

# Optimism is a Nonnegligible Factor Associated With Compliance to Urate Lowering Therapy in Patients With Gout: A Prospective Study

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## Research article

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# Abstract

**Background:** Optimism has different effects on patients with chronic rheumatic disease. Gout is an increasingly prevalent disorder around the world, while the compliance to urate lowering therapy (ULT) of gout patients is poor. The objective of this study was to assess the optimism of gout patients. Contributors to optimism and poor compliance were also explored.

**Methods:** A total of 530 gout patients, 174 ankylosing spondylitis (AS) patients, 60 rheumatoid arthritis (RA) patients and 324 healthy volunteers were included. Optimism, anxiety, and depression were measured by the life orientation test-revised (LOT-R), self-rating anxiety scale (SAS) and self-rating depression scale (SDS). Demographic and disease characteristic were recorded, including education, residence, disease duration, etc. Severity of pain in the involved joints was assessed by the visual analog scale (VAS). Concentration of serum uric acid (SUA) was collected at baseline and the last examination within the follow-up. Compliance to ULT was investigated by the medication possession ratio (MPR) in 3 months. The contributors to optimism and poor compliance were detected by the multivariate and binary logistic regression analysis.

**Results:** The LOT-R score of gout patients was higher than AS and RA patients, but there was no statistical difference between gout patients and healthy controls. The SAS and SDS score of gout patients were lower than AS and RA patients, while the SDS score of gout patients was higher than healthy controls. The mean disease duration and VAS score were 5.0 (2.0-7.3) years and 2.0 (0.0-4.0). Percentage of gout patients with an MPR<0.8 was 55.1%. Insufficient education contributed to optimism in gout patients. Insufficient education, living in countryside, higher concentration of SUA and higher LOT-R score led to poor compliance to ULT.

**Conclusion.** The optimism of gout patients is greater compared with AS and RA patients. The compliance to ULT is poor, which ascribes to optimism. Furthermore, the optimism of gout patients may attribute to insufficient education.

## Background

The prevalence of gout is approximately 1–3% of the population around the world [1, 2]. Long term serum uric acid (SUA) controlled is the key strategy for the management of gout. The recommendations and guidelines of gout worldwide emphasize the importance of treatment of hyperuricemia. It is required that long term SUA should be controlled below 360  $\mu\text{mol/L}$  and 300  $\mu\text{mol/L}$  for those with the deposition of monosodium urate crystals in joints or surrounding tissues [3].

Despite treat to SUA target is considered as a therapeutic target for gout patients, studies from many countries and regions have reported that gout management was still poor with low achievement of treatment targets [4–7]. For example, the prevalence of hyperuricemia, considering the main etiology of gout, increases more than 10 times from early 1980 to 2006 in China [8]. Besides, data of 6814 gout patients registered by the Chinese Rheumatism Data Center reported that the rate of reaching standard of

SUA level in gout patients after 3 months of treatment was only 29.12% in China, while the 1 month and 6 months follow-up rate were only 20.7% and 3.9% in 2016. Despite a good agreement on the treatment of gout, medication compliance, representing the process of taking drugs according to prescriptions, is considered as one of obstacle treatment to target [9–11]. In a cohort study of Western Sweden, only 1/3 of gout patients received urate lowering therapy (ULT) within the first year of gout diagnosis, and merely 1/4 of them continued ULT within the first 2 years [12]. A study from South Australia involved 2531 patients with gout also reported that only 55% patients continued ULT treatment [13]. Besides, a study reported that the compliance to allopurinol was only 56% [14].

Compliance of patients plays a central role in the treatment of chronic disease, which raises a great discussion in the whole medical field [15]. A previous study found that compliance of gout patients was the poorest compared with several common chronic diseases including hypertension, hypothyroidism, diabetes and hypercholesterolemia [16]. Besides, several studies found gout patients with older age and more comorbidity had better medication compliance [17–19].

Psychological status not only has a great impact on the quality of life of healthy people, but also on the outcome of patients with chronic disease. Anxiety and depression are common in patients with rheumatic disease liked gout, ankylosing spondylitis (AS) and rheumatoid arthritis (RA) [20–22]. Previous studies have reported that patients with AS or RA had a higher level of anxiety and/ or depression than healthy people, while anxiety and/ or depression were related to their quality of life. Optimism is defined as the propensity to look forward to a better future. Several studies reported that optimism was associated with health-related quality of life in patients with different chronic rheumatic diseases [23–25]. For example, a study reported that optimism was positively associated with quality of life in patients with axial spondyloarthritis and chronic low back pain [26]. However, few studies had investigated the association between optimism and compliance and the contributors to optimism in gout patients.

This study was to assess the optimism in gout patients. Therefore, we evaluated the relationship between optimism and clinical variables as well. Finally, we attempted to determine the contributors to optimism and poor compliance in gout patients.

## Methods

### Study population

Patients were identified from the rheumatologists at the Guangdong Second Provincial General Hospital from August 2018 to October 2019. Patients aged 18 years or older were considered to have gout, AS and RA according to 2015 American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) Criteria for gout, Modified New York Classifications Criteria for AS and 2010 ACR/ EULAR Criteria for RA, respectively [27–29]. The healthy controls, required not having a history of rheumatic disease, were selected from the Department of Physical Examination Center of the same hospital. Our analysis concentrated on new patients of ULT, which was defined as no dispensing of ULT in the prior 6 months.

This study was agreed by the ethics committee of the Guangdong Second Provincial General Hospital (2018-SYX-003).

## Data collection

Baseline demographic assessment was accomplished by a trained investigator using designed questionnaires including age, gender, body mass index (BMI), education and residence. Clinical data contained disease duration, tophi, comorbidity including hypertension, diabetes, hyperlipidemia, and chronic kidney disease (CKD). The concentration of SUA was collected at baseline and the last examination within the follow-up. The pain of the involved joints was assessed by the visual analog scale (VAS) at baseline. The score ranged from 0 to 10, and a higher score meant more pain [30].

Compliance to ULT of gout patient was measured by the medication possession ratio (MPR) in this study, while the MPR was used similarly to measure compliance to ULT in other studies [14, 31, 32]. The MPR was calculated as the total number of days supply of medication dispensed during the observed day divided by the number of days between first and last prescription. The MPR was determined according to the outpatient prescription record, while the observed days was set as 90 days. Based on this definition, the MPR might be greater than 100% if patients refilled before their drugs run out, and the MPR was regarded as 100% in this situation. Poor compliance to ULT was defined as the  $MPR < 80\%$ .

All participants completed a series of questionnaires to measure their optimism, anxiety, and depression in the week before the baseline. The life orientation test-revised (LOT-R) is used to assess the optimism of the gout patients and the controls. The LOT-R has been confirmed to be reasonable in healthy individuals and in those with varied chronic diseases [33, 34]. This is a measure of expectation about positive outcomes in general, using a 5-point scale from 0 (strongly disagree) to 4 (strongly agree). The LOT-R consists of 10 questions of which 4 questions are filler items not used in scoring. Of the six items that are scored, three are in a positive direction and three are in a negative direction. The total score ranges from 0 to 24, while higher LOT-R score reflects more optimistic life orientation. The self-rating anxiety scale (SAS) and the self-rating depression scale (SDS) are originated to evaluate the severity of anxiety and depression. They have been applied to the study of patients with different chronic rheumatic diseases including AS and systemic lupus erythematosus [21, 35]. The SAS and SDS range from 20 to 80, and the standard score is obtained by multiplying the total score by 1.25. Higher score means more psychological anxiety and depression.

## Statistical analyses

The Statistical Package for Social Science (SPSS) software version 21 was used for statistical analyses. Categorical variables are presented as percentages (%), while continuous variables are shown as mean and standard deviation. Firstly, the Mann-Whitney U test and Student's t test were used to compare the differences between groups and subgroups. Therefore, the Spearman rank correlation analysis was used to determine the relationship between psychological characteristic and the other variables. Finally, multivariate and binary logistic regression analysis were used to analyse the contributors to optimism

and poor compliance in gout patients, with factors involved in the model with  $p < 0.05$  in the univariate and Spearman analysis. Statistical significance was considered when  $p < 0.05$ , while all tests were two-tailed.

## Results

The demographic and psychological characteristic of 530 gout patients, 174 AS patients, 60 RA patients, and 324 healthy controls matched by education were presented in Additional file 1. The gout patients and healthy controls were also matched by age and gender ( $p > 0.05$ ). After comparing the psychological variables, the LOT-R score of gout patients was higher than AS and RA patients ( $p < 0.05$ ). There was no significant difference of the LOT-R score between the gout patients and the healthy controls ( $p > 0.05$ ). The SAS and SDS score of gout patients were lower than AS and RA patients ( $p < 0.05$ ), while the SDS score of gout patients was higher than healthy controls ( $p < 0.05$ ).

The clinical characteristic of 530 patients were shown in Table 1. More than half of the patients were male (96.4%) and living in the city (70.9%). Most patients suffered from comorbidity (62.1%) and nearly a quarter of patients had tophi (24.5%). The mean disease duration and VAS score were 5.0 (2.0-7.3) years and 2.0 (0.0-4.0). Among the 530 gout patients, only 320 gout patients (60.4%) returned and retested the SUA in 90 days, while 55.1% of all gout patients had an MPR  $< 0.8$ .

Table 1  
Demographic and clinical characteristic of 530 gout patients

<b>Variables</b>	<b>Gout patients(n = 530)</b>
Age, years, mean (SD)	41.4 (12.3)
Gender, male, n (%)	511 (96.4)
BMI, kg/m <sup>2</sup> , mean (SD)	25.8 (3.7)
Years of education	
≤ 9 years n (%)	318 (60.0)
> 9 years n (%)	212 (40.0)
Residence	
City, n (%)	376 (70.9)
Countryside, n (%)	154 (29.1)
Stage of gout	
Acute phase, n (%)	36 (6.8)
Others: intercritical phase or chronic phase, n (%)	494 (93.2)
Disease duration, years, mean (IQR)	5.0 (2.0-7.3)
Tophi, n (%)	130 (24.5)
Comorbidity, n (%)	329 (62.1)
Hypertension, n (%)	94 (17.7)
Diabetes, n (%)	38 (7.2)
Hyperlipidemia, n (%)	267 (50.4)
CKD, n (%)	72 (13.6)
VAS, mean (IQR)	2.0 (0.0–4.0)
Baseline SUA, μmol/L, mean (SD)	501.1 (147.1)
Follow-up patients, n, (%)	330 (60.4)
Follow-up SUA, μmol/L, mean (SD) <sup>a</sup>	363.3 (46.3)
At SUA target, n (%) <sup>a</sup>	127 (40.0)
ULT drugs	
Febuxostat, n (%)	404 (76.2)

Variables	Gout patients( <i>n</i> = 530)
Allopurinol, <i>n</i> (%)	43 (8.1)
Benzbromarone, <i>n</i> (%)	26 (4.9)
Others, <i>n</i> (%)	57 (10.8)
ULT compliance	
MPR < 0.8, <i>n</i> (%)	292 (55.1)
MPR ≥ 0.8, <i>n</i> (%)	238 (44.9)

*SD* standard deviation, and the data that meet the normal distribution are shown as mean (*SD*), *BMI* body mass index, *IQR* interquartile range, and the data that did not meet the normal distribution are shown as median (*IQR*), *CKD* chronic kidney disease, *VAS* visual analog scale, *SUA* serum uric acid, *ULT* urate lowering therapy, *MPR* medication possession ratio

<sup>a</sup> base on the 320 patients that returned and retested the *SUA* during the observed day

In this study, the 530 gout patients were divided into four subgroups according to their compliance to *ULT* and the stage of gout, which were displayed in Additional file 2. Patients with poor compliance had a higher concentration of baseline *SUA*, *VAS*, and *LOT-R* score and lower *SAS* and *SDS* score ( $p < 0.05$ ).

Besides, poor

compliance was also related to education, residence, tophi, and hyperlipidemia ( $p < 0.05$ ). Finally, patients suffering acute gout attack were found to have higher *VAS* and *SAS* score ( $p < 0.05$ ). The stage of gout was not associated with optimism in this study ( $p > 0.05$ ).

The result of the Spearman correlation analysis was shown in Table 2. Among the 530 gout patients, baseline *SUA* and disease duration positively correlated with the *LOT-R* score, while the relationship between the *MPR* of *ULT* therapy and *LOT-R* score was negative ( $p < 0.05$ ). Meanwhile, the *SAS* score positively correlated with *VAS* ( $p < 0.05$ ).

Table 2  
Correlations between psychological and demographic, clinical characteristic of gout patients

Variables	LOT-R score		SAS score		SDS score	
	<i>r</i>	<i>p</i> value	<i>r</i>	<i>p</i> value	<i>r</i>	<i>p</i> value
Age	0.000	0.994	0.081	0.063	0.057	0.191
BMI	0.064	0.149	0.012	0.792	-0.027	0.543
Disease duration	-0.106	0.015	-0.015	0.735	0.034	0.439
VAS	0.034	0.432	0.154	< 0.001	0.052	0.228
Baseline SUA	0.131	0.003	0.024	0.578	0.018	0.671
MPR	-0.536	< 0.001	0.038	0.382	0.044	0.313
LOT-R score	1		-0.123	0.005	-0.251	< 0.001
SAS score	-0.123	0.005	1		0.498	< 0.001
SDS score	-0.251	< 0.001	0.498	< 0.001	1	

*LOT-R* life orientation test-revised, *SAS* self-rating anxiety scale, *SDS* self-rating depression scale, *BMI* body mass index, *VAS* visual analog scale, *SUA* serum uric acid, *MPR* medication possession ratio. The result of stepwise multiple and binary and regression analysis were shown in Table 3 and Table 4. All factors with  $p < 0.05$  in the univariate analysis were included in the models. Insufficient education ( $p < 0.001$ ) contributed to optimism in gout patients. Besides, insufficient education ( $p = 0.046$ ), living in countryside ( $p = 0.002$ ), high concentration of SUA ( $p = 0.001$ ) and LOT-R score ( $p < 0.001$ ) contributed to poor compliance to ULT.

Table 3  
Stepwise multiple regression analysis of LOT-R score in gout patients

Variables	B	SE	OR	OR%95CI	<i>p</i> value
Years of education					
≤ 9 years	1.394	0.371	0.249	0.120–0.513	< 0.001

*LOT-R* life orientation test-revised, *B* beta, *SE* standard error, *OR* odds ratio, *CI* confidence interval

Model included all factors with  $p < 0.05$  in the Spearman analysis except SAS and SDS score

Table 4  
Stepwise binary regression analysis of MPR < 0.8 in gout patients

Variables	B	SE	OR	OR%95CI	p value
Years of education					
≤ 9 years	0.394	0.198	0.674	0.457–0.994	0.046
Residence					
Countryside	0.659	0.217	1.934	1.265–2.956	0.002
SUA	0.002	0.001	1.002	1.001–1.004	0.001
LOT-R	0.376	0.048	1.457	1.325–1.602	< 0.001

MPR medication possession ratio, B beta, SE standard error, OR odds ratio, CI confidence interval, SUA serum uric acid, LOT-R life orientation test-revised

Model included all factors with  $p < 0.05$  in the univariate analysis

## Discussion

Despite widespread guidelines and recommendations around the world have highlighted the importance of long-term control of SUA in preventing gout attacks and delaying joint damage in gout patients [4], majority of gout patients involved in this study were found to have poor compliance to ULT. This study emphasized that optimism was negatively related to compliance to ULT, and insufficient education contributed to optimism in gout patients. To our best knowledge, this is the first study reporting that optimism negatively related to compliance in gout patients.

In terms of the demographic variables between the gout patients and other controls, we found that the average age of gout patients was higher than that of AS patients and lower than RA patients. Meanwhile, the male sex composition ratio of gout patients was higher than that of RA patients. No previous studies had reported the influence of age and gender on optimism in gout patients, but this study found that age and gender did not contribute to optimism in gout patients. Besides, it was found that optimism of gout patients was higher than that of AS and RA patients. The result revealed that gout patients were more optimistic about their disease than AS and RA patients. A recent study reported that optimism correlated with improvement in disease activity in patients with arthritis [36]. We speculated that symptoms of AS and RA patients were persistent and chronic, while symptoms of gout patients were mostly paroxysmal.

Anxiety of gout patients was higher than healthy controls in this study, while the anxiety correlated with the compliance, the stage of gout and pain. A previous study reported that the anxiety of gout patients was associated with education, disease duration, stage of gout, pain, and tophi, which was consistent with our study [37]. Although anxiety did not independently correlate with compliance to ULT, we could find that psychological factors had different degrees of influence on compliance in gout patients.

It was also found that optimism contributed to poor compliance to ULT in this study, indicating that optimism had negative effects on compliance of gout patients. Interestingly, this conclusion was inconsistent with previous studies on optimism of patients with chronic disease. Optimism is helpful in some diseases, especially cardiovascular disease. A study from America involved 6808 participants reported that higher optimism was associated with a lower risk of heart failure incident [35]. Besides, a study involving 1529 patients with chronic disease pointed out that optimism played a positive role in the quality of life of patients with various chronic diseases [36]. Optimists are more likely to participate in health-promoting behaviors like exercising more, eating healthier diets and quitting smoking [36]. However, blind optimism may make patients show insufficient attention to their disease, or even ignore the doctor's advice for medication and follow-up visit. Serlachius et al indicated that low pessimism rather than high optimism was associated with cardiovascular health. Besides, low pessimism was associated with not smoking, taking part in physical exercise, and eating a healthy diet [38]. For gout patients, blind optimism may lead to poor curative effect of ULT and eventually irreversible joint and organ damage. These results did not discount the effect of ULT, but emphasized the non-ignorable role of optimism in gout patients.

This study also concluded that the education negatively correlated with optimism in gout patients. A previous study had also reported that insufficient education was a risk factor to poor compliance [7]. We assumed that most gout patients with limited education had little comprehension to their disease, and did not fully understand the importance of controlling SUA at target.

There were some limitations in this study. First and foremost, we did not retest the optimism of gout patients after the observation period. A previous study pointed out that, in contrast to depression, optimism was one of the components of personality and was relative stable [39]. In addition, the follow-up rate of gout patients in this study was low. Therefore, the concentration of follow-up SUA may be higher than that in this study actually. However, the follow-up rate of gout patients in this study was still higher than most domestic studies [12, 13]. Finally, the observation period of gout patients in this study was only 90 days, while the ULT and SUA standard of gout patients were long-term and lifelong. Therefore, a larger sample size and longer follow-up period were necessary to study the influence of optimism on compliance in gout patients.

## Conclusions

This study has highlighted the association between optimism and compliance to ULT, and contributors to optimism and poor compliance in gout patients. The optimism of gout patients is similar to healthy controls, but significantly higher than AS and RA patients. Most of the gout patients in this study have poor compliance to ULT. In gout patients, optimism negatively correlates with compliance to ULT. Insufficient education contributes to optimism. Insufficient education, living in countryside, high concentration of SUA and optimism contribute to poor compliance to ULT. These results emphasize the influence of optimism on compliance to ULT in gout patients.

# Abbreviations

SUA: serum uric acid; ULT: urate lowering therapy; AS: ankylosing spondylitis; RA: rheumatoid arthritis; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism; BMI: body mass index; CKD: chronic kidney disease; VAS: visual analog scale; MPR: medication possession ratio; LOT-R: life orientation test-revised; SAS: self-rating anxiety scale; SDS: self-rating depression scale.

# Declarations

## Ethics approval and consent to participate

This study was agreed by the ethics committee of the Guangdong Second Provincial General Hospital (2018-SYX-003). The subjects gave their written consent before they were included in this study.

## Consent for publication

Not applicable.

## Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Competing interests

The authors declare that they have no competing interests.

## Funding

Not applicable.

## Authors' contributions

All authors of this study made significant contributions to the current work. WZ was involved in the design of this study, data interpretation, statistical analysis and drafting of this manuscript. ZH was involved in the conception and design of this study, data explanation and critical appraisal of the drafts of this manuscript. YH, QH, SC, XL, ZZ and YL were involved in the in data acquisition and collection of this study. TL was involved in the design and conception of this study, critical appraisal of the drafts of this manuscript. All authors read and approved the final manuscript.

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