Psychological state is related to remission of Boolean-based definition of patient global assessment in patients with rheumatoid arthritis

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博士論文

Psychological state is related to remission of Boolean-based definition of patient global assessment in patients with rheumatoid arthritis

（Boolean 基準における患者全般改善評価の寛解には

関節リウマチ患者の心理状態が関連する）

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房間　美恵

Psychological state is related to remission of Boolean-based definition of patient global assessment in patients with rheumatoid arthritis

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Abstract

Objective: To evaluate whether psychological state is related to Boolean-based definition of patient global assessment (PGA) remission in patients with rheumatoid arthritis (RA).

Methods: Patients with RA who met the criteria of SJC≤1, TJC≤1 and CRP≤1 were divided into 2 groups, PGA remission group (PGA≤1cm) and non-remission group (PGA>1cm). Anxiety was evaluated utilizing the Hospital Anxiety and Depression Scale-Anxiety (HADS-A), while depression was evaluated with HADS-Depression (HADS-D) and the Center for Epidemiologic Studies Depression Scale (CES-D). Comparison analyses were performed between PGA remission group and non-remission group in HADS-A, HADS-D and CES-D.

Results: Seventy-eight patients satisfied with SJC≤ 1, TJC≤ 1 and CRP≤ 1. There

were no significant differences between PGA remission group (n=45) and non-remission group (n=33) in age, sex, disease duration, Steinbrocker's class and stage. HADS-A, HADS-D and CES-D were significantly lower in PGA remission group compared with those in non-remission group (p=0.034, p=0.0088, p=0.0017, respectively).

Conclusion: Patients with RA who do not meet PGA remission criterion despite good disease condition were in poor psychological state compared with those who satisfied Boolean-based definition of clinical remission. Support for psychological state might be effective for improvement of PGA, resulting in attainment of true remission.

(196<200 letters)

INTRODUCTION

The American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) presented the ACR/EULAR provisional definition of remission in rheumatoid arthritis (RA) for clinical trials in 2011 and the clinical remission in Boolean criteria requires scores of less than 1 on swollen joint counts (SJC), tender joint counts (TJC), CRP and patient global assessment (PGA) (1).

Development of biologic agents such as TNF inhibitors and IL-6 inhibitor has improved disease activity of RA and inhibited progression of destruction of bone and cartilage in patients with RA (2). Moreover, there are many reports suggesting improvement of quality of life (QOL) as well as clinical and radiographic improvement in patients with RA treated with biologics (3) (4). However, we often encounter patients with RA whose PGA is higher than 1, even though their SJC, TJC and CRP are less than 1. It is reported that PGA is not solely influenced by RA disease activity (5) and that PGA is a limiting factor for reaching remission (6).

Meanwhile, there are many reports suggesting that patients with RA are often related with poor psychological condition. Anxiety is common in patients with RA (7) (8) (9). Depression is also related with prevalence rates ranging from 13% to 20% in patients with RA (10) (11) and may exacerbate pain and disease activity (12). Although there are many evidences that psychological state may be related with patients with RA, the influence of psychological state on PGA is not well demonstrated.

In this study, we evaluate whether psychological state is related to Boolean-based definition of PGA remission for patients with RA.

PATIENTS AND METHODS

Patients with RA who fulfilled the 1987 revised criteria of ACR for RA (13) or the 2010 ACR/ EULAR classification criteria for RA (14) were enrolled in this study. Patients in Yukioka Hospital and NTT West Osaka Hospital in Osaka, Japan were selected for enrollment with the approval of the ethics committees of these hospitals, and informed consent was obtained from all the patients.

SJC, TJC, PGA and CRP were examined. Among patients with RA enrolled, those who fulfilled Boolean remission of SJC (≤1), TJC (≤1) and CRP (≤1mg/dl) were selected. These patients were divided into 2 groups, the PGA remission group (PGA≤1cm) and the PGA non-remission group (PGA>1cm).

Anxiety and depression were examined utilizing the Hospital Anxiety and Depression Scale-Depression (HADS-D) and HADS-Anxiety (HADS-A), respectively. HADS is a 14-item scale consisting of two 7-item subscales measuring depression and anxiety on a 4-point response scale (15) (16). Subscale scores range from 0 to 21, with higher scores indicating higher levels of depression and/or anxiety. Scores from 0 and 7 represent no cases; those from 8 to 10 indicate a possible case, and those from 11 to 21 suggest a probable case of depression/anxiety (15) (16). Depression was also evaluated with the Center for Epidemiologic Studies Depression Scale (CES-D). CES-D is a 20-item scale designed to measure depressive symptoms experienced in the past week. Scores range from 0 to 60, with a cut-off of 16 indicative of probable clinical depression (15) (17).

Comparison analyses were performed between the PGA remission group and the PGA non-remission group using HADS-A, HADS-D and CES-D as well as taking into consideration age, gender, disease duration, functional class & stage, MTX dosage and ratio of biologics usage.

Statistical analysis

Data was analyzed using Wilcoxon rank-sum test, Peason Chi-square test and Fisher's exact test. A probability value of less than 0.05 was considered significant. Data analysis was performed using the statistical software EZR version 2.14.

RESULTS

Patients' characteristics

One hundred twelve patients with RA (18 males and 94 females) were recruited. Among these patients enrolled, those with RA who satisfied with SJC ≤ 1, TJC ≤ 1 and CRP ≤ 1 were 78 patients (17 males and 61 females). These patients were evaluated in this study. Patients' characteristics were as follows: median [min-max] of age (54.0, [27-83] years old), disease duration (7.34, [0.3-30] years), TJC (0.0, [0-1]), SJC (0.0, [0-1]), PGA (8.0, [0-57]) and EGA (4.0, [0-33]) (Table 1).

Patients' psychological characteristics

Psychological characteristics were as follows: median [min-max] of HADS-A (2.0, [0-15]), HADS-D (3.0, [0-16]) and CES-D (12.0, [0-36]) (Table 2).

Comparison of patients' characteristics between PGA remission group and PGA non-remission group

Patients characteristics of the PGA remission group (n=45) and the PGA non-remission group (n=33) were as follows: median [min-max] of age (52.0, [29-83] & 55.0, [27-81] years) and disease duration (7.0, [0.25-27] & 8.0, [0.58-30] years), male/female (9/36 & 8/25 patients).

There was no statistically significant difference between the PGA remission group and the PGA non-remission group in age, sex, disease duration, Steinbrocker's class and stage (p=0.381, p=0.783, p=0.923, p=0.392 and p=0.215, respectively) (Table 3).

There was also no significant difference in MTX dosage (p=0.358) and ratio of patients treated with biologics (p=0.612) between in PGA remission group and non-remission group (Table 3).

Comparison of HADS-Anxiety and HADS-Depression between the PGA remission group and the PGA non-remission group

Anxiety and depression evaluated with HADS-A and HADS-D were compared between the PGA remission group and the PGA non-remission group. HADS-A was significantly lower in the PGA remission group compared with that in the PGA non-remission group (median [min-max]; 2.0, [0-12], 4.0, [0-15], respectively, p=0.017) (Figure 1A). HADS-D was also significantly lower in the PGA remission group compared with that in the PGA non-remission group (median [min-max]; 1.0, [0-12], 3.0, [0-16], respectively, p=0.007) (Figure 1B)

Comparison of CES-D between the PGA remission group and the PGA non-remission group

Another measure of depression, CES-D, was compared between the PGA remission group and the PGA non-remission group (Figure 1C). CES-D was also significantly lower in the PGA remission group compared with that in the PGA non-remission group (median [min-max]; 9.0, [0-27], 13.0, [0-36], respectively, p=0.001).

DISCUSSION

In our study, there were statistically significant differences in psychological parameters between the PGA remission group and the PGA non-remission group in patients with RA who met ACR/EULAR joint and CRP criteria for remission (≤ 1 SJC, ≤ 1 TJC and ≤ 1 CRP). Anxiety evaluated with HADS-A was significantly lower in the PGA remission group compared with the PGA non-remission group. Similarly, depression evaluated with HADS-D and CES-D was also statistically lower in the PGA remission group compared with the PGA non-remission group. This data indicates that psychological states such as depression and anxiety are related to PGA.

It has been demonstrated that anxiety and depression were related to pain in patients with RA (18) (19). Pain is also reported to correlate with patient perception, PGA (20). Therefore, our findings indicating that PGA is correlated with psychological conditions such as anxiety and depression are in agreement with the previous reports. Non-inflammatory factors including back pain and fatigue were reported to contribute to higher PGA and a large proportion of patients not in remission by ACR/EULAR criteria had high PGA related to non-inflammatory issues (21). Our data also support this report because psychological states such as anxiety and depression belong to non-inflammatory factors.

In 2012, EULAR published recommendations for the role of the nurse in the management of chronic inflammatory arthritis (22). In these recommendations, the importance of identification, assessment and address of psychological issues to minimize the chances of patients' anxiety and depression is advocated. There are several reports suggesting the efficacy of nurses' interventions for patients' psychological states. Nurses' intervention, by applying principles of self-management

and cognitive behavioral therapy, over a period of three months for patients 60 years or older with depression complicated with either type II diabetes mellitus (DM) or chronic obstructive pulmonary disease (COPD), was associated with less anxiety, better self-efficacy skills, daily functioning and social participation (23). Another study of nurses' intervention was conducted with patients suffering from head and neck cancer (HNC). A problem-focused intervention aimed at helping patients to manage the physical, psychological, and social consequences of HNC was performed for patients with HNC in six bimonthly 45-minute counseling sessions. After one year, the level of depression was significantly lower in the intervention group than in the control group (24). Similarly, for RA patients with anxiety or depression, nurses' psychological support described above may be important to minimize their poor psychological state.

The rate of depression may be higher in patients newly diagnosed with RA compared with those with established RA (25). It has been reported that psychosocial acceptance of the diagnosis of RA varies greatly by individuals, and poor adjustment to this diagnosis contributes to the onset of depressive symptoms (10) (26). Moreover, Sharpe L, et al. suggest that the concept of a psychological 'window of opportunity' may exist (27). Therefore, we believe that it is crucial to provide suitable psychological support for patients diagnosed with RA to prevent development of depression. In addition, we argue that anxiety and depression must be identified in patients with established RA in order to provide suitable psychological support. We would like to propose that "psychological remission", meaning the state of being free from psychological conditions such as anxiety and depression, should be a requirement to attain "true remission".

In conclusion, this is the first report suggesting that patients with RA who do not meet the PGA remission criterion despite a good clinical condition may be suffering

from poor psychological state, while patients who satisfied Boolean-based definition of clinical remission appear to be in a good psychological state. Support for patients' psychological well-being may be effective in preventing the onset of depression or alleviating depression and improving PGA, ultimately resulting in attainment of true remission.

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Conflict of Interest: None

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Figure legends

Figure 1. Comparison of HADS-Anxiety, HADS-Depression and CES-D between PGA remission group and PGA non-remission group

(A) Comparison of HADS-Anxiety; HADS-A was significantly lower in PGA remission group compared with that in PGA non-remission group. (B) Comparison of HADS-Depression; HADS-D was significantly lower in PGA remission group compared with that in PGA non-remission group. (C) Comparison of CES-D; CES-D was significantly lower in PGA remission group compared with that in PGA non-remission group. Statistical analysis was performed with Wilcoxon rank sum test.

Table 1

Patient characteristics

Clinical variables	n=78
Age , years [range]	54.0 [27-83]
Gender (female / male)	61 / 17
Disease duration , years	7.34 [0.3-30.0]
Function class 1 : 2 : 3 : 4	12 : 60 : 6 : 0
Function stage 1 : 2 : 3 : 4	13 : 41 : 8 : 16
Tender joint count (28-joint count) (TJC)	0.0 [0-1]
Swollen joint count (28-joint count) (SJC)	0.0 [0-1]
Patient global assessment (PGA)	8.0 [0-57]
Evaluator global assessment (EGA)	4.0 [0-33]
CDAI	1.85 [0-8]
Patient pain assessed with VAS (Pain-VAS)	8.0 [0-60]
	median [min-max]

Table 2

Psychological characteristics

Clinical variables	n=78
HADS-Anxiety	2.0 [0-15]
HADS-Depression	3.0 [0-16]
CES-D	12.0 [0-36]
	median [min-max]

Table 3

Comparison of patient characteristics between PGA remission group and PGA non-remission group

n = 78	PGA remission group (n=45)	PGA Non-remission group (n=33)	p-value
Age , years [range]	52.0 [29-83]	55.0 [27-81]	0.381‡
Gender (male / female)	9 / 36	8 / 25	0.783†
Disease duration , years	7.0 [0.25-27]	8.0 [0.58-30]	0.923‡
Function class 1 : 2 : 3 : 4	8 : 35 : 2 : 0	4 : 25 : 4 : 0	0.392*’
Function stage 1 : 2 : 3 : 4	8 : 26 : 3 : 8	5 : 15 : 5 : 8	0.215*’
MTX dosage (mg/week)	4.0 [0-14]	6.0 [0-14]	0.358‡
DMARDs (+ / -)	7 / 38	4 / 29	0.752†
Biologics (+ / -)	34 / 11	23 / 10	0.612†
			median [min-max]
	‡Wilcoxon rank sum test *’ Peason Chi-square test(1+2 vs 3+4)		
	† Fisher’s exact test PGA: Patient global assessment		

Figure 1