUA-mediated insulin resistance mechanism

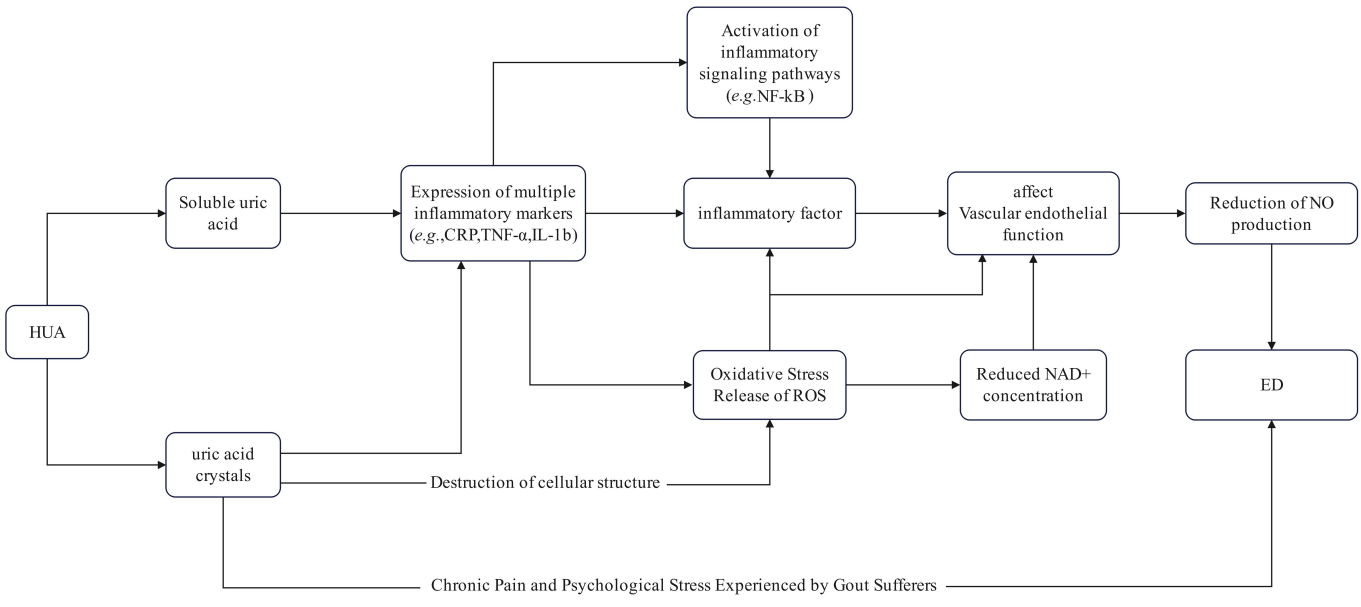
Hyperuricemia (HUA) activates NADPH oxidase (NOX) by promoting angiotensin II (Ang II) expression, inducing oxidative stress [38]; inhibits IRS1 (Insulin Receptor Substrate 1)/Akt (Protein Kinase B, PKB) phosphorylation leading to insulin resistance (IR), which subsequently activates uric acid transporter (URAT1) to reduce uric acid excretion [39]; reduces NO release and increases endothelin-1 (ET-1) by blocking the PI3K (Phosphatidylinositol 3-kinases)/Akt/eNOS pathway and affecting L-arginine transport, while simultaneously impairing testosterone synthesis [40].

The "oxidative stress-inflammation-metabolism" triad axis mechanism proposed by included studies has biological plausibility and is supported by clear evidence. Fig. 2 mechanism: HUA inhibits NO synthesis (Salavati *et al.* [26] observed elevated UA in coronary heart disease patients with comorbid ED, $p = 0.034$) [19]; Fig. 3 mechanism: uric acid crystals activate inflammatory factors (Ticoalu *et al.* [21] found that HUA increased ED risk by 4-fold in hypertensive patients) [20]; Fig. 4 mechanism: HUA mediates insulin resistance



HUA (hyperuricemia)
RAS (Renin Angiotensin System)
XO (Xanthine oxidase)
NOX (NADPH oxidase)
NCXmito (Sodium-calcium exchanger)
ROS (Reactive Oxygen Species)
ADMA (Asymmetric Dimethylarginine)
ED (Erectile Dysfunction)

FIGURE 2. Mechanism by which hyperuricemia inhibits nitric oxide synthesis through oxidative stress and inflammatory response, leading to erectile dysfunction.



CRP: C-Reactive Protein; TNF-α: Tumor Necrosis Factor-alpha; IL-1b: Interleukin-1beta ; NF-kB: Nuclear Factor kappa-light-chain-enhancer of activated B cells; NAD+: Nicotinamide Adenine Dinucleotide; HUA: hyperuricemia; NO: Nitric Oxide; ED: Erectile Dysfuncton; ROS: Reactive Oxygen Species.

FIGURE 3. Mechanism of hyperuricemia damaging vascular endothelial function through inflammatory pathways and oxidative stress.

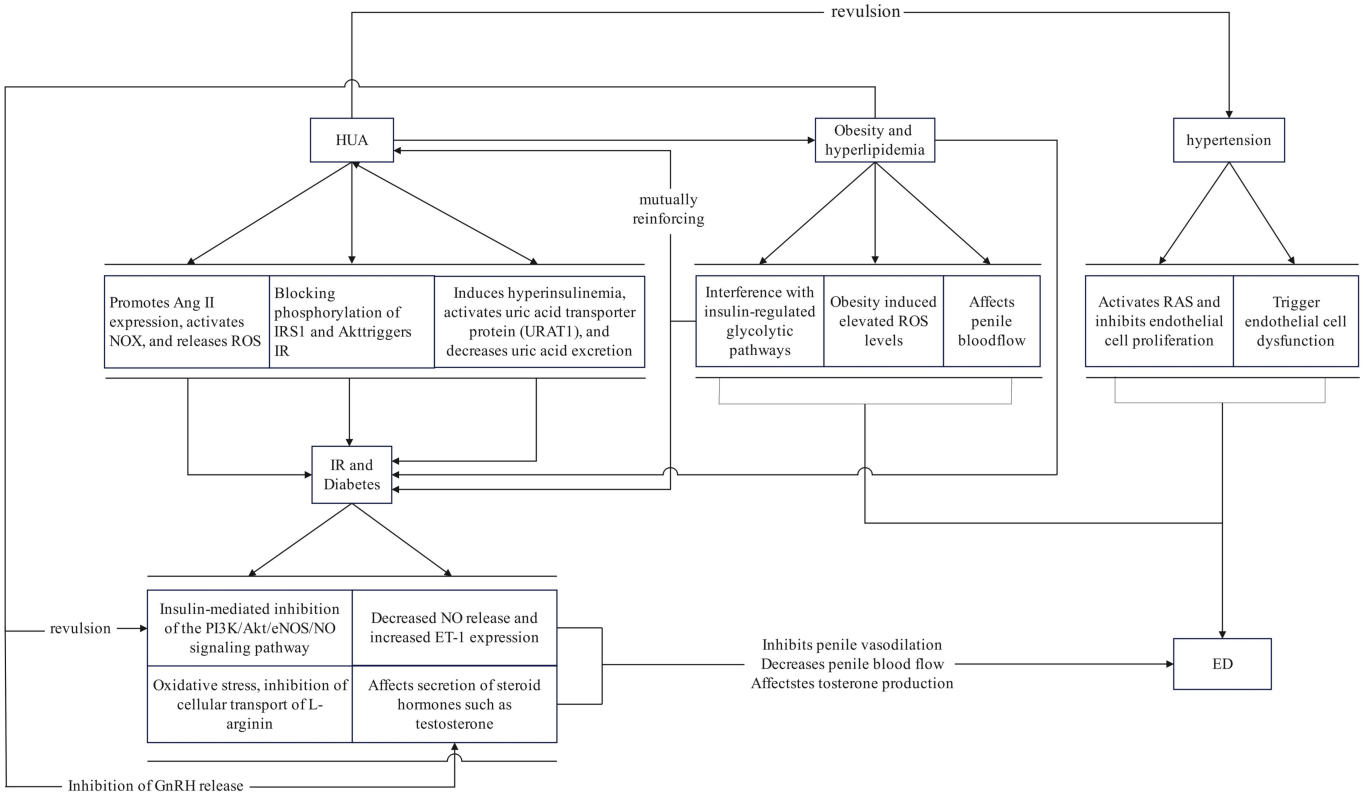


FIGURE 4. Molecular pathways by which hyperuricemia mediates insulin resistance and vascular endothelial dysfunction.

(Korean study confirmed that IR is an independent predictor of ED in gout patients, OR = 1.62) [26].

5.4 Explanation of contradictory results

Gao *et al.*'s [24] study based on the Chinese general population reached the opposite conclusion, suggesting that serum uric acid has a protective effect on ED (OR = 0.998) [23]. This contradiction may reflect the biphasic biological effects of uric acid: at physiological concentrations, uric acid serves as an important antioxidant, accounting for approximately 60% of plasma antioxidant capacity; however, when pathologically elevated, it becomes a pro-oxidant and pro-inflammatory factor [41]. Additionally, this study was based on the general population rather than clinical patients, which may involve population selection differences. Differences in genetic background, dietary patterns, and environmental factors may also affect uric acid metabolism and vascular reactivity.

5.5 Impact of methodological heterogeneity

The high heterogeneity in hyperuricemia definitions is an important finding of this review. Only 6.3% of studies used the international standard definition (>7.0 mg/dL), while 93.7% used non-standardized definitions, including relative grouping methods (18.8%), disease proxy methods (18.8%), and undefined definitions (56.3%). This inconsistency in definitions may lead to systematic bias in association strength, affecting the comparability and clinical translational value of results.

The limitations of study design should not be overlooked. Cross-sectional studies accounted for 75%, which cannot establish temporal relationships or causal inference. The uneven geographic distribution (62.5% from Asia) limits the global applicability of results. Furthermore, 62.5% of studies focused on specific disease populations, which may overestimate association strength.

5.6 Clinical significance

Based on existing evidence, the association between hyperuricemia and ED has important clinical significance, particularly in patients with comorbid cardiovascular metabolic diseases. However, the evidence is insufficient to support routine uric acid screening for all ED patients or uric acid-lowering therapy as first-line treatment for ED. Further research is needed before routine clinical application can be supported [42]. Clinical management should adopt a comprehensive cardiovascular risk assessment strategy, as hyperuricemia and ED may jointly reflect underlying endothelial dysfunction and metabolic disorders.

For patients with both hyperuricemia and ED, focus should be placed on modifiable cardiovascular risk factors, including management of hypertension, diabetes, dyslipidemia, and lifestyle factors. The benefits of uric acid-lowering therapy need to be further validated through prospective intervention studies.

5.7 Study limitations

This review has several important limitations. First, the heterogeneity in study design and populations excluded the possibility of quantitative meta-analysis, limiting precise estimation of effect sizes. Second, cross-sectional studies dominated, making it impossible to establish causal relationships. Third, the non-uniform definition of hyperuricemia affected the comparability of results. Fourth, geographic distribution bias may limit the universal applicability of results. Finally, the possibility of publication bias cannot be excluded.

5.8 Future research directions

Future research should prioritize large-sample, multicenter prospective cohort studies using standardized hyperuricemia definitions (>7.0 mg/dL) and ED assessment tools. Intervention studies should evaluate the impact of uric acid-lowering therapy on erectile function to determine causality and clinical relevance. Mechanistic studies should explore dose-response relationships between uric acid levels and erectile function, particularly potential non-linear relationships. Genetic studies may help explain differences between populations and identify high-risk individuals.

6. Conclusion

Existing evidence supports an association between hyperuricemia and erectile dysfunction, particularly in patients with comorbid cardiovascular metabolic diseases. High-quality cohort studies show that gout patients have a 16% increased risk of ED, but the independence of this association remains controversial. The "oxidative stress-inflammation-metabolism" triad axis mechanism synthesizes previous mechanistic links into an integrated conceptual framework and has biological plausibility but requires more mechanistic studies for validation. In clinical practice, the potential association between the two should be emphasized by adopting comprehensive cardiovascular risk management strategies rather than simple uric acid-lowering therapy. Future high-quality prospective studies and intervention trials are needed to determine causal relationships and optimal treatment strategies.

AVAILABILITY OF DATA AND MATERIALS

All data supporting the conclusions of this article are contained within the article and its references. Additional data may be requested from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

ML, SAH and XYS—designed the research study; wrote the manuscript. ML and XYS—performed the research. JDZ and YOY—provided help and advice on writing the final version of the manuscript. The manuscript's editing revisions were made with input from all authors. All authors reviewed and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This scoping review analyzed previously published data and did not involve new human or animal subjects. Therefore, institutional ethical approval was not required.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Zhu D, Pham QM, Wang C, Colonnello E, Yannas D, Nguyen BH, *et al*. Erectile dysfunction and oxidative stress: a narrative review. International Journal of Molecular Sciences. 2025; 26: 3073.

[2] Pellegrino F, Sjoberg DD, Tin AL, Benfante NE, Briganti A, Montorsi F, *et al*. Relationship between age, comorbidity, and the prevalence of erectile dysfunction. European Urology Focus. 2023; 9: 162–167.

[3] De Leonardis F, Colalillo G, Finazzi Agrò E, Miano R, Fuschi A, Asimakopoulos AD. Endothelial dysfunction, erectile deficit and cardiovascular disease: an overview of the pathogenetic links. Biomedicines. 2022; 10: 1848.

[4] Piao W, Zhao L, Yang Y, Fang H, Ju L, Cai S, *et al*. The prevalence of hyperuricemia and its correlates among adults in China: results from CNHS 2015–2017. Nutrients. 2022; 14: 4095.

[5] Yang S, Liu H, Fang XM, Yan F, Zhang Y. Signaling pathways in uric acid homeostasis and gout: from pathogenesis to therapeutic interventions. International Immunopharmacology. 2024; 132: 111932.

[6] Park K, Gupta NK, Olweny EO, Schlesinger N. Beyond arthritis: understanding the influence of gout on erectile function: a systematic review. Urology. 2021; 153: 19–27.

[7] Nie Q, Liu M, Zhang Z, Zhang X, Wang C, Song G. The effects of hyperuricemia on endothelial cells are mediated via GLUT9 and the JAK2/STAT3 pathway. Molecular Biology Reports. 2021; 48: 8023–8032.

[8] Xavier FE. Nitrergic perivascular innervation in health and diseases: focus on vascular tone regulation. Acta Physiologica. 2020; 230: e13484.

[9] Wang W, Zhao S, Zhou R, Yu PZ, Pan SY, Huan PF, *et al*. Associations between metabolic syndrome and erectile dysfunction: evidence from the NHANES 2001–2004. Frontiers in Public Health. 2025; 13: 1543668.

[10] Halomoan R, Christopher J. Hyperuricemia and the risk of hypertension: a systematic review and meta-analysis. Journal of Hypertension. 2023; 41: 875–885.

[11] Wang W, Jing Z, Liu W, Zhu L, Ren H, Hou X. Hyperuricaemia is an important risk factor of the erectile dysfunction: a systematic review and meta-analysis. Andrologia. 2022; 54: e14384.

[12] Li K, Li K, Yao Q, Shui X, Zheng J, He Y, *et al*. The potential relationship of coronary artery disease and hyperuricemia: a cardiometabolic risk factor. Heliyon. 2023; 9: e16097.

[13] Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, *et al*. Updated methodological guidance for the conduct of scoping reviews. JBI Evidence Synthesis. 2020; 18: 2119–2126.

[14] Khalil H, Jia R, Moraes EB, Munn Z, Alexander L, Peters MDJ, *et al*.

Scoping reviews and their role in identifying research priorities. Journal of Clinical Epidemiology. 2025; 181: 111712.

[15] Veroniki AA, Hutton B, Stevens A, McKenzie JE, Page MJ, Moher D, *et al*. Update to the PRISMA guidelines for network meta-analyses and scoping reviews and development of guidelines for rapid reviews: a scoping review protocol. JBI Evidence Synthesis. 2025; 23: 517–526.

[16] Zhang Y, Huang L, Wang D, Ren P, Hong Q, Kang D. The ROBINS-I and the NOS had similar reliability but differed in applicability: a random sampling observational studies of systematic reviews/meta-analysis. Journal of Evidence-Based Medicine. 2021; 14: 112–122.

[17] Rojas M, Guilera G, Arias-Patiño E, Barrios M, Gómez-Benito J. Methodological considerations in cross-sectional studies validating the International Classification of Functioning, Disability and Health (ICF) Core-Sets: a systematic review. Disability and Rehabilitation. 2025; 47: 1912–1931.

[18] Vallejo-Medina P, Saffon JP, Álvarez-Muelas A. Colombian clinical validation of the International Index of Erectile Function (IIEF-5). Sexual Medicine. 2022; 10: 100461.

[19] Chen YF, Lin HH, Lu CC, Hung CT, Lee MH, Hsu CY, *et al*. Gout and a subsequent increased risk of erectile dysfunction in men aged 64 and under: a nationwide cohort study in Taiwan. The Journal of Rheumatology. 2015; 42: 1898–1905.

[20] Solak Y, Akilli H, Kayrak M, Aribas A, Gaipov A, Turk S, *et al*. Uric acid level and erectile dysfunction in patients with coronary artery disease. The Journal of Sexual Medicine. 2014; 11: 165–172.

[21] Ticoalu JHV, Kandarina I, Rizal DM, Setiabudi IDPP. Relationship between hyperuricemia and erectile dysfunction on hypertension patients. Journal of the Medical Sciences. 2019; 51: 152–158.

[22] Tuokko AT, Murtola T, Korhonen P, Kaipia A. Hyperuricemia is not an independent predictor of erectile dysfunction. Sexual Medicine. 2021; 9: 100319–100319.

[23] Jun Wang Y, He Chen Y, Fan LL. The association between uric acid and erectile dysfunction in US adults: NHANES 2001–2004. BMC Nephrology. 2024; 25: 189.

[24] 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. Scientific Reports. 2017; 7: 2087.

[25] Salem S, Mehrsai A, Heydari R, Pourmand G. Serum uric acid as a risk predictor for erectile dysfunction. The Journal of Sexual Medicine. 2014; 11: 1118–1124.

[26] Salavati A, Mehrsai A, Allameh F, Alizadeh F, Namdari F, Hosseinian M, *et al*. Is serum uric acid level correlated with erectile dysfunction in coronary artery disease patients? Acta Medica Iranica. 2016; 543: 173–175.

[27] Kim JH, Chung MK, Kang JY, Koh JH, Lee J, Kwok SK, *et al*. Insulin resistance is an independent predictor of erectile dysfunction in patients with gout. The Korean Journal of Internal Medicine. 2019; 34: 202–209.

[28] Barassi A, Corsi Romanelli MM, Pezzilli R, Dozio E, Damele CAL, Vaccalluzzo L, *et al*. Levels of uric acid in erectile dysfunction of different aetiology. The Aging Male. 2018; 21: 200–205.

[29] Schlesinger N, Lu N, Choi HK. Gout and the risk of incident erectile dysfunction: a body mass index-matched population-based study. The Journal of Rheumatology. 2018; 45: 1192–1197.

[30] Xia DS, He Q, Wang L, Mao DQ, Xia W, Lu CZ, *et al*. Relationship between serum uric acid and erectile dysfunction and endothelial injury in male patients with hypertension. Tianjin Medical Journal. 2020; 48: 1–5. (In Chinese)

[31] Fan J, Peng T, Hui J, Ding W, He B, Zhang H, *et al*. Erectile dysfunction in type-2 diabetes mellitus patients: predictors of early detection and treatment. Urologia Internationalis. 2021; 105: 986–992.

[32] Zhang Q, Chen W, Yun C, Wang J. The application value of serum 25(OH)D_3, uric acid, triglyceride, and homeostasis model assessment of insulin resistance in male patients with hyperuricemia combined with hypogonadism. BMC Endocrine Disorders. 2021; 21: 102.

[33] Tong Q, Du Y, Cui R, Chen M, Wang SI, Wei JC, *et al*. Risk of erectile dysfunction in male patients with gout treated with febuxostat or allopurinol: a propensity score-matched cohort study. Drugs. 2022; 82: 1717–1726.

[34] Du GW, Niu PN, Yang ZX, Zhang XH, He JC, Liu T, *et al*. Association between metabolic parameters and erection in erectile dysfunction patients with hyperuricemia. Asian Journal of Andrology. 2025; 27: 482–487.

[35] Long H, Jiang J, Xia J, Jiang R, He Y, Lin H, *et al*. Hyperuricemia is an independent risk factor for erectile dysfunction. The Journal of Sexual Medicine. 2016; 137: 1056–1062.

[36] Zhong CS, Zeng B, Qiu JH, Xu LH, Zhong MY, Huang YT, *et al*. Gout-associated monosodium urate crystal-induced necrosis is independent of NLRP3 activity but can be suppressed by combined inhibitors for multiple signaling pathways. Acta Pharmacologica Sinica. 2022; 43: 1324–1336.

[37] Allen M, Wood A, Sheffield D. The psychology of erectile dysfunction. Current Directions in Psychological Science. 2023; 32: 487–493.

[38] Suvorava T, Metry S, Pick S, Kojda G. Alterations in endothelial nitric oxide synthase activity and their relevance to blood pressure. Biochemical Pharmacology. 2022; 205: 115256.

[39] Alaaeldin R, Abdel-Rahman IAM, Hassan HA, Youssef N, Allam AE, Abdelwahab SF, *et al*. Carpachromene ameliorates insulin resistance in HepG2 cells via modulating IR/IRS1/PI3k/Akt/GSK3/FoxO1 pathway. Molecules. 2021; 26: 7629.

[40] Li J, Zhang W, Zhu S, Shi F. Nitric oxide synthase is involved in follicular development via the PI3K/AKT/FoxO3a pathway in neonatal and immature rats. Animals. 2020; 10: 248.

[41] Allegrini S, Garcia-Gil M, Pesi R, Camici M, Tozzi MG. The good, the bad and the new about uric acid in cancer. Cancers. 2022; 14: 4959.

[42] Chen H, Feng WD, Feng JL, Zhao C, Gao ZX, Wang B. Association of serum uric acid with male sexual hormones and erectile dysfunction: a bidirectional 2-sample Mendelian randomization analysis. Sexual Medicine. 2024; 12: qfae051.

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