Associations of perceived social support and positive psychological resources with fatigue symptom in patients with rheumatoid arthritis

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Abstract

Objective

This study aimed to assess the association between perceived social support (PSS) and fatigue and the roles of hope, optimism, general self-efficacy and resilience as mediators or moderators on PSS-fatigue association among Rheumatoid Arthritis (RA) patients in China.

Methods

A multi-center, cross-sectional study was conducted withinpatients diagnosed with RA in northeast China, in which 305 eligible inpatients were enrolled. The Multidimensional Fatigue Inventory, Multidimensional Scale of Perceived Social Support, Herth Hope Index, Life Orientation Test Revised, General Self-Efficacy Scale and Ego-Resiliency Scale were completed. The associations of PSS, hope, optimism, general self-efficacy and resilience with fatigue and the moderating roles of these positive psychological constructs were tested by hierarchical linear regression. Asymptotic and resampling strategies were utilized to assess the mediating roles of hope, optimism, general self-efficacy and resilience.

Results

The mean score of the MFI was 57.88 (SD = 9.50). PSS, hope, optimism and resilience were negatively associated with RA-related fatigue, whereas DAS28-CRP was positively associated. Only resilience positively moderated the PSS-fatigue association (B = 0.03, β = 0.13, P<0.01). Hope, optimism and resilience may act as partial mediators in the association between PSS and fatigue symptoms (hope: a*b = -0.16, BCa 95%CI: -0.27, -0.03; optimism: a*b = -0.20, BCa 95%CI: -0.30, -0.10; resilience: a*b = -0.12, BCa 95%CI: -0.21–0.04).

Conclusions

Fatigue is a severe symptom among RA patients. Resilience may positively moderate the PSS-fatigue association. Hope, optimism and resilience may act as partial mediators in the association. PSS, hope, optimism and resilience may contribute as effective recourses to alleviate fatigue, upon which PSS probably has the greatest effect.

Introduction

Rheumatoid arthritis (RA) is a common autoimmune disease, mainly manifested as chronic, symmetric and progressive multi-arthritis, with a prevalence of 0.3–1.0% worldwide [1] and nearly 0.37% in China [2]. Fatigue is regarded as an extra-articular symptom and is the most common complaint besides pain among RA patients, with prevalence of 42%-80% or even more [3]. One study found that 57% patients have identified fatigue as the most important problem [4]. In RA patients, fatigue is considered as a chronic, complex, unpredictable, frustrating and overwhelming experience, typically not associated with excessive exertion and poorly relieved by rest [3–6]. Its exact etiology remains barely understood but is considered to be multidimensional. In addition to the inflammation itself, other researches have concluded that social factors, gender, cognition and emotion, impaired sleep patterns, pain, and environmental factors may also be related to the onset of fatigue [7, 8]. Because fatigue is a symptom of subjective experience, self-assessment is the most commonly used descriptive tool. Fatigue is also often considered to be a multi-dimensional framework. For example, some consider fatigue consists of 5 dimensions: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue; meanwhile, some considers 4 dimensions: cognitive, physical, emotional and living with fatigue [9].With tremendous adverse consequences, fatigue penetrates every corner of daily routines and poses a substantial humanistic and financial burden on the overall quality of life, thus decreasing patients' general well-being [1].

However, no specific pharmacological strategies have been discovered to produce meaningful improvements in the symptom to date. An 8-year follow-up concluded that the clinical influence of the severity of inflammation (for instance, inflammation markers and disease activity) on fatigue was actually quite small despite being statistically correlated [6]. Additionally, many studies have suggested that even when the inflammation was under control as indicated by low disease activities or achieving the desirable goal of remission, the fatigue wasn't remarkably alleviated. Therefore, because no evidence exists to support the improvement by available medications, research on the psychosocial strategies may become a task of top priority to relieve RA-related fatigue [10, 11].Social support is defined as a helpful resource that can meet an individual's urgent needs and is provided by a network of others, such as family members, friends, colleagues and other communities [12]. Social support may be divided into 2 groups: perceived social support (PSS), the subjective support that individuals may experience, emphasizing the individual's self-understanding, experience and feelings of social support from different sources; and enacted social support (ESS), which refers to the objective, practical and visible support, including direct physical assistance and assistance from a social network [13]. It has been suggested that PSS can play a greater role on physical health than ESS [14]. Social support directly and moderately exerts beneficial effects on the health-related quality of life in RA patients [8, 12]. One study found that approximately one-fifth of patients with RA had been on bad terms with their family and friends due to fatigue [15]. Another study concluded that RA patients usually considered themselves short of sufficient social support

[16], which should highlight its impact on fatigue symptoms. According to a recent systematic review, several results have demonstrated that more social support indeed had a positive influence on fatigue outcomes in RA [17]. However, that conclusion haven't been confirmed due to the small quantity of available relevant studies, indicating that further research is required.

As a consequence of emerging positive psychology in recent decades, beyond the limited positive effects of external social factors, some internal psychological constructs, such as hope, optimism, general self-efficacy and resilience, have been attributed increasing recognition of playing positive roles among clinical research and trials [18]. Further, social support can improve the characteristics of these positive psychological variables, to reduce the effects of these traits on social support.

Hope, as a positive cognitive-affective process, is considered to be multidimensional and dynamic; it refers to the ability of an individual to strive to realize their future goals despite a sense of uncertainty [19]. Many studies have demonstrated that an individual's level of personal hope is related to mental development and health conditions, which could improve mental physical health. Hope is an important part of treatment process, by helping patients overcome difficulties and relieve stress, thereby alleviating the suffering. Perceived social support is one of the most important factors affecting the level of hope [20]. Hope may have a positive effect on outcomes of different disease populations [18, 21]. One study reported that those patients with greater feelings of hope suffered from less fatigue, demonstrating that bolstering hope may result in less fatigue in chronic illness [22].

Optimism refers to an individual's tendency to maintain positive expectations of future events with an inclination towards believing that there is more good than bad in any situation [23]. Optimists tend to evaluate development trends and results of things with positivity [24]. Optimism is a positive subjective experience, and is an important subject in the field of positive psychology. According to Dr. Martin Seligman, optimism can be cultivated and is aimed at stimulating people's inner strength and good qualities to help people to maximize their potential and maintain an overall better condition. Developing an optimistic attitude has become one of the most important ways to improve person's health [25]. Researches have suggested that optimism might exert direct impacts on inflammatory and immune responses [26] and suggested possible associations between optimism and two rheumatic diseases: Ankylosing spondylitis and chronic low back pain, by potentially improving health-related quality of life, especially mental health [23].

According to Schwarzer, the definition for general self-efficacy is that an individual's capacity to convince himself to achieve success by accomplishing one or a series of actions in various situations [27]. It refers to an individuals' overall confidence when coming across challenges or confronting new things [28, 29]. People with higher general self-efficacy always set higher goals, make more effort and are reluctant to give up. It is considered to be an important psychological resource, and it directly and indirectly affects the physical and mental health-related of quality of life in patients with arthritis. Some researches have concluded that with lower self-efficacy, arthritis-related symptoms such as pain and fatigue become more severe [8, 17]. However, little similar research has been carried out in mainland China due to a lack of intervention programs for general self-efficacy [8].

Resilience is defined as a person's capacity to adapt to anexisting situation when under pressure or confronted with a critical condition instead of stagnating in the original state [30], which has been a hot topic in positive psychology for many years. Psychologists believe that resilience is the main reason why patients with the same physical status have different feelings about their own quality of life and that better resilience can help patients to respond quickly to the physical and psychological adjustment in the face of disease [31]. Many researchers have suggested that resilience, as a dynamic process, is not always innate and may be learned in certain

circumstances [32]. Moreover, acquired environment, such as education and intervention training, probably has a greater impact on individuals' resilience than congenital genetics. For example, positive intervention can promote the improvement of the resilience and contribute to an individual's development [33]. Increasingly, researches have illuminated that resilience, contributecd as a defense mechanism or protective factor, is associated with emotional adjustment and could prevent patients from experiencing distress or at least reduce it [30, 34]. Additionally, resilience is related to fatigue in different disease populations [35, 36].Although the newly emerging field of positive psychology is under rapid development, almost none research has been conducted to evaluate the associations among PSS, positive psychological constructs and fatigue in patients with RA. Furthermore, if they are interrelated, little is known about the the specifics of how they interact with one another. More importance should be attached to PSS and psychological constructs as possibilities to alleviate symptoms of fatigue in RA.

Therefore, in accordance with the analysis above, the objective of the present study are as follows:

1. To assess the effect of PSS on fatigue among RA patients, simultaneously adjusting for related factors including demographic and clinical variables.

2. To assess whether hope, optimism, general self-efficacy and resilience moderate or mediate the association between PSS and fatigue.

Materials and methods

Study design and sample

From December 2014 to January 2016, a multi-center and cross-sectional study was conducted in successive inpatients diagnosed with RA. Patients were recruited at the Department of Rheumatology at Shengjing Hospital of China Medical University, Central Hospital of Benxi, General Hospital of Fushun Mining Bureau and Sujiatun Central Hospital of Shenyang, which are characterized as key medical centers that gathers substantial numbers of patients in Liaoning Province and even in northeast China. The protocol of research was inspected and authorized by the Committee on Human Experimentation of each hospital and complied with current ethical standards. Each patient signed the informed consent.

Patients diagnosed with RA based on ACR/EULAR 2010 met the inclusion criteria as follows: (1) $\geq$ 18 years of age; (2) had clear consciousness and cognition(be able to answer questions on persons, time and places within 30s); (3) were able to consciously complete questionnaires. The exclusion criteria included: (1) had a psychiatric history and intellectual injury (e.g. depression, anxiety, schizophrenia and other psychiatric disorders); (2) were taking psychotropic drugs; (3) were suffering from other severe illness(diseases which are at acute stage threatening patients'safety of life and have a serious impact on fatigue besides RA).

All eligible patients enrolled in the research voluntarily and anonymously. They indicated their understanding the objectives and procedures of the research as described by Rheumatologists-in-charge and relevant residents. Each patient signed the informed consent form. Questionnaires were completed by the patient himself or with the help of others under the guidance of investigators. Specifics of patients' conditions were evaluated by physicians including duration of early morning stiffness (EMS), swollen joint counts (SJC) and tender joint counts (TJC). The clinical data was collected from medical records comprising C-reaction protein (CRP) and erythrocyte sedimentation rate (ESR).

There were 325 patients recruited as potential subjects at the initial stage, and 12 respondents subsequently refused to cooperate. Eight respondents with more than 30% of missing

information were removed, with an effective response rate of 93.8%. Ultimately, 305 subjects qualified for the research.

Measurement of fatigue

The degree of fatigue was measured by the Chinese version of the Multidimensional Fatigue Inventory (MFI-20) [37]. The MFI, containing 20 items with scores ranging from 20 to 100, comprised of 5 diverse dimensions: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue with 4 items each. The score for each item is in accordance with the degree of each individual's specific condition on a 5 point scale. The higher the total score, the higher the degree of fatigue is. The Chinese version of MFI has been applied to patients with high reliability and validity [8, 38]. The Cronbach 's α value of the MFI was 0.91 in the current study.

Measurement of PSS

The Multidimensional Scale of Perceived Social Support (MSPSS) was utilized to evaluate PSS [39]. The MSPSS consists of 12 items and 3 subscales with 4 items each concerning family support, friend support and support from others (such as relatives, colleagues and community leaders). The score of each item is given on a 7-point Likert scale, ranging from (1) 'very strongly disagree' to (7) 'very strongly agree'. The total scale score ranges from 12 to 84. The higher the total score, the higher the extent of social support perceived by the patient. High reliability and validity have been confirmed among various Chinese patients[40, 41]. The Cronbach 's α value of the MSPSS was 0.95 in the current study.

Measurement of hope

The Herth Hope Index (HHI) is a simplified psychometrical instrument to measure the extent of a patient's hopefulness [42]. The HHI consists of 12 items and 3 subscales with 4 items each: temporality and future, positive readiness and expectancy, and interconnectedness. The score of each item is graded with a 4-point Likert scale, ranging from (1) 'very strongly disagree' to (4) 'very strongly agree'. Each item is summed to yield a total score ranging from 12 to 48. The higher the total score, the greater the extent of hopefulness. The Chinese version of HHS has been demonstrated to have good validity and reliabilityand be suitable for various Chinese patients [18, 43]. In this research, the Cronbach 's α value of the HHI was 0.82.

Measurement of optimism

The Life Orientation Test Revised (LOT-R) is the most widely applied test for measuring optimism [44], with high degree of reliability and validity when used with various Chinese patients [18, 41]. The LOT-R comprises 10 items, including 6 scored items and 4 filler items. Among the 6 meaningful items, 3 are optimistic statements indicating positive expectations of future life, and 3 statements are pessimistic ones framing negative expectations. Each item is employed on a 5-point Likert scale, ranging from (1) 'very strongly disagree' to (5) 'very strongly agree '. A total score is calculated as the final outcomes ranging from 6 to 30. The higher the score, the more optimistic the patient is understood to be. In our research, the Cronbach 's α value of the LOT-R was 0.86.

Measurement of general self-efficacy

General self-efficacy was evaluated by the Chinese version of General Self-Efficacy Scale (GSES) [45], which is widely used among patients in China [43, 46]. The GSES comprises of

10 items with scores given on a 4-point Likert scale, ranging from (1) 'completely incorrect' to (4) 'completely correct'. The summed up total score of the GSES ranges from 10–40, with higher scores indicating higher patient confidence. With high validity and reliability, the Cronbach 's α value of the GSES was 0.80 in the current study.

Measurement of resilience

Resilience was evaluated by the Chinese version of the Ego-Resiliency Scale (ERS) [47]. The ERS consists of 14 items. The score of each item is evaluated on a 4-point Likert scale, ranging from (1) 'does not apply at all' to (4) 'completely apply '. The total scale score ranges from 14 to 56, with higher scores indicating higher levels of resilience and swifter recovery from emergencies. The ERS fits for different Chinese populations with high validity and reliability [48, 49], with the a Cronbach 's α value of 0.88 in the current study.

Demographic characteristics

Demographic variables included age, gender, marital status, educational level, employment and monthly income per capita. Marital status was sorted into 2 groups: married/cohabited and single/divorced/widowed/separated. Educational level was classified as junior high school or below, senior high school and junior college or above. Employment was sorted into 3 groups as unemployment, part-time and full-time. Clarified as 3 groups also, monthly income per capita was also classified into three groups of <3,000, 3,000–3,999 and ≥4,000 Yuan (RMB).

Clinical variables

Clinical data included family history of RA, anemia, compliance of taking medicine, presence of other chronic comorbidities, duration of RA, EMS, TJC, SJC, CRP and ESR. Family history, anemia and other chronic comorbidities were grouped as either yes or no. Compliance of taking medicine was sorted into 3 groups: never, sometimes and always. Duration of suffering RA was classified as: 1, 2–5, 6–10 and >10 years. EMS was categorized as: <0.5, 0.5–1 and >1 hour. The disease activity was evaluated by ESR and DAS28-CRP. Based on CRP, TJC and SJC, DAS28-CRP was calculated according to the formula:

DAS28-CRP = [0.56*sqrt(TJC28)+0.28*sqrt(SJC28)+0.36*ln(CRP+1)]*1.10+ 1.15 and was sorted into 4 groups: clinical remission ≤2.6, low level of disease activity 2.6–3.2, moderate level 3.2–5.1 and high level >5.1.

Statistical analysis

Statistical analysis was carried out by SPSS 13.0 software and P<0.05 (two-tailed) was viewed as statistically significant. Descriptive statistics were used to process the demographic, clinical and psychological variables manifested with number (n), percentage (%), mean and standard deviation (SD). Independent sample t-test and one-way analysis of variance (ANOVA) were utilized to evaluate the variations in fatigue concerning the demographics and clinical variables. Pearson's correlation was applied to evaluate correlations among continuous variables.

Hierarchical regression analysis was applied to explore the associations of PSS, hope, optimism, general self-efficacy, and resilience with fatigue along with the moderating roles of internal psychological variables on the PSS-fatigue association involved in demographic and clinical variables, of which variables with P<0.25 as indicated by univariate analysis were added to the regression model besides age and gender. Demographic and clinical variables were included in Block 1, with PSS in Block 2, and hope, optimism, general self-efficacy and

resilience in Block 3. Finally, the products of PSS with internal psychological constructs were employed in Block 4. If the interaction effect was statistically significant, simple slope analyses were conducted to visualize the interaction term.

Asymptotic and resampling strategies were employed to explore whether hope, optimism, general self-efficacy and resilience mediated the PSS-fatigue association. A bias-corrected and accelerated 95% confidence interval (BCa 95% CI) for each mediation was conducted with the bootstrap estimate on a basis of 5,000 bootstrap samples, in which exclusion of 0 implied that the variables indeed contributed as mediating factors to take effect.

Variables in the models were standardized before regression analysis to eliminate differences among scale scores. Multicollinearity was verified involving variance inflation factor (VIF).

Results

Descriptive statistics

The processed data of demographic and clinical characteristics and group differences among the different categories are displayed in Table 1.

There were 3 times as many females as there were males, and there was no difference of fatigue with regard to gender. Among all patients, married/cohabited people accounted for 87.54 of patients, who suffered less severity of fatigue than the single/divorced/widowed/separated patients (t = 3.00, P<0.01). Only 21.31% held a junior college degree or above, and no distinction of fatigue was discovered among people with different educational status. Unemployed patients were the largest group in terms of job status with 61.97%, and employment was found to affect the severity of fatigue (F = 3.07, P<0.05). Differences in monthly income per capita exerted certain impacts on fatigue as well (F = 6.96, P<0.01).

There were no statistically significant differences discovered between the associations of fatigue with family history, anemia, duration of RA, DAS28-CRP and compliance of taking medicine. Patients whose duration of EMS was in a range of 0.5–1 hours suffered from the least severity of fatigue compared to other groups (F = 3.53, P<0.05).

Correlations among continuous variables

The correlations among age, ESR, DAS28-CRP, PSS, positive psychological constructs and fatigue-the dependent variable are displayed in Table 2. The mean value of fatigue was 56.88 (SD = 9.50). The average age of RA patients was 57.80 (SD = 12.46). Age, ESR and DAS28-CRP were positively correlated with the independent variable carrying great significance. Meanwhile, PSS, hope, optimism, general self-efficacy and resilience were all significantly negatively correlated with fatigue.

Hierarchical regression analysis

The results of hierarchical regression analysis are displayed in Table 3. In Block 1, age and other chronic comorbidities were negatively associated with fatigue, whereas the monthly income per capita and DAS28-CRP had a positive association. However, in Block 2 among the demographic and clinical variables, only DAS28-CRP was found to have a positive association with fatigue (B = 0.90, β = 0.15, P<0.01), and similar results were shown both in Blocks 3 and 4. Meanwhile, as shown in Block 2, there was a significant negative correspondence between PSS and fatigue as hypothesized (B = -0.76, β = -0.76,P<0.01) and PSS accounted for 49.7% of the variance of fatigue. In Block 3, hope, optimism and resilience were all negatively associated with fatigue while general self-efficacy was not (hope:

Table 1. Demographic and clinical characteristics and group differences of fatigue.

Variables	n	%	Fatigue		F/t value	P value
			Mean	SD		
Total	**305**		**56.88**	**9.50**		
Demographic variables						
Gender					0.50	0.619
Men	69	22.62	56.38	9.93		
Women	236	77.38	57.03	9.39		
Marital status					2.97**	0.003
Married/cohabited	267	87.54	56.28	9.27		
Single/divorced/widowed/separated	38	12.46	61.11	10.14		
Educational level					0.09	0.915
Junior high school or below	105	34.43	56.56	9.37		
Senior high school	135	44.26	57.04	10.04		
Junior college or above	65	21.31	57.06	8.63		
Employment					3.07*	0.048
Unemployment	189	61.97	57.70	9.52		
Part-time	76	24.92	56.53	9.35		
Full-time	40	13.11	53.68	9.18		
Monthly income per capita (yuan)					6.60**	0.002
<3000	111	36.39	54.34	8.29		
3000–3999	124	40.66	58.60	10.19		
≥4000	70	22.95	57.84	9.28		
Clinical variables						
History					0.79	0.430
Yes	8	2.62	54.25	7.61		
No	297	97.38	56.95	9.55		
Anemia					0.77	0.440
Yes	125	41.0	57.38	9.09		
No	180	59.0	56.53	9.79		
Duration (years)					0.36	0.786
≤1	89	29.2	56.24	6.28		
2–5	84	27.5	57.48	5.55		
6–10	54	17.7	57.50	4.01		
>10	78	25.6	56.54	6.38		
EMS (hours)					3.53*	0.030
<0.5	100	32.8	57.44	9.66		
0.5–1	73	23.9	54.34	7.89		
>1	132	43.3	57.86	9.96		
DAS28 CRP					2.44	0.065
≤2.6	30	9.8	54.43	8.23		
2.6–3.2	28	9.2	56.11	9.18		
3.2–5.1	145	47.5	56.17	9.52		
>5.1	102	33.4	58.81	9.70		
Other chronic comorbidities					1.53	0.127
Yes	197	52.2	56.26	9.43		
No	108	47.8	58.00	9.57		
Compliance					0.24	0.790
Never	181	59.34	56.57	9.52		

(*Continued*)

Table 1. (*Continued*)

Variables	n	%	Fatigue		F/t value	P value
			Mean	SD		
Sometimes	121	39.67	57.33	9.50		
Always	3	0.98	57.33	11.59		

PSS: perceived social support; SD: standard deviation; ESR: erythrocyte sedimentation rate; DAS28 CRP: DAS28 C-reaction protein;

*P<0.05,

**P<0.01.

B = -0.52, β = -0.20 P<0.01; optimism: B = -0.70,β = -0.25 P<0.01; resilience: B = -0.31, β = -0.18 P<0.01), together accounting for additional 6.6% of the variance playing a predictive role in fatigue. In Block 4, apart from the negative association of PSS, hope, optimism and resilience with fatigue, the product of PSS and resilience was positively associated with fatigue (B = 0.03, β = 0.13,P<0.01), accounting for additional 1.4% of the variance of fatigue. Simple slope analysis revealed that when resilience is lower, the association between PSS and fatigue becomes stronger. In other words, the associations between PSS and fatigue were gradually reduced in the low (1 SD below the mean, B = -0.52, β = -0.52, P<0.01), mean (B = -0.36, β = -0.37, P<0.01) and high (1 SD above the mean, B = -0.21, β = -0.21, P<0.01) groups of resilience. The interaction was visualized in Fig 1.

Furthermore, the absolute value of β coefficient of PSS in Block3 (β = -0.34) was much smaller than that in Block2(β = -0.76) suggesting a lesser effect of PSS exerted on fatigue, indicating that the 4 positive psychological constructs could indirectly affect the association of PSS with fatigue as potential mediators.

Hope, optimism and resilience seem to act as mediators in the association between PSS and fatigue. The associations between PSS and hope, optimism, general self-efficacy along with resilience are referred to as 'a', the associations between hope, optimism, general self-efficacy along with resilience with fatigue after controlling for PSS are referred to as 'b', the value of their mediating effects, referred to as 'a*b' products and 'a, b, a*b' products along with their BCa 95% CI are displayed in Table 4.

Hope, optimism and resilience not only had significant and positive associations with PSS, but also exerted direct effects on fatigue after controlling for predictor variables, indicating

Table 2. Correlations among continuous variables.

Variables	Mean(SD)	Min	Max	r (Fatigue)
Age (years)	57.8(12.46)	21	83	0.19**
DAS28 CRP	4.57(1.53)	1.56	8.13	0.17**
ESR (mm/hour)	42.05(22.99)	2	117	0.18**
PSS	64.07(9.58)	37	84	-0.80**
Hope	36.81(3.56)	24	46	-0.79**
Optimism	22.04(3.39)	16	29	-0.78**
General self-efficacy	18.27(3.62)	10	40	-0.57**
Resilience	34.16(5.46)	23	56	-0.69**

SD: standard deviation; Min: minimum; Max: maximum; r (Fatigue): the correlation with fatigue; PSS: perceived social support; ESR: erythrocyte sedimentation rate; DAS28 CRP: DAS28 C-reaction protein;

**P<0.01.

Table 3. Associations of PSS, positive psychological constructs with fatigue and moderating roles of positive psychological constructs.

Variables	Block 1			Block 2			Block 3			Block 4		
	B	SE	β	B	SE	β	B	SE	β	B	SE	β
Gender	1.20	1.27	0.05	0.85	0.79	0.04	0.45	0.71	0.02	0.18	0.70	0.01
Age (years)	0.13	0.06	0.18*	0.05	0.04	0.07	0.05	0.03	0.06	0.04	0.03	0.06
Marital status	-4.40	1.57	-0.14**	-1.20	0.99	-0.04	-0.35	0.90	-0.01	-0.06	0.88	0.00
Employment												
Employment 1	1.61	1.45	0.07	0.54	0.90	0.02	0.66	0.82	0.03	0.35	0.80	0.02
Employment 2	-0.75	1.94	-0.04	-0.25	1.21	-0.02	0.12	1.09	0.00	0.28	1.07	0.01
Monthly income per capita (yuan)												
Monthly income per capita 1	4.27	1.20	0.22**	0.64	0.77	0.03	0.20	0.69	0.01	-0.20	0.68	-0.01
Monthly income per capita 2	5.02	1.41	0.23**	-0.04	0.91	0.00	-0.13	0.81	0.00	-0.65	0.81	-0.03
EMS (hours)												
EMS 1	-3.76	1.42	-0.16*	-1.52	0.89	-0.07	-0.92	0.80	-0.04	-0.77	0.80	-0.03
EMS 2	-0.78	1.30	-0.03	-0.25	0.81	-0.01	-0.31	0.73	-0.01	-0.35	0.71	-0.02
DAS28 CRP	0.95*	0.41	0.15*	0.90	0.25	0.15**	0.84	0.23	0.14**	0.84	0.23	0.14
ESR	0.04	0.03	0.09	0.02	0.02	0.04	0.01	0.01	0.02	0.01	0.01	0.02
Other chronic comorbidities	-2.73	1.15	-0.14*	-0.77	0.72	-0.04	-0.05	0.66	-0.01	-0.08	0.65	-0.01
PSS				-0.76	0.04	-0.76**	-0.34	0.06	-0.34**	-0.36	0.06	-0.37**
Hope							-0.52	0.17	-0.20**	-0.44	0.17	-0.16*
Optimism							-0.70	0.16	-0.25**	-0.58	0.17	-0.21**
General Self-efficacy							0.18	0.12	0.07	0.12	0.13	0.04
Resilience							-0.31	0.09	-0.18**	-0.36	0.09	-0.20**
PSS*Hope										-0.02	0.01	-0.06
PSS*Optimism										-0.02	0.02	-0.04
PSS*General self-efficacy										0.00	0.02	0.00
PSS*Resilience										0.03	0.01	0.13**
F	5.51**			47.76**			49.87**			42.83**		
df	(12, 292)			(13, 291)			(17, 287)			(17, 287)		
R2	0.19			0.68			0.75			0.76		
adjusted R2	0.15			0.67			0.73			0.74		
ΔR2	0.19**			0.50**			0.07**			0.01**		

PSS: Perceived social support; Gender: men vs. women; Marital status: single/divorced/widowed/separated vs. married/cohabited; Employment 1: part-time vs. unemployment; Employment 2: full-time vs. unemployment; Monthly income per capita 1: 3000–3999 vs. <3000; Monthly income per capita 2: ≥4000 vs. <3000; EMS 1: 0.5–1 vs. <0.5; EMS 2: >1 vs. <0.5; Other chronic comorbiditites: no vs. yes; ESR: erythrocyte sedimentation rate; DAS28 CRP: DAS28 C-reaction protein;

* P<0.05,

** P<0.01.

that hope, optimism and resilience could act as mediators affecting the association between PSS and symptoms of fatigue (hope: a*b = -0.16, BCa 95%CI: -0.27,-0.03; optimism: a*b = -0.20, BCa 95%CI: -0.30, -0.10; resilience: a*b = -0.12, BCa 95%CI: -0.21,-0.04). Although general self-efficacy was positively associated with PSS, it did not have significant influence. Thus, general self-efficacy did not seem to mediate the association of PSS with fatigue.

Using the formula: (a*b)/total effect, the proportion of indirect effects of PSS on fatigue through mediators accounting for total effects could be calculated. With respect to fatigue, the proportions of mediating roles of hope, optimism, and resilience were 20.7%, 25.7% and 15.2% respectively.
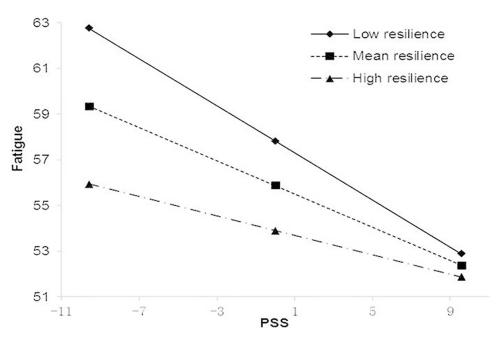
Fig 1. Moderating effect of resilience on PSS-fatigue association.

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Discussion

In our research, the mean score of the MFI was much higher than that of the general population [50], demonstrating that fatigue is indeed serious in RA. Furthermore, Our results were corresponded with previous research of RA patients such as that in the Netherlands and Denmark [51, 52]. Similar research has never been conducted in China, sot no comparison may presently be made in the same population. Although the current study lacks without control groups of patients suffering from other diseases, the scores above are at a medium-high level with regard to related researches carried out among other clinical populations [53–56]. PSS had a significantly negative association with fatigue, accounting for almost half of the variance concerning its predicting role, indicating that less severity of fatigue might be experienced among RA patients when acquiring more positive assistance from others. Compared with the US and Egypt, RA patients in the UK and the Netherlands seemed to be dealing with their fatigue by themselves without seeking help from others, thus suffering from greater severity of

Table 4. Mediating roles of positive psychological constructs on the PSS-fatigue association.

Mediators	a	b	a*b value	BCa95%CI	c'	c
Hope	0.80**	-0.20**	-0.16	(-0.27, -0.03)	-0.34	-0.76
Optimism	0.78**	-0.25**	-0.20	(-0.30, -0.10)		
General self-efficacy	0.67**	0.07	0.05	(-0.04, 0.13)		
Resilience	0.66**	-0.18**	-0.12	(-0.21, -0.04)		

PSS: Perceived social support; BCa 95% CI: Bias-corrected and accelerated 95% confidence interval; a: PSS → Hope/Optimism/ General Self-efficacy/ Resilience; b: Hope/Optimism/ General Self-efficacy/Resilience → Fatigue; a*b: Product of a and b; c: PSS → Fatigue; c': PSS → Hope, Optimism, General Self-efficacy and Resilience→ Fatigue. Gender, age, marital status, employment, monthly income per capita, duration of early morning stiffness (EMS), DAS28 CRP, erythrocyte sedimentation rate (ESR), and other chronic comorbidities were covariates.

**P<0.01.

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symptoms [5, 57–59]. A Chinese study reported that social support, as a direct or indirect factor, played an important predicting role in health-related quality of life both physically and psychologically[8]. But some researches have reported that patients with RA always lack adequate social support [15, 16], probably because RA is incurable with a prolonged course, causing even deformity and physical disability in the final stage. Furthermore, most patients suffering RA are usually involved in restricted social activities, contributing to less support from the society [15, 57]. Therefore, social support may be quite relevant to RA-related fatigue and could probably relieve it to a large extent. The current study has shown that, hope, optimism and resilience, contributed as mediators and affected the PSS-fatigue association by accounting for a proportion of the variance in predicting fatigue, indicating that RA patients might experience less severity of fatigue when they had higher levels of hope, optimism and resilience. However, research and evidence regarding their impact among patients with RA is quite rare.

RA patients burdened by a prolonged course of disease, achieve hope not by relying on any exact target but by attaching importance to present or future possibilities, as well as themselves or others they viewed to be important, which is different from the usual "goal orientation" [60]. When going through declining functioning even physical disability in the progress of the disease, it is hope that contributed to the intrinsic strength that beings patients the courage to confront reality with a positive attitude. Meanwhile, hope can promote patients' adaption to the difficult condition, rather than extricating themselves from it. Therefore, higher level of hope could probably relieve fatigue among RA patients.

Apart from its contribution as a personality trait, optimism also acts as an explanatory pattern bound up with positive prospects [61], exerting desirable influences on psychological health. Optimism exerts considerable impacts on accommodation with chronic disease, such as RA, making it great beneficial to the physical functioning among patients in a direct or indirect way [62]. Further, RA patients with a higher level of optimism achieved a better emotional status [63, 64], indicating that a positive and optimistic mood can alleviate fatigue to a certain extent. Higher level of optimism resulted in less pain, thus improving the wellbeing among RA patients [63]. But researches demonstrated that RA patients did have worse expectations of their fatigue symptoms [65]. As a result, optimism probably has an impact on RA-related fatigue.It was shown that resilience was expected to predict and evaluate fatigue symptom among cancer patients [36]. Although resilience was studied only in a few studies of RA, a consensus was reached that higher level of resilience was beneficial for RA patients [66, 67] and a study reported that resilience was positively associated with PSS [68]. In our research, resilience not only acted as a mediator by playing a predictive role, but it also positively moderated on the PSS-fatigue association, indicating that with higher levels of resilience, the association between PSS and fatigue might be more close among RA patients. Therefore, improving resilience could probably alleviate fatigue among RA patients.

Although negatively correlated to fatigue in univariate analysis, self-efficacy did not have statistical significance in the regression analysis. However, previous researches have reported that patients with higher levels of self-efficacy suffered from less fatigue severity in RA [8, 17]. This difference maybe because the effect of self-efficacy was covered by other psychological variables. However, another study also indicated that the association between self-efficacy and fatigue was not confirmed by multivariate analysis [17]. Therefore, further research should be conducted to explore its exact effect in RA-related fatigue.

The current study provided the preliminary possibility of building a core-positive high-order psychological construct to alleviate fatigue in RA patients by utilizing the individual positive construct of hope, optimism and resilience. Therefore, several clinical implications might be concluded according to this study. First, fatigue is a serious among RA patients, and much

more attention should be paid to detecting and treating its symptoms by Chinese rheumatologists. Besides, social support may be taken into account seriously with regard to the alleviation of RA-related fatigue. In addition, a whole new perspective could emerge on the application of a model to improve positive psychological resources and relieve fatigue in RA patients by utilizing the protective effects of social support, hope, optimism and resilience. As the present study has demonstrated, social support, hope, optimism and resilience all probably have positive impacts on alleviating fatigue, so non-pharmacological treatments with regard to RA-related fatigue may focus on social support and positive psychological interventions mainly targeting hope, optimism and resilience. As for social support, family, friends and society should pay more attention to these patients, and doctors should show more solicitude as well. Encouragements from doctors can enhance patients confidence during treatments and improve their compliance, thereby relieving fatigue symptoms remarkably [4, 6]. Online interactions aimed at acquiring more social support have also been shown to be beneficial to RA patients, which can also be recommended [12]. As for hope, optimism and resilience, these positive psychological constructs may keep patients maintain a positive and optimistic attitude towards confronting reality and coordinating with doctors, thus managing fatigue symptoms successfully. Therefore, adequate social support and positive psychological interventions targeting hope, optimism and resilience should probably be attached great importance to alleviate fatigue symptoms among RA patients. However, there are still several limitations in our research. First, self-reporting measures were applied to evaluate patients' conditions and some of them fulfilled the questionnaires with the help of others due to illiteracy, which might lead to recall and reporting bias affecting the associations among variables. Therefore, efficacious control measures were required, such as the guarantee of anonymity, measuring instruments with high reliability and validity and emphasizing to patients there was no right or wrong answer. Second, our research was conducted in northeast China at various multicenters, but whether the results may be generalized to other populations with different cultural backgrounds requires further study. Third, the cross-sectional method applied in our research only provided the general condition of patients at the exact time point of investigation, thus restricting the evaluation of casual links among the variables. Therefore, prospective longitudinal studies need to be studied to further verify our conclusions.

Conclusions

Fatigue is a severe symptom among RA patients. Only resilience was shown to probably positively moderates the PSS-fatigue association. Hope, optimism and resilience may act as partial mediators in the association between PSS and fatigue. PSS, hope, optimism and resilience may contribute as effective recourses to alleviate fatigue, with PSS showing the greatest possible effect. Adequate social support and positive psychological interventions targeted at hope, optimism and resilience should probably be attached great importance to alleviate fatigue symptom among RA patients.

Supporting information

S1 File. STROBE_checklist_v4_combined_PlosMedicine.
(DOCX)

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Author Contributions

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Investigation: NX TZ RH.

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Therapy (Fatigue) (FACIT-F), Multi-Dimensional Assessment of Fatigue (MAF), Multi-Dimensional Fatigue Inventory (MFI), Pediatric Quality Of Life (PedsQL) Multi-Dimensional Fatigue Scale, Profile of Fatigue (ProF), Short Form 36 Vitality Subscale (SF-36 VT), and Visual Analog Scales (VAS). Arthritis care & research. 2011; 63 Suppl 11:S263–86. Epub 2012/05/25.

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