

**ORIGINAL ARTICLE** 

# Assessment of electronic health literacy and its association with self-management among gout patients: A cross-sectional study

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#### ABSTRACT

**Objectives:** This study aimed to assess electronic health (eHealth) literacy and self-management ability among gout patients in China and analyze their correlation.

**Patients and methods:** A cross-sectional study was conducted on 168 male gout patients (mean age: 44.5±13.8 years, range, 22 to 76 years) using a gout patient self-management assessment scale and the Chinese version of eHealth Literacy Scale between August 2020 and February 2021. The correlation between eHealth literacy and gout self-management was examined. Multivariate regression analysis was conducted to identify the predictors of gout patients' self-management ability.

**Results:** The scores of eHealth literacy and self-management were  $28.56\pm1.72$  and  $3.59\pm0.78$ , respectively, which were both in the medium level, with the lowest score in the lifestyle management dimension. Pearson's correlation analysis showed that eHealth literacy was significantly and positively associated with the total score of gout self-management and its four dimensions. Literacy in eHealth ( $\beta$ =0.399, p<0.001, 95% confidence interval [CI]: 0.023-0.069), living with family members ( $\beta$ =0.336, p=0.001, 95% CI: 0.313-1.234), living in an urban area ( $\beta$ =0.312, p=0.005, 95% CI: 0.191-1.022), and having college or a higher level of education ( $\beta$ =0.268, p=0.016, 95% CI: 0.032-0.302) were the significant predictors of gout patients' self-management ability, explained 30.6% of the total variance.

**Conclusion:** Literacy in eHealth was the most significant predictor of gout self-management ability. Gout patients had the lowest score in the perceived ability of searching and applying online health-related information, indicating that both the quantity and quality of gout-specific information needs to be enlarged in electronic resources. Healthcare providers could design and implement eHealth literacy interventions to strengthen patients' gout self-management ability.

Keywords: Cross-sectional study, gout, Health literacy, self-management.

Gout is a common chronic inflammation that occurs due to the accumulation of monosodium urate crystals in both articular and nonarticular structures.<sup>1</sup> The urate crystals result in intermittent episodes of gout flares (acute inflammatory arthritis) that trigger intense joint pain, immobility, and subsequent psychosocial distress, including emotional suffering and decreased productivity at work.<sup>2</sup> Over time, patients with persistent hyperuricemia could develop further symptoms, such as chronic gouty arthritis and joint damage. Additionally, gout is commonly accompanied by various conditions, such as cardiovascular disease, chronic kidney disease, and osteoporosis.<sup>3</sup> Gout patients also have increased risk of developing urological cancer, such as bladder and renal carcinoma.<sup>4</sup> The prevalence of gout is increasing both globally and in China in recent decades.<sup>5</sup> A meta-analysis showed that the pooled prevalence of gout in mainland China was 1.1% between 2006 and 2009, and it rose to 1.3% between 2010 and 2016, with a trend of occurrence among the young age group.<sup>6,7</sup>

Gout is a treatable and chronic progressive disease. Many factors contribute to hyperuricemia and gout, including dietary exposure to purinerich foods (e.g., red meat, seafood, and alcohol) and sugar-sweetened beverages.<sup>5</sup> Urate-lowering therapy (ULT) is the primary treatment to maintain serum uric acid concentrations at an unsaturated

level to prohibit formation and dissolution of crystals.<sup>3,8</sup> The overarching principles for gout treatment include managing acute attacks and eliminating urate crystals through lifelong lowering of serum uric acid below a target level.<sup>9</sup> Allopurinol is recommended as a first-line ULT, while colchicine, nonsteroidal anti-inflammatory drugs, and glucocorticoids are recommended as first-line drugs for acute gout flare treatment.<sup>10,11</sup> Initiating treatment as early as possible during an acute gout attack can significantly improve the effectiveness in gout management.<sup>12</sup> The approach of "pill in the pocket" (taking oral colchicine with different dosages over time) has the potential to greatly reduce the treatment duration for gout patients and alleviate the pain caused by gout attacks.<sup>11</sup> Therefore, effective gout management measures comprising appropriate use of ULTs, diet, and lifestyle modification are crucial to reducing the occurrence of gout flares and associated diseases.<sup>13</sup> Gout patients need relevant knowledge and skills to perform these self-management behaviors.<sup>14,15</sup> However, gout management is suboptimal in many countries, including China.<sup>3</sup> For instance, studies reported that gout patients often received inadequate education from healthcare providers due to time constraints and hence were unlikely to obtain personalized advice for optimal selfmanagement.<sup>16</sup> Under these circumstances, some gout patients tend to utilize the internet to seek information to support their self-management efforts, particularly in the context of rapid technological development.<sup>13</sup>

Currently, easy access to the internet and mobile devices enables people to search for and acquire electronic health (eHealth)-related information. Accordingly, eHealth and mobile health resources, such as mobile applications, have been developed and show promise in terms of promoting self-management of chronic diseases, including gout.<sup>14,17,18</sup> However, the accuracy, credibility, and quality of health information on the internet are varying. For instance, studies found that only a few web-based patient information resources provide accurate information on gout, and only one app includes all recommendations to facilitate self-management of gout.<sup>17,19</sup> Consequently, patients need eHealth literacy to properly use health information for effective gout self-management.

Literacy in eHealth was defined as the ability to seek, search, understand, and appraise healthrelated information from electronic resources and apply the knowledge to address health problems in a networked world.<sup>20</sup> A lot of research analyzed the influence of health literacy on health outcomes among patients with chronic diseases. such as hypertension and chronic pain.<sup>21,22</sup> For example, a study found that health literacy was a major determinant of self-management among early-stage chronic kidney disease compared to illness perception and self-efficacy.<sup>23</sup> Nonetheless, relatively rare research focused on eHealth literacy among gout patients in the information era. This study aimed to investigate the current state of eHealth literacy and self-management among gout patients in China and explore the association between the two variables.

### **PATIENTS AND METHODS**

In this cross-sectional study, participants were recruited from a gout specialist outpatient clinic at the affiliated hospital of Qingdao University. The clinic was one of the biggest gout diagnosis and treatment centers in China. The inclusion criteria of participants were as follows: (*i*) being diagnosed with gout by a physician according to the American Rheumatism Association diagnostic criteria;<sup>24</sup> (*ii*) being aged ≥18 years; (*iii*) being able to read and speak Chinese; (*iv*) having no cognitive impairment.

Demographic information, such as age, marital status, and educational level, and disease characteristics, such as disease duration, times of gout flares, and number of visiting doctors, were evaluated. Two multiple choice questions were utilized to assess patients' sources of knowledge about gout and their belief of effective sources of knowledge.

The gout patient self-management assessment scale was developed by the research team to measure self-management ability among gout patients.<sup>25</sup> It included 41 items in four dimensions of disease treatment management (13 items; e.g., "I do not regulate the type and dosage of gout medication on my own"), dietary management (12 items; e.g., "I strictly limit the intake of high purine foods, such as shellfish, animal organs, meat soup, hot pot soup, and fish skin"), lifestyle

management (nine items; e.g., "I choose and adjust exercise methods and amounts based on age, disease condition, and weather") and psychosocial management (seven items; e.g., "I actively regulate the negative emotions caused by gout, such as confiding in family and friends, diverting attention"). Each item was evaluated on a 5-point Likert scale ranging from 1 (never) to 5 (always), with a total score of 41 to 205, with higher scores representing higher selfmanagement levels. The scale had good reliability and validity. The Cronbach's alpha of the total scale was 0.962, and that of the four dimensions was 0.893-0.950. The content validity index of the total scale was 0.905. In factor analysis, values with an eigenvalue exceeding 1 explained 68.5% of total variance, and the factor loading coefficients of the 41 items ranged between 0.435 and 0.827.

The eHealth Literacy Scale (eHEALS) was developed by Norman and Skinner<sup>26</sup> to assess eHealth literacy for a wide range of populations and contexts. The Chinese version of eHEALS was translated by Chinese scholars<sup>27</sup> and has been used among different populations. It showed acceptable reliability and validity, with Cronbach's alpha being 0.913 and the loading coefficients of the eight items being 0.692-0.869.27 It consists of eight items pertaining to self-perceived health literacy. with each item being evaluated by a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). The total score ranges from 8 to 40, with higher scores indicating higher levels of eHealth literacy. According to previous research, the cutoff for high eHealth literacy was set at 26, and this score being <26represents a low eHealth literacy level.<sup>28</sup>

The researchers conducted the study after obtaining permission from the hospital. A paperbased questionnaire was distributed to patients at the gout specialist outpatient clinic between August 2020 and February 2021. Uniform instructions were used to explain the study's aims to the participants. It took 10 to 15 min to finish the questionnaire for each participant. Participants filled in the questionnaire and returned it to the researchers on the spot. A total of 178 male patients were recruited for participation, and 10 questionnaires were excluded due to incomplete data. As a result, 168 male patients (mean age:  $44.5\pm13.8$  years, range, 22 to 76 years) with valid questionnaires were included for data analysis, with an effective response rate of 94.3%.

#### Statistical analysis

The sample size was calculated using the G\*power version 3.1.9.2 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). With an effect size (f2) of 0.15, alpha of 0.05, power of 0.85, and 13 potential predictors, the minimum sample size was calculated as 144. Considering 15% of invalid questionnaire, the required sample size was determined to be 166.

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was applied to check the normality of data, which showed that self-management and eHealth literacy followed a normal distribution. Descriptive analysis was employed to describe the sociodemographic and disease information of the participants. An independent sample t-test, analysis of variance, and independent sample R-by-C table were utilized. Chi-square tests were used to compare differences between groups. Pearson's correlation analysis was performed to examine the correlation between eHealth literacy and gout self-management. Multivariate step-by-step linear regression analysis was used to identify salient factors associated with gout self-management ability. Multicollinearity test was performed on the data before linear regression. Both the variance inflation factors (1.007-1.197) and tolerance limit (0.836-0.973) met the cut-off points of <10 and >0.10, respectively, indicating that independent variables can be reasonably entered into multivariate analysis. Statistical significance was established at a *p*-value < 0.05.

#### RESULTS

#### Common method deviation test

Harman's single-factor test was applied to assess the potential common method deviation caused by the self-report questionnaire method in this study. The test evinced 16 factors with eigenvalues >1, and the variation explained by the first factor was 31.65%, which was below the critical value of 40%. This demonstrates that the effect of common method deviation would not influence the data results.

# Demographic and clinical characteristics of the participants

The majority of the participants were younger than 60 years (85.8%), married (80.9%), lived with others (90.1%), and from an urban area (83.1%). Above half of the participants (46.1%)

had gout for less than five years, and 21.3% of the participants experienced gout flares for over four times within the most recent year. Most of the participants (86%) were overweight and obese. The detailed information is presented in Table 1.

### Sources of knowledge about gout

The participants reported that their current knowledge about gout was mainly from

				Low eHealth		High eHealth			
Variables	Categories	n	%	n	%	n	%	$\chi^2$	р
Age (year)	<45	87	51.9	18	20.7	69	79.3	2.555	0.279
	45-59	57	33.9	12	21.1	45	78.9		
	≥60	24	14.2	10	41.7	14	58.3		
Residence	Urban area	140	83.1	28	20.0	112	80.0	4.670	0.031
	Rural area	28	16.9	13	46.4	15	53.6		
Marital status	Single	32	19.1	8	25.0	24	75.0	0.016	0.899
	Married	136	80.9	34	25.0	102	75.0		
Employment status	Unemployment	38	22.5	21	55.3	17	44.7	12.711	<0.00
	Employment	130	77.5	21	16.2	109	83.8		
Educational level	Higher school or less	75	44.9	26	34.7	49	65.3	4.127	0.042
	College education or higher	93	55.1	15	16.1	78	83.9		
Body mass index (kg/m²)	Normal	23	14.0	6	26.1	17	73.9	0.279	0.87
	Overweight	49	29.0	14	28.6	35	71.4		
	Obesity	96	57.0	22	22.9	74	77.1		
	<5,000	65	46.2	30	46.2	35	53.8	11.861	0.008
Fomily, monthly, income (week)	5,000-7,500	40	23.8	6	15.0	34	85.0		
Family monthly income (yuan)	7,500-10,000	36	21.4	4	11.1	32	88.9		
	>10,000	27	16.1	4	14.8	23	85.2		
(	Live alone	15	9.0	2	13.3	13	86.7	0.000	0.19
Living arrangement	Live with family members	153	91.0	42	27.5	111	72.5	2.886	
	<5	77	46.1	13	16.9	64	83.1	4.006	0.13
Duration of gout (years)	5-10	51	30.2	20	39.2	31	60.8		
	>10	40	23.7	7	17.5	33	82.5		
Firess of gout flows	<4	132	78.7	30	22.7	102	77.3	1.120	0.29
Times of gout flare	≥4	36	21.3	13	36.1	23	63.9		
No. of visiting doctors	<4	127	75.3	36	28.3	91	71.7	1.000	0.165
No. of visiting doctors	≥4	41	24.7	6	14.6	35	85.4	1.929	
No. of hospitalization	0	142	84.3	34	23.9	108	76.1	0.132	0.741
	1	26	15.7	7	26.9	19	73.1		

health professionals and the internet (65.1%). The participants reported that they perceived mobile applications (32.7%) as more effective and acceptable in helping their disease self-management compared to traditional educational approaches, such as written materials, lectures, and follow-up calls.

# Electronic health literacy level and influencing factors

The total eHealth literacy score was  $28.56\pm1.72$ , with a mean item score of  $3.59\pm0.78$ , indicating a moderate level of eHealth literacy. As shown in Table 2, the mean scores of four items were comparably lower. Namely, patients reported less knowledge of available health resources on the internet, where to find helpful health resources on the internet, how to find helpful health resources on the internet to answer health questions.

With 26 points as the cutoff, 75.3% of the participants had higher eHealth literacy. The chi-square test showed that eHealth literacy level was significantly different among the participants by residence, employment status, educational level, and family monthly income (Table 1). Participants living in an urban area, employed participants, those with higher education, and those with higher family income had higher eHealth literacy. Other variables such as age, marital status, and duration of gout were not identified as significant factors

influencing the level of eHealth literacy among this group.

Self-management ability of gout patients and influencing factors.

The total score on the self-management assessment scale was  $166.56\pm29.68$  among the participants, indicating a moderate level of self-management ability. The mean item scores of the four dimensions of disease treatment management, psychosocial management, diet management, and lifestyle management were  $4.18\pm0.73$ ,  $3.91\pm0.97$ ,  $3.70\pm0.84$ , and  $3.60\pm0.87$ , respectively.

The independent sample t-test showed significant differences between groups of patients by residence, living arrangement, and educational level. Patients living in urban areas, living with family members, with college or a higher degree reported higher levels of self-management ability than those living in a rural area (t=2.239, p=0.026), living alone (t=-2.477, p=0.015), and with high school or less education (t=-2.159, p=0.031), respectively.

### Correlation between self-management skill and eHealth literacy

Pearson's correlation analysis showed that eHealth literacy was significantly and positively associated with the total score of gout selfmanagement and its four dimensions. The correlation coefficients ranged from 0.225 to 0.571, as shown in Table 3.

Table 2. The score of eHealth literacy scale among the participants						
eHea	th literacy scale (eHEALS) items	Mean±SD	Ranking			
Q1	I know what health resources are available on the internet.	$3.46 \pm 0.35$	7			
Q2	I know where to find helpful health resources on the internet.	$3.49 \pm 0.32$	6			
Q3	I know how to find helpful health resources on the internet.	$3.55 \pm 0.38$	5			
Q4	I know how to use the internet to answer my health questions.	$3.45 \pm 0.34$	8			
Q5	I know how to use the health information I find on the internet to help me.	3.67±0.29	2			
Q6	I have the skills I need to evaluate the health resources I find on the internet.	3.62±0.32	4			
Q7	I can tell high quality health resources from low quality health resources on the internet.	3.68±0.27	1			
Q8	I feel confident in using information from the internet to make health decisions.	3.64±0.27	3			
	Total eHealth literacy score	28.56±1.72				
SD: St	andard deviation.					

Table 3. Correlation between self-management ability and eHealth literacy					
	eHealth lit	eHealth literacy score			
Variables	r	р			
Score of disease treatment management	0.571	< 0.001			
Score of diet management	0.246	0.020			
Score of lifestyle management	0.344	0.001			
Score of psycho-social management	0.225	< 0.001			
Total score of gout self-management	0.506	< 0.001			

Table 4. Multivariate linear regression analysis on gout self-management ability								
Variables	В	SE	β	t	р	95% CI	Tolerance	VIF
Constant	-0.265	0.725		-0.366	0.716	-1.713-1.182		
eHealth literacy	0.046	0.012	0.399	3.975	< 0.001	0.023-0.069	0.871	1.148
Living with family members (ref. Living alone)	0.773	0.231	0.336	3.352	0.001	0.313-1.234	0.860	1.163
Living in urban area (ref. Living in rural area)	0.606	0.208	0.312	2.912	0.005	0.191-1.022	0.756	1.323
College education or higher (ref. Higher school or less)	0.167	0.068	0.268	2.475	0.016	0.032-0.302	0.680	1.470

B: Unstandardized coefficient; SE: Standard error; B: Standardized coefficient; CI: Confidence interval; VIF: Variance inflation factor; F=8.830, p<0.001, R: 0.588, R<sup>2</sup>: 0.345, adjusted R<sup>2</sup>: 0.306.

#### Multivariate linear regression analysis on gout self-management ability

With independent variables identified as being statistically associated with self-management ability by univariate analysis, multivariate linear regression analysis was conducted to determine the predictive factors of gout self-management ability. The analysis found that eHealth literacy ( $\beta$ =0.399, p<0.001) was the most significant factor predicting the change in gout patients' self-management ability, followed by living with family members ( $\beta$ =0.336, p=0.001), living in urban areas ( $\beta$ =0.312, p=0.005), and with college or higher education ( $\beta$ =0.268, p=0.016). The four predictors explained 30.6% of the total variance in self-management (Table 4).

#### DISCUSSION

The advancement of the internet and smartphones provides new opportunities for patients to obtain online health-related information. With the rapidly increasing amount of online health information that is of mixed content and quality in the age of information technology,<sup>29</sup> the ability to seek, understand, appraise, and apply online information is crucial for patients to make well-informed health-related decisions.<sup>30</sup> Promoting adequate levels of eHealth literacy is essential in the health sector due to increasing reliance on digital technologies.<sup>31</sup> Based on the knowledge gap of the relationship between eHealth literacy and self-management ability among gout patients, this study explored the eHealth literacy level and its association with self-management ability among Chinese gout patients in the context of the rising incidence of gout and its occurrence among a younger population.

Participants in this study reported a moderate level of eHealth literacy, which is similar to the Chinese high school students  $(28.58\pm7.00)^{27}$  and higher than Chinese community-dwelling older people  $(12.08\pm7.68)$ .<sup>32</sup> This may be explained by the majority of gout patients in the present study being young people, which accords with the epidemiological data about the increasing

incidence of gout among young individuals.<sup>6</sup> Previous research also reported that younger patients had higher eHealth literacy than older patients.<sup>33</sup> This may be because young individuals are more capable of accessing internet-based health information and are more literate in the use of eHealth than older individuals.

Nonetheless, the eHealth literacy score of gout patients in the present study was lower than that of kidney and liver transplant recipients (mean score:  $30.88\pm5.37$ )<sup>34</sup> and patients with chronic obstructive pulmonary disease in the USA (mean score: 29.1±5.72).<sup>35</sup> The difference suggests that eHealth literacy among gout patients in China needs to be improved to enable them to make well-informed health decisions and effective gout self-management. Furthermore, in the eight items of eHEALS, gout patients in the present study showed a low level of perceived ability in searching and applying online health-related information. By contrast, gout patients had relatively higher scores in distinguishing between high- and low-quality health resources on the internet and confidence to use internet information to make health decisions. These results were distinctive from the two aforementioned studies in the USA,<sup>34,35</sup> in which kidney and liver transplant recipients and chronic obstructive pulmonary disease patients reported relatively higher scores in health information search and application, while they observed relatively lower scores in differentiating health information sources and confidence to use the information to make health decisions. This disparity indicates that the current availability of reliable electronic resources about gout is limited for Chinese gout patients. A recent survey also found that 47.1% of the gout patients in China were unsatisfied with mobile healthcare service they used.<sup>36</sup> For this reason, the quantity and quality of gout-specific electronic information need to be enlarged to meet patients' needs. Health professionals are accordingly supposed to be involved more in developing online goutrelated resources, as well as the appraisal and validation of related electronic information.

Gout patients from urban areas, employed individuals, with college education or higher levels of education, and with higher family income had a higher level of eHealth literacy, signifying that socioeconomic status was a factor in eHealth literacy. This finding aligns with previous studies.<sup>37,38</sup> and confirms that patients with higher socioeconomic status may be more concerned about personal health, and thus, they use more means, including the internet, to acquire information for gout management. This finding addressed the inequality generated by the difference in infrastructure between rural and urban areas and the associated employment status. Therefore, in related intervention programs, more emphasis needs to be placed on unemployed gout patients from rural areas with lower education. Health professionals can help patients filter through various sources of eHealth information and take into account outreach services to patients from rural areas.

The correlation analysis revealed that eHealth literacy was positively correlated with overall gout self-management ability, as well as the four dimensions. Furthermore, linear regression analysis demonstrated that eHealth literacy was a major factor predicting self-management gout ability compared to socioeconomic status, including living arrangement, residence, and educational level. Other studies also demonstrated that eHealth literacy as a personal resource was closely linked with health behaviors. For instance, eHealth literacy had a direct effect on self-care behaviors among Taiwanese patients with type II diabetes,<sup>39</sup> was a key predictor of self-care behaviors among homebound older adults.<sup>40</sup> and positively predicted health-promoting lifestyle among older Chinese adults.<sup>41</sup> The underlying mechanism was that patients with better ability to search and acquire online information were more capable of utilizing the information to support their self-management behaviors. The present study consolidates the closely positive relationship between eHealth literacy and self-management for patients with chronic diseases. Simultaneously, gout patients in the present study perceived mobile applications as more effective and acceptable in helping their disease self-management compared to traditional approaches. The findings suggested that interventions to improve gout patients' eHealth literacy could be an effective way to strengthen their gout self-management ability via boosting their ability to search and use webbased health information about gout care.

Gout patients in this study reported a moderate level of overall self-management ability, while had lowest mean score in dimension of lifestyle management. This finding suggests that managing the lifestyle was the most difficult aspect for gout patients. Gout is a disease closely related to lifestyle and lifestyle modification is the core of gout treatment, particularly for early-detected patients. Previous qualitative research also found that lifestyle management.<sup>42</sup> Consequently, future eHealth literacy programs need to cover more specific information concerning lifestyle modification for gout patients.

This study has several limitations. First, participants were recruited using convenience sampling from the affiliated hospital of Qingdao University, and all participants were male. Although this result accords with the fact that the prevalence of gout is greatly higher in males than in females,<sup>3</sup> the generalizability of the findings may be limited. Second, eHEALS is a self-reported measurement of perceived proficiency in finding, critiquing, and applying eHealth information,<sup>26</sup> which does not necessarily represent patients' actual abilities when using health information technology. Future research could incorporate qualitative data to supplement quantitative data on eHealth literacy, with consideration of collecting data about sources of eHealth information and problems confronting patients to obtain a rich understanding of patients' experiences. Third, this study focused on the association between self-management and eHealth literacy, while other influencing factors, such as social support, self-efficacy,<sup>14</sup> and digital competence,<sup>38</sup> were not included in this study. Therefore, a more nuanced relationship between eHealth literacy and self-management among patients with gout needs to be uncovered in future research.

In conclusion, gout patients in China had a moderate level of eHealth literacy, with a particularly low score in perceived ability in searching and applying online health-related information. Gout patients showed a poor ability in lifestyle management compared to other dimensions of self-management. Literacy in eHealth was the most significant predictor of gout self-management ability among patients. Therefore, improving eHealth literacy in gout Arch Rheumatol

patients would be beneficial for them to manage gout in the information era. Based on the findings, healthcare professionals need to address the inclusion of specific information about gout and provide support of evidence-based and updated online information retrieval, judgment, and utilization for gout patients, with a focus on coverage of lifestyle management in relevant programs.

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

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

**Author Contributions:** Conceptualization: T.L., X.Y.Y.; Data curation, writing-original draft: J.Z.Q., X.Y.Y.; Formal analysis, software: J.Z.Q., T.L.; Investigation, methodology: J.Z.Q., X.Y.Y.; Writing-review and editing: T.L. All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication.

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