

EPIDEMIOLOGY/RISK FACTORS

The Role of the “Anti-Inflammatory” Couple for the Management of Hyperuricemia With Deposition

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ABSTRACT

Introduction: Gout is the most prevalent inflammatory crystal arthropathy worldwide and is a chronic disease requiring strict, lifelong adherence to drug therapy and healthy lifestyles. Gout has a heavy burden on the patient’s sexual health, owing to the associated inflammatory status, long-term complications, and chronic pain; however, the effects of gout also extend to the partner’s sexual health.

Aims: We aimed to investigate how the presence of a partner could influence the complex interaction between risk factors for sexual dysfunctions in gout in order to define novel strategies to improve sexual health and disease management.

Methods: Clinical and experimental data on the role of the couple in chronic diseases, as well as on the association between gout and sexual health, were searched through Pubmed.

Main outcome measures: Evidence from studies describing how the presence of a couple and leveraging sexual health can improve management and clinical outcomes for chronic diseases.

Results: Treatment adherence can improve the sexual health of gout patients and their partners; likewise, by leveraging sexual health, it would be possible to promote better health-seeking behaviors, ultimately improving gout management.

Clinical implications: Promoting awareness of the sexual health relevance of gout can potentially be a pivotal strategy to improve disease management and prevent the progression of sexual dysfunctions from subclinical to overt forms.

Strengths and limitations: Identifying a bidirectional association between sexual health and disease management paves the way for improved disease control and can potentially prevent the development of sexual dysfunctions in couples affected by gout. However, the relevance of the couple has not been adequately addressed in gout management, and most evidence comes from other chronic diseases.

Conclusion: Improving gout management results in better sexual health, and vice-versa promoting better sexual health can improve disease control for gout. The presence of a partner improves the behavioral well-being of gout patients, with beneficial effects on both sexual health and gout management. **Sansone A, Reisman Y, Meto S, et al. The Role of the “Anti-Inflammatory” Couple for the Management of Hyperuricemia With Deposition. Sex Med 2022;10:100562.**

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INTRODUCTION

Gout, the clinical representation of hyperuricemia with deposition, is the most prevalent inflammatory crystal arthropathy worldwide.¹ Recent studies suggest an increasing trend for this condition,^{2–4} with an estimated prevalence of 3–4% in Europe and the USA, over 6% in some Oceanic-Pacific ethnic groups.^{5–9} The expanding presence of risk factors in the western population, such as obesity, metabolic syndrome, and dietary changes, has been advocated as one of the plausible reasons for this trend. However, gout is not a recent disease. It was historically known as “the disease of kings” or the “rich men’s disease”, as in the past, only wealthy

individuals could afford a “rich” diet heavy in meat.¹⁰ To the present date, being this disease more easily found in marginal lifestyles adopting trash food, alcohol abuse, and lacking physical activity, it cannot be consistently considered a disease of the elites. Undoubtedly, changes in socioeconomic milieu may have had a profound impact on its prevalence: between 1990 and 2017, the rates of gout both globally and in China were increasing, but with a significantly larger extent for males in China than globally.¹¹ This was proportional to the adoption of Western lifestyles, mirrored by an increased average body mass index.

Gout is a typical non-communicable chronic disease (NCD), generated by important genetic and predisposing factors, but also associated with socio-demographic characteristics (age, gender) and the behaviors mentioned above, and not rarely comorbid with other NCDs (metabolic, renal and cardiovascular diseases, etc.).¹² Gout is a chronic condition potentially leading to decreased mobility, persistent pain, and impaired quality of life.¹⁰ Several studies have provided evidence of how gout can impair health-related quality of life (HR-QoL).^{13–15} This impairment may be due to its disease-specific features such as excruciatingly painful attacks, their frequency and the number of joints involved, pain in between attacks, long-term joint damage due to accumulation of tophi, or, when the untreated disease progresses to more severe forms, to the amputation. A US veterans study found that gout was associated with poorer HR-QoL, functional limitation, higher mortality, and increased primary care visits and inpatient utilization.¹⁶ Hence, gout is not only a metabolic disease but has important psychosocial aspects that may dramatically affect its impact and final clinical outcome.

Although only recently considered as a part of the general one, sexual health could be regarded as a marker of the psychosocial milieu associated with NCDs in general and of gout in particular and, at the same time, a marker of the consequences of gout itself.¹⁷ Not only do the underlying shared risk factors (such as aging, sedentary lifestyle, obesity, metabolic syndrome, and hypertension) potentially contribute to an impaired sexual life, but also gout itself can potentially have devastating effects on the patient’s ability to have intercourse.¹⁷ In the present narrative review, we aim to focus on aspects of hyperuricemia with deposition that should be considered in order to increase awareness of the potential risks for sexual health, not only in the affected patients but also in their partners. We also aim to discuss literature suggesting that the involvement of the couple in the clinical management of gout can potentially improve patient care and prevent, or delay, the onset of sexual dysfunctions; at the same time, promoting sexual health in such patients can be a crucial strategy to improve clinical outcomes and disease management. This paper will therefore start with a “primer” on gout pathophysiology before moving to the actual burden of gout on the couple, to the beneficial and adverse effects of a partner (or loss thereof) on compliance to gout therapy, to the consequences of gout on sexual health as well as on the general and sexual quality of life and,

finally, to the potential strategies involving sexual health to promote better lifestyles.

Literature Search Strategy

Peer-reviewed publications were identified through a PubMed search using the search terms “sexual dysfunction”, “erectile dysfunction”, “premature ejaculation”, “gout”, “chronic disease”, “couple”, and “hyperuricemia”. The search was completed in May 2022 and was limited to articles published in English. Relevant articles were identified based upon the expertise and clinical experience of the authors. Additional papers were retrieved by reviewing references from cited works.

Gout: a brief primer.

Gout is a disease resulting from the deposition of monosodium urate (MSU) crystals in target organs and tissues, which occurs when the concentration of serum uric acid (UA) increases over the 6.8 mg/dl solubility threshold. Several environmental factors can also affect the actual threshold for the deposition of MSU crystals, including temperature and pH.^{18,19} Not all individuals with hyperuricemia develop crystal deposition or the consequent acute inflammatory response²⁰; additional factors, such as genetics, underlying inflammatory background, or pre-existing fiber damage, can potentially affect the mechanisms leading to the progression from silent hyperuricemia to asymptomatic crystal deposition, and subsequently to acute gout flares and chronic gouty arthritis.²¹ In fact, the prevalence of hyperuricemia in the US population is more than 3.5 times higher than that of gout, proving that the presence of elevated serum UA is not enough to result in the development of the disease.

Gout is also characterized by a relapsing-remitting course, with extended times of silent hyperuricemia interspersed with intermittent episodes of acute crystal-associated inflammatory arthritis.¹⁰ During these periods of “intercritical gout”, the MSU crystals persist in the target organs and tissues: the inflammatory response is toned down, but chemokines persist, suggesting that low-grade inflammation is still present following the resolution of the acute phase.²² Moreover, there is growing experimental evidence that supports a relationship between high concentrations of UA and endothelial dysfunction,^{23,24} a typical target of a number of chronic inflammations.

The main goals of the medical treatment of gout include minimizing the inflammation and pain of an acute gout attack, and preventing future gout flares by lowering serum UA levels. Xanthine oxidase inhibitors (XOIs), including allopurinol and febuxostat, are first-line agents for the prevention of acute attacks. Uricosuric agents are an appropriate adjunctive therapy or second-line agent when XOIs are contraindicated or poorly tolerated.²⁵ Recently, several third-line agents (e.g., pegloticase) have become available for the treatment of refractory gout.²⁵

Despite a good pharmacological efficacy and tolerability, as in the majority of the chronic treatments for NCDs,^{26,27} treatment adherence is remarkably poor for gout patients,^{28,29} even worse

than in other chronic diseases.³⁰ This can be possibly due to the relapsing-remitting course of the disease, which might give some patients the false belief of being free from disease, despite being in one of the intercritical periods. Another possible explanation for the poor treatment adherence lies in the possible combination of lacking “tangible” effects and the presence of side effects. Antihypertensive drugs are a paramount example of this mechanism²⁶: hypertension, by itself, can often be asymptomatic, whereas side effects from several antihypertensive treatments are frequent and can impair QoL.³¹ Education and behavioral interventions have often been considered among the possible strategies available to clinicians to improve this negative scenario,^{26,32} but with limited efficacy.

Gout, the “Third Wheel” in the Couple: Issues and Challenges

Gout is almost twice as prevalent in men than in women⁹ and, as with the majority of NCDs, is strictly associated with other unmodifiable factors, such as genetics and age, with prevalence steadily increasing in elderly individuals.¹⁰ However, modifiable factors also play a major role. A recent study demonstrated that, compared to age-matched controls, male gout patients are significantly more likely to be overweight or obese, to have diabetes and hypertension, and to have more health-risk behaviors, such as binge-drinking, previous use of tobacco products, and sedentary lifestyle.³³ Interestingly, all the mentioned aspects are well-known major risk factors for sexual dysfunction, particularly erectile dysfunction (ED).³⁴ While research on the relationship between female gout and female sexual dysfunction is still in its infancy,³⁵ the epidemiology and risk factors make, in principle, gout a condition primarily affecting male sexual function. However, it would be reductive to consider only the affected patient as an individual whose sexual health has been impaired by gout: indeed, the partner is also facing, indirectly, the burden of the disease. For the sake of simplicity, let's consider a heterosexual couple in which the male partner is affected by gout, and the female partner is relatively healthy. The first gout flare, being a sudden event with few (if any) premonitory signs, is potentially a source of concern and anxiety for both members of the couple – even more if the flare occurs at the wrong time, e.g., during celebration times (when flare-triggering, purine-containing foods and beverages are likely to abound). The resulting distress is expected to affect the couple – or, rather, the “dyad” – before diagnosis and in the subsequent weeks of uncertainty following treatment onset. Anxiety is a powerful trigger for sexual dysfunction in men^{36–38} and women,^{39–41} and can therefore worsen the couple's sexual health. As such, it becomes clear that while gout is – in this case – affecting only half of the couple, both partners have to face the likely consequences in terms of intimacy.¹⁷

Following ULT initiation, lifestyle changes are also likely required to reduce the chances of relapse¹⁰ and, at the same time, can potentially be beneficial for the couple's sexual health.⁴²

For example, the Mediterranean diet, rich in fiber, antioxidants, and mono-unsaturated fatty acids, can improve UA levels and reduce inflammatory status and oxidative stress.⁴³ The same diet has improved erectile function.^{44,45} Likewise, physical exercise has beneficial effects on gout⁴⁶ as well on male and female sexual health and function,^{47,48} possibly also mediated by its effect on body weight and inflammatory status⁴⁵: the effects of physical exercise on the endocrine milieu can promote a favorable anti-inflammatory profile, increasing levels of anti-inflammatory cytokines (such as IL-10) and reducing levels of pro-inflammatory cytokines such as TNF- α , IL-6, and IL-1 β ,^{49,50} positively acting on both gout and sexual health. In fact, to simplify, gout produces chronic and acute inflammation, both major pathogenetic mechanisms of sexual dysfunction.⁵¹ Also, for this reason, Park and coll. correctly proposed that all gout patients should be assessed for ED.⁵² This tenable advice is fortified by the concept that the couple's sexual health could act as an “anti-inflammatory” mechanism positively affecting gout itself and its inflammatory consequences with respect to the adherence to both lifestyle changes and the prescribed pharmacological treatments.

May the Marital Life Modify Therapeutical Compliance and Adherence?

Compliance and adherence to lifestyle changes in gout are often poor due to limited awareness of purine-rich foods and beverages⁵³ or to the physical disability limiting physical exercise during gout flares and chronic arthropathy.⁵⁴ Additionally, during intercritical periods, the perception of having “overcome” the disease can also be a further reason for poor treatment adherence: treatment compliance (including strict and careful observance of the prescribed lifestyle changes) is usually higher for acute rather than chronic diseases,²⁶ and is particularly low for gout.⁵⁵ The presence of a partner can be beneficial in these regards. In fact, according to the “theory of social causation”,⁵⁶ being married is accompanied by better health behaviors and greater attention to individual well-being. This becomes even more pronounced for gout, as the preventive effects are more likely to occur in men than in women.⁵⁶ In several chronic lifestyle-related diseases, such as the many NCDs, the presence of a partner can increase adherence to prevention and treatment, with married couples having better compliance.^{57–61} The shared responsibilities improve treatment outcomes and adherence to therapy, as proven in chronic conditions.^{62–64} Positive partners act, in fact, as “reminders” for treatment continuation and can motivate their significant others to maintain healthy behaviors, as proven by the lower cardiovascular risk and mortality associated with marital status.^{65–67} Surprisingly, the potential role of the partner has not been adequately addressed by studies investigating treatment adherence in gout.²⁹ In a vicious circle, gout impairs sexual health, which can in turn progressively worsen self-care, and leads to partner distancing, resulting in worse adherence to treatment which ultimately promotes the progression of both sexual dysfunctions and gout itself (Figure 1).

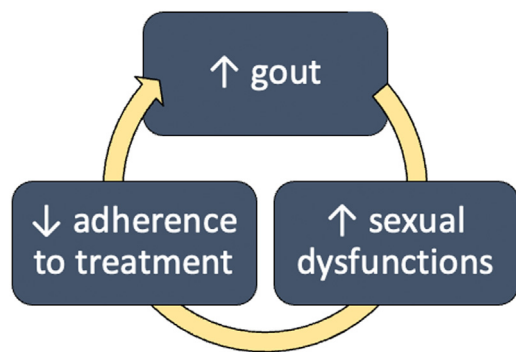


FIGURE 1. The vicious circle associating gout, sexual dysfunctions, and treatment adherence.

Effects of Partner Loss and Distancing on Sex-Gout Outcomes

On the contrary, conflicts in the couple are likely to affect treatment compliance negatively,⁶⁸ and the loss of a partner is associated with worse health outcomes.⁶⁵ Several reasons for the preventive effects of the couple have been hypothesized: marriage is associated with a shorter delay in seeking medical treatment, and the presence of a partner also results in better economic, behavioral, mental, and emotional well-being.^{65,69} The emotional distress due to partner loss can influence the inflammatory phenotype driving depression pathogenesis⁷⁰: the same inflammatory cytokines TNF- α , IL-6, and IL-1, whose concentration is also regulated by testosterone levels,⁵⁰ are involved in the immune response occurring in gout flares. Therefore, losing a partner has adverse effects from both a behavioral and a biochemical point of view on the gouty inflammation and its management.

When extreme, this mechanism is well recognized as the “Widowhood effect”, i.e., the increased morbidity and the decreased male survival following the death of a spouse.^{71–74} Elegantly, Corona et al. demonstrated that the absence of a partner or their lacking sexual interest in a patient with ED produces delayed referral to andrology clinics, late assessment of ED comorbidities, more risky behaviors, and, as a final consequence, more inflammation and more NCDs.⁷⁵

It is worth mentioning, however, that the loss of a partner does not exclusively mean their passing. Negative effects on different health outcomes occur even following divorce.⁷⁶ The association between sexual health and divorce is a complex one: while indeed sexual dysfunctions are a relatively frequent factor involved in marriage breakdown,⁷⁷ it is also true that they might be consequences of a dysfunctional relationship,^{36,78,79} in which the “partner stress” (i.e., marital conflict⁶⁸) can ease progression from subclinical^{80,81} to overt, clinically manifest sexual dysfunction.⁸² As stated, TNF- α , IL-6, and IL-1 are involved in the immune response to the loss of a partner. These cytokines also have a role in the development of sexual dysfunction, most notably ED,^{83,84} by inducing endothelial

dysfunction and reducing nitric oxide availability. To an extent, this low-grade inflammation is mediated by several prothrombotic agents, which further contribute to worsening sexual health for both men and women.^{85,86,17} In summarizing: the inflammatory status prominently featured in gout is exacerbated by further “inflammatory” psycho-social factors, such as lack of partner’s interest, partner loss, and consequent depression, which can worsen sexual health. All such determinants are mutually associated, and measures aimed at preserving sexual health can, by transforming the “inflammatory” couple into the “anti-inflammatory” one, be a key strategy to improve outcomes for all other underlying conditions.

Diagnosing and Curing the Couple’s Gout-Related Sexual Dysfunctions

For all these reasons, we recommend exploring the couple’s sexual life in all patients with gout. This could be easily done by well-validated psychometric tools, as reported in Table 1.⁸⁷ In this perspective, it is crucial to make all possible efforts to explore not only each partner individually but also the couple as a unit. Based on the initial screening, sexual function could be investigated by focused physical examination and laboratory and instrumental tests aiming to identify the severity of the symptom (subclinical, mild, moderate, severe), to identify the comorbidity with other sexual dysfunctions, to find other comorbid NCDs and risk factors, and to ascertain the impact of the sexual symptom in the general QoL and in the mood of the couple itself.⁷⁹

On these bases, a tailored therapy is always advised, starting from the transformation of vicious into virtuous lifestyles (i.e., smoking cessation, quitting illegal drugs, reducing alcohol dramatically, shifting to healthier diets, and increasing physical activity) and then addressing other possible needs (i.e., prescribing testosterone in hypogonadal patients or psychotherapies for subjects with psychopathological traits).

Prescription of the gold therapeutic standard for ED, i.e., type 5 phosphodiesterase inhibitors (PDE5Is), is highly advised in the subject with gout and inability or reduced capacity to obtain or maintain the erection in the presence of proper erotic stimuli.⁸⁸ This therapy needs to be tailored to the couple’s clinical profile.^{89,90} While PDE5Is do not display any particular warning concerning gout or relative therapies,⁹¹ some patients may be better prescribed with the PDE5I with the best safety profile, such as avanafil,^{92,93} others with the drug with the best vascular properties, such as sildenafil⁹⁴, also in its newest orodispersible, intimacy sparing, pharmacological form,^{95,96} and others with the long-acting tadalafil either in the on-demand regimen, as used for the other PDE5Is, or in the low-dose, daily regimen, peculiar for this drug.⁹⁷

Interestingly, a significant positive correlation has been found between PDE5I use and allopurinol, hydrochlorothiazide, nicotine, and alcohol use confirming that ED is a major problem in gout, hypertension, smoking, and drinking, respectively, but also

TABLE 1. Diagnosing gout-related sexual dysfunctions of the couple

TOOL	TYPE	TARGET GENDER	ADDRESSED SYMPTOMS AND FUNCTIONS	REF
International Index of Erectile Function (IIEF)	SRQ	Male	Erection; Orgasm; Desire; Intercourse satisfaction; Overall satisfaction	130
Sexual Health Inventory for Men (SHIM)	Scr	Male	Erection (function)	131
Erection Hardness Score (EHS)	Scr	Male	Erection (hardness)	132
Female Sexual Function Index (FSFI)	SRQ	Female	Desire; Subjective Arousal; Lubrication; Orgasm; Satisfaction; Pain	133
Female Sexual Function Index-6 (FSFI-6)	Scr	Female	Screeners for the presence of a female sexual dysfunction	134
Female Sexual Distress Scale-Revised (FSDS-R)	SRQ	Female	Questionnaire exploring the sexual distress induced by the partner's premature ejaculation	135
Premature Ejaculation Diagnostic Tool (PEDT)	SRQ	Male	Ejaculation	136
Masturbation Erection Index (MEI)	SRQ	Male	Erection during self-erotism	137
Masturbatory Premature Ejaculation Diagnostic Tool (MPEDT)	SRQ	Male	Ejaculation during self-erotism	138
Orgasmometer	Scr	Male	Orgasm	139
Orgasmometer-F	Scr	Female	Orgasm	140
Structured Interview on Erectile Dysfunction (SIEDY)	Str Int	Male in the couple	Erection in the context of the couple	141
Dyadic Adjustment Scale (DAS)	SRQ	Couple	Quality of relationship as dyadic satisfaction; dyadic cohesion; dyadic consensus and affectional expression.	142

Psychometric well-validated and clinically sound tools for diagnosing couple's sexual health in gout. The majority of them are diagnostic tools designed for self-administration (self-reported questionnaire: SRQ), some are screeners (Scr), also validated for self-administration, to be used in large populations, and some others are designed as structured interviews (Str Int) driven by an interviewer. Note that the majority of the tools here listed have not been used yet in the gout setting. However, it would be advisable to adopt them in all couples experiencing NCDs in general and gout in particular as well to use them in future research on the impact of gout in the couple's sexual health. The majority of these diagnostic tools have been originally validated in the heterosexual setting, and this should be considered a major limit to be overcome by future research.

indirectly suggesting the safety of the association of PDE5I with the mentioned drugs and substances in these real-life contexts.⁹⁸

Both diagnosis and therapy of ED, or other couple's sexual symptoms, may have further advantages. Careful screening of sexual health gives the doctor "baseline" evidence, useful for the follow-up of the chronic disease itself. Although yet to be demonstrated, progressive improvement or worsening of the metabolic profile may be mirrored by parallel changes in sexual health. In diabetes, another metabolic NCD sharing many risk factors and comorbidities with gout, this relationship is very strong, and erectile function is to be considered an efficient biomarker of diabetic complications and glycemic control and vice-versa.^{99,100} Studies are needed to ascertain the same in gout.

Moreover, a successful therapy of gout-related sexual dysfunction may also produce unexpected advantages for the treatment of gout itself, as discussed in the following paragraphs.

Improving Gout Management by Leveraging Sexual Health

There is ample evidence suggesting that sexual health can benefit many conditions, from psychological distress¹⁰¹ to general health.¹⁰² From a broader point of view, it is generally assumed

that sexual health is also a reliable hallmark of cardiovascular and metabolic health and a predictor of future cardiovascular mortality.^{103–105} While most people having sexual dysfunctions do not immediately seek sexual health advice and treatment,^{106–108} the sudden onset of ED can potentially be the proverbial "canary in the coal mine",¹⁰⁹ predicting future cardiovascular events.¹¹⁰ This is unsurprising, given that sexual dysfunctions (ED in particular) and cardiovascular diseases share the same modifiable risk factors, such as sedentary lifestyle, obesity, smoking, and dyslipidemia.^{111,34} However, gout also shares many of these risk factors, and different guidelines have advocated lifestyle modifications for its clinical management.¹⁰ Such changes in daily behaviors are often difficult to maintain for gout patients, resulting in poor adherence¹⁰; however, providing sexual consultations to gout patients, and explaining the extent to which these interventions can promote better sexual health, could possibly improve patient compliance. Additionally, as one partner's sexual health inevitably bears on the other¹¹² and lifestyle interventions generally involve the couple, it would be beneficial to involve both members of the couple in sexological consultations.¹¹³

A typical representation of this concept is provided by the smoking habit in the couple and how the couple may dramatically improve the attempt to quit tobacco. While the first

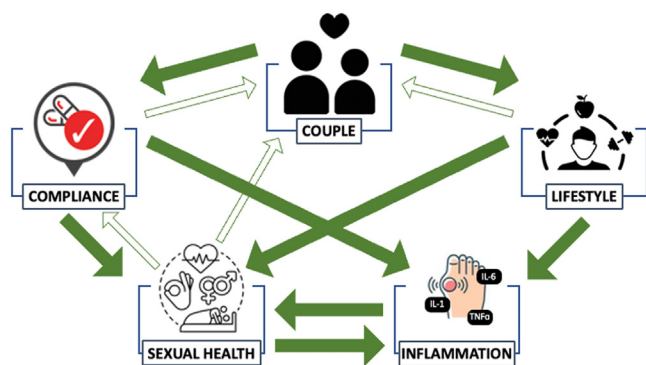


FIGURE 2. The fundamental role of the couple in the management of the gout-related sexual dysfunctions.

cigarettes are frequently partner-driven, volitional processes to quit smoking or at least to adopt harm reductive strategies¹¹⁴ have been demonstrated to spill over to their partners positively.^{115,116} Hence, improved health behavior changes often occur in a dyadic context of romantic relationships.¹¹⁷ Therefore, by leveraging both the patient's and the partner's sexual health, it would be possible to promote better health-seeking behaviors, resulting in better gout management (Figure 2).

Sexual and General Quality of Life in Gout Patients

Last but not least, it is mandatory to consider the possible negative effects of gout on the psychological status of the affected individual and, by extent, on their family members, especially the partner.

Gout has a significant impact on patients' lives. Beyond pain and functional limitations, it increases anxiety and depressive disorders and affects sexual function, sleep, social relationships, emotional health, and work.¹¹⁸ Patients may feel helpless and frustrated and tend to social isolation.^{119,120} Shame, embarrassment, and stigma may lead to minimization of the impact of the disease.^{119,120}

Moreover, gout affects not only the patient's quality of life but also the partner's and other family members'. Dependency on the family members during flares or physical disability can be important.¹¹⁹

Sex is an essential contributor to QOL, and the sexual quality of life of gout patients is negatively affected,¹²¹ as expected based on the presence of both organic and non-organic risk factors. Therefore, the sexual health of the couple is endangered, owing to the association between the two partners' sexual function.^{122–124} Promoting compliance to treatment, including drug therapy and better lifestyles, would thus be beneficial to the sexual health of the couple: making both partners actively involved in the clinical management of gout by leveraging sexual health can result in improved quality of life for the couple.

Finally, addressing the sexual life of the couple may also have positive effects. Gout, along with other rheumatological diseases,

such as osteoarthritis, fibromyalgia, rheumatoid arthritis, and low back pain, is a major driver of the use of illegal drugs (cocaine, hallucinogen, amphetamine, or sedative/anxiolytic/hypnotic¹²⁵) and alcohol.¹²⁶ It is unclear how this figure precedes and may have a causal relationship or, on the contrary, may represent unmet needs or unsatisfied expectations of patients with rheumatic diseases. In any case, the same substances have a direct negative effect on the ability to obtain and maintain an erection, further reducing the level of the couple's sexual QoL (SQoL).^{127,128} The clinical management of the sexual symptom in the couple would *bona fide* increase the therapeutical alliance with the partner in reducing these dysfunctional abuses, and further motivate the patient to follow the correct prescriptions more carefully, thus reducing the use of illegal substances and the abuse of alcohol.

Conclusion: the Anti-Inflammatory Couple

Hyperuricemia with deposition is a subtle and multifaceted disease that, after long periods of (apparent) clinical silence, manifests itself in a violent and potentially devastating way affecting the general quality of life of the patient and his partner but also, and specifically, of the quality of sex life.

It is a typical clinical picture named in Italy as “the dog eating its own tail”, which can be idiomatically translated in English as: “it's a catch-22”. The patient with gout has impaired sexual life, and at the same time the subject with poor sexual health is much less motivated to adopt virtuous behaviors to prevent gout and to follow the long-term pharmacological therapy.

In this article, we aimed to prove the importance of sexual health as a powerful surrogate marker of the HR-QoL and of the couple as a powerful tool for prevention and for providing a solid reinforcement of motivation towards lifestyle improvement and for the correct use of drugs. In fact, romantic partners significantly influence their reciprocal health behaviors.

Patients seldom voluntarily mention sexual disorders to their clinicians, and unfortunately, many doctors are not educated in sexual medicine and therefore feel capable of interviewing neither the patient nor the partner about sexual symptoms.¹²⁹ The patient perceives this lack of scientific and clinical interest in sexual function (biologically speaking, the most important of all) as a poor prognosis. When, on the contrary, the doctor motivates his patients to follow lifestyle changes or chronic therapies by suggesting that these can have very positive effects on sexual and marital life, therapeutic compliance is expected to improve and the patient, especially if not young, interprets the message of the doctor as a good prognosis. The patient perceives two positive signs: the first says that if the doctor is concerned about the sexual symptom, there is still a lot to do, and the second signal acts precisely as a formidable motivational element reinforced within, and by, the couple.

For the dog to really stop eating its tail, however, robust and direct scientific evidence correlating improved control of serum

UA (e.g., with febuxostat) to a reduced prevalence of sexual symptoms is needed. This will further prove that the couple is considered a powerful and effective “anti-inflammatory” therapeutic target, which increases and amplifies the drugs’ efficacy with adoption of a virtuous lifestyle and better adherence to prescriptions. At present, specific studies aimed at addressing the relationship between gout and sexual dysfunction are still missing. Likewise, there is insufficient evidence on the impact of gout on the couple’s quality of life. As gout shares many similarities with other chronic conditions, it can be assumed that a typical “phenotype” can affect sexual health outcomes for the couple. Still, more studies are needed to address this literature gap.

The bidirectional link between gout and sexual dysfunction, i.e., how gout can have negative consequences for sexual health and how acting on promoting healthy sexual life may improve clinical and therapeutical outcomes of gout, is, therefore, a promising new chapter of sexual medicine, in which research will continue more and more in the years to come.

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