

Psychological Flexibility and Depression in Advanced CKD and Dialysis



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Rationale & Objective: Depression is prevalent and highly associated with mortality among patients with chronic kidney disease (CKD). Psychological flexibility can be captured as acceptance in psychology, and its improvement by behavioral therapy is associated with reduced depression in some clinical settings. However, no study has been reported on patients with CKD. This study aimed to examine the association between psychological flexibility and depression in patients with CKD.

Study Design: Cohort study.

Setting & Participants: This multicenter study of 5 hospitals in Japan included patients with nondialysis stage 3-5 CKD or stage 5D CKD receiving hemodialysis or peritoneal dialysis.

Predictor: Psychological flexibility measured using the 7-item Acceptance and Action Questionnaire (AAQ-II).

Outcomes: The prevalence and incidence of depression after 1 year, which was defined by a score ≥ 16 points on the Center for Epidemiologic Studies Depression (CES-D) questionnaire.

Analytical Approach: Gamma regression was used in the examination of correlates of the psychological flexibility value. Modified Poisson regression models were fit for the prevalence and incidence of depression.

Results: The cross-sectional and longitudinal analyses included 433 and 191 patients, respectively. Lower (ie, worse) psychological flexibility levels were associated with hemodialysis and peritoneal dialysis. Higher (ie, better) psychological flexibility levels were associated with lower prevalence of depression (per 5-point increase; adjusted prevalence ratio, 0.75; 95% CI, 0.70-0.80) and lower incidence of depression (per 5-point increase; adjusted risk ratio, 0.72; 95% CI, 0.61-0.85).

Limitations: Depression was assessed using the CES-D questionnaire. Cultural differences may exist in the interpretation of AAQ-II scores.

Conclusions: Better psychological flexibility was associated with lower prevalence and incidence of depression in patients with CKD. Further studies are warranted to determine the possible prevention and treatment of depression by the development of behavioral interventions to improve psychological flexibility.

Visual Abstract included

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Depression is highly prevalent in patients with chronic kidney disease (CKD) and significantly affects mortality.^{1,2} The clinical relevance of depression has been demonstrated by its high prevalence; interview-based as-

Editorial, p. 673

sessments revealed that 22.8% of patients with stage 5D CKD and 21.4% of patients with stage 1-5 CKD exhibit depression.³ In addition, patients with CKD often consider depression a more important outcome than survival.⁴ Treatment methods such as selective serotonin reuptake inhibitors and nonpharmacologic interventions (ie, cognitive behavioral therapy) have not shown consistent efficacy among patients with CKD,^{5,6} partially due to the difficulty adjusting antidepressant doses.⁷ Thus, focusing on psychological factors may provide an alternative for understanding the mechanisms of depression among patients with CKD.⁷ Targeting psychological flexibility, which has rarely been investigated in patients with CKD, could be a therapeutic option.

Psychological flexibility is conceptualized as the ability to completely contact the present moment and change or

persist in behaviors to pursue identified values.⁸ According to this definition, psychological flexibility encapsulates “acceptance,” which is the ability to be open to personal experiences such as unpleasant sensations, thoughts, and feelings without altering their frequency or contents.⁸ In this context, acceptance does not refer to the acceptance of the disability or disease; rather, it specifically refers to the acceptance of inner thoughts and feelings that have grown, over a lifetime, due to chronic illness. Recently, acceptance has been measured by psychological flexibility using the 7-item Acceptance and Action Questionnaire-II (AAQ-II).⁹ Emerging evidence indicates that an improvement in psychological flexibility by behavioral therapy is associated with a decrease in depression among patients with other chronic diseases, such as Crohn disease.^{10,11} Considering the similarity of psychological distress and burden (ie, burden from the disease itself and self-care) among many chronic illnesses, a focus on psychological flexibility should be applicable to depression observed in patients with CKD. Thus, it is possible that patients with CKD with better psychological flexibility could accept painful daily self-care and/or dialysis-related symptoms more easily and therefore are more likely to be resistant to depression.

PLAIN-LANGUAGE SUMMARY

In patients with kidney disease, daily self-care and dialysis-related symptoms can be painful experiences and depression is common. Therefore, a longitudinal study was conducted to determine whether patients with advanced chronic kidney disease and dialysis were less likely to develop depression with greater psychological flexibility, and a cognitive acceptance of the patient's experience as it is. It was observed that better psychological flexibility correlated with patients experiencing less depression. This finding is important for the prevention of depression in advanced chronic kidney disease and dialysis because behavioral therapy can increase psychological flexibility.

However, to our knowledge, studies on the relationships between CKD, psychological flexibility, and depression are inadequate. Clarifying these associations is of clinical importance because characterizing patients with low psychological flexibility can lead to the establishment of nonpharmacologic behavioral interventions to improve psychological flexibility and effectively treat and prevent depression.

Therefore, using data from the Hope Trajectory and Disease Outcome Consortium (HOTDOC) Study, a multicenter cohort study was conducted to examine the correlates of psychological flexibility, which were measured using the AAQ-II. In addition, associations between psychological flexibility and prevalence and incidence of depression in a cohort of patients with a wide range of CKD severities were evaluated.

METHODS

Setting and Participants

The HOTDOC Study was a multicenter cohort study conducted at 5 outpatient general community hospitals with nephrology centers (Japanese Red Cross Medical Center, Tokyo; Inagi Municipal Hospital, Tokyo; JCHO Nihonmatsu Hospital, Fukushima; Shirakawa Kosei General Hospital, Fukushima; and the St Marianna University Hospital, Kanagawa).

The HOTDOC Study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional review boards of St Marianna University (number 3209) and Fukushima Medical University (number 2417). Written informed consent was obtained from each participant.

Inclusion criteria were as follows: (1) nondialysis stage 3-5 CKD or stage 5D CKD treated by hemodialysis or peritoneal dialysis; (2) receiving nephrology care at the participating center for dietary instruction, medication prescription, kidney function monitoring, and/or dialysis treatment; and (3) the ability to respond

to the questionnaire survey. Patients with dementia were excluded.

Exposure

The exposure was acceptance, which was measured as psychological flexibility using the AAQ-II.⁹ The AAQ-II is a unidimensional construct that includes 7 items, scored using a 7-point Likert scale. AAQ-II captures the willingness of the patient to be in contact with unpleasant private experiences at the present moment, their acceptance of these experiences, and the ability to persist in behavior related to their identified values (sample items: "My painful experiences and memories make it difficult for me to live a life that I would value"; Table S1). Patients were asked to score each item on a scale of 1 to 7, with 1 and 7 meaning "never true" and "always true," respectively. Total scores ranged from 7 to 49. In this study, the total score was reversed such that lower and higher scores indicated worse and better psychological flexibility, respectively.^{10,12,13} The Japanese version of the AAQ-II was validated by Shima et al¹⁴ and was demonstrated to have good reliability (coefficient alpha = 0.88) and concurrent validity. Permission for the use of this scale was obtained from the last author (Prof H. Kumano).

Outcomes

The main outcome was depression, which was measured using the Japanese version of the Center for Epidemiologic Studies Depression scale (CES-D).¹⁵ The CES-D is composed of 20 items, which are scored using a 4-point Likert scale. Patients were asked to choose one of the following responses for each item: "less than 1 day" (0 point), or "5-7 days" (3 points). The coefficient alpha for the CES-D was 0.84.¹⁵ Total scores can range from 0 to 60; in this study, a total score ≥ 16 was considered to indicate depression.¹⁶ For the cross-sectional analysis, the outcome was the prevalence of depression among all participants. The incidence of depression 1 year after the baseline survey among patients who experienced no depression at baseline was considered the outcome in the longitudinal study.

Measurement of Covariates

Confounding variables were those suspected of being associated with either depression or psychological flexibility, based on evidence from the literature. These variables included age, sex, impaired performance status, diabetic nephropathy as the primary kidney disease, treatment status (nondialyzed, peritoneal dialysis, or hemodialysis), comorbid conditions (such as cardiovascular disease, cerebrovascular disease, and malignancy), working status as a proxy for economic status, and the presence of family.⁷ Performance status was assessed by attending physicians using the Zubrod Scale.¹⁷ Impaired performance status was defined as a score ≥ 2 (ambulatory > 50% of waking hours or occasional assistance when

moving). The presence of family was evaluated by the patient's yes or no response to the question "Do you have any family?" Working status was assessed with the question "During the past 4 weeks, did you work at a paying job?" to which patients responded either yes or no. The questionnaire was administered at each facility, and patients were asked to complete it at home. In the event that patients could not write due to visual impairment or physical disability, they were asked to verbally complete the form with the aid of a trained research assistant who did not inform patients of the hypothesis.

Statistical Analyses

All statistical analyses were conducted using Stata/SE, version 15 (Stata Corp). Baseline characteristics were described for patients included for cross-sectional analysis, and histograms were constructed for the total AAQ-II score (ie, score before reversal; higher score indicates worse psychological flexibility).

Associations between baseline characteristics and total AAQ-II scores were analyzed using a generalized linear model with gamma distribution and log-link function to provide unbiased estimates because the total AAQ-II score demonstrated a heavily right-skewed distribution. A Box-Cox test was used to confirm the appropriateness of the log-link function (ie, natural log transformation), which symmetrically transforms the outcome variables. In addition, the modified Park test was used to confirm that the specification of the gamma distribution with a log-link had the best fit.¹⁸

To derive adjusted mean differences in AAQ-II score from the model, the average marginal effects of all participants (ie, an average of the individual marginal effect) were calculated using the following step. First, predicted AAQ-II scores of participants with a categorical variable fixed at a specific category (eg, hemodialysis) were calculated in the estimated model while keeping all other variables fixed at their original values. Second, predicted AAQ-II scores, for which every patient was treated such that he or she represents participants with the categorical variable fixed at a reference category (eg, nondialysis) were similarly obtained. Last, the average marginal effect was obtained as the mean of the difference in predicted AAQ-II scores for the 2 groups. Similarly, the average marginal effect for continuous variables was obtained as the difference between predicted AAQ-II scores following an increase in a continuous variable by a specific unit (eg, a 1-year increase in age) and predicted AAQ-II scores with the continuous variable fixed at the original value, while all other variables were fixed at their original values.^{19,20} CIs were generated using the delta method.

The associations between the reversed AAQ-II score (higher score indicates better psychological flexibility) and depression at baseline were analyzed using a modified Poisson regression to estimate the adjusted prevalence ratio. This is because depression in CKD is common, and

prevalence ratio could not be approximated by odds ratios in this situation.²¹ Age, sex, diabetic nephropathy, treatment status, impaired performance status, comorbid conditions, working status, and the presence of family were entered into the multivariate analyses as covariates. Subsequently, the association between the reversed AAQ-II score and incidence of depression at the 1-year follow-up was analyzed using a modified Poisson regression to estimate the adjusted risk ratio.²¹ Covariates were identical to those in the cross-sectional analysis. Sensitivity analysis was conducted to determine the association between the reversed AAQ-II score and incidence of depression using a penalized maximum likelihood logistic regression model, which allows the analysis of a small number of outcomes.²² $P < 0.05$ was considered statistically significant for all analyses.

RESULTS

Characteristics of Study Participants

Among 461 participants, 433 were included in the cross-sectional analysis, whereas 28 were excluded due to incomplete or missing responses to the reversed AAQ-II score or CES-D score (Fig 1). Baseline characteristics are shown in Table 1. Mean age was 66.7 years, and 139 (32%) patients were women. Mean AAQ-II score was 39.5 (standard deviation [SD], 7.9), while mean CES-D score was 13.4 (SD, 8.6). The histogram of the total AAQ-II score (before reversal) suggests that AAQ-II distribution was right-skewed (Fig 2). One hundred forty-four patients experienced depression at baseline, with a prevalence of 33.3%.

Cross-Sectional Analysis

Correlations between baseline characteristics and higher "total" AAQ-II (ie, worse psychological flexibility) scores are shown in Table 2. Patients receiving peritoneal dialysis or hemodialysis demonstrated high total AAQ-II scores compared with nondialyzed patients (adjusted mean difference, 2.26 [95% CI, 0.23-4.28] points; 3.16 [95% CI, 1.39-4.94] points, respectively). Effect sizes of peritoneal dialysis or hemodialysis on total AAQ-II score, as determined by Cohen *d*, were 0.28 and 0.40, respectively.²³ On the contrary, other variables were not associated with AAQ-II score. In the covariate-adjusted modified Poisson regression model, a 5-point higher AAQ-II score (after reversal, indicating better psychological flexibility) was associated with lower likelihood of developing depression (adjusted prevalence ratio, 0.75 [95% CI, 0.70-0.80]; Table 3).

Longitudinal Analysis

Of patients without depression at baseline ($n = 289$), 93 did not participate in the follow-up survey because of referral to other facilities ($n = 18$), death ($n = 17$), hospitalization during the 1-year follow-up survey ($n = 3$), or

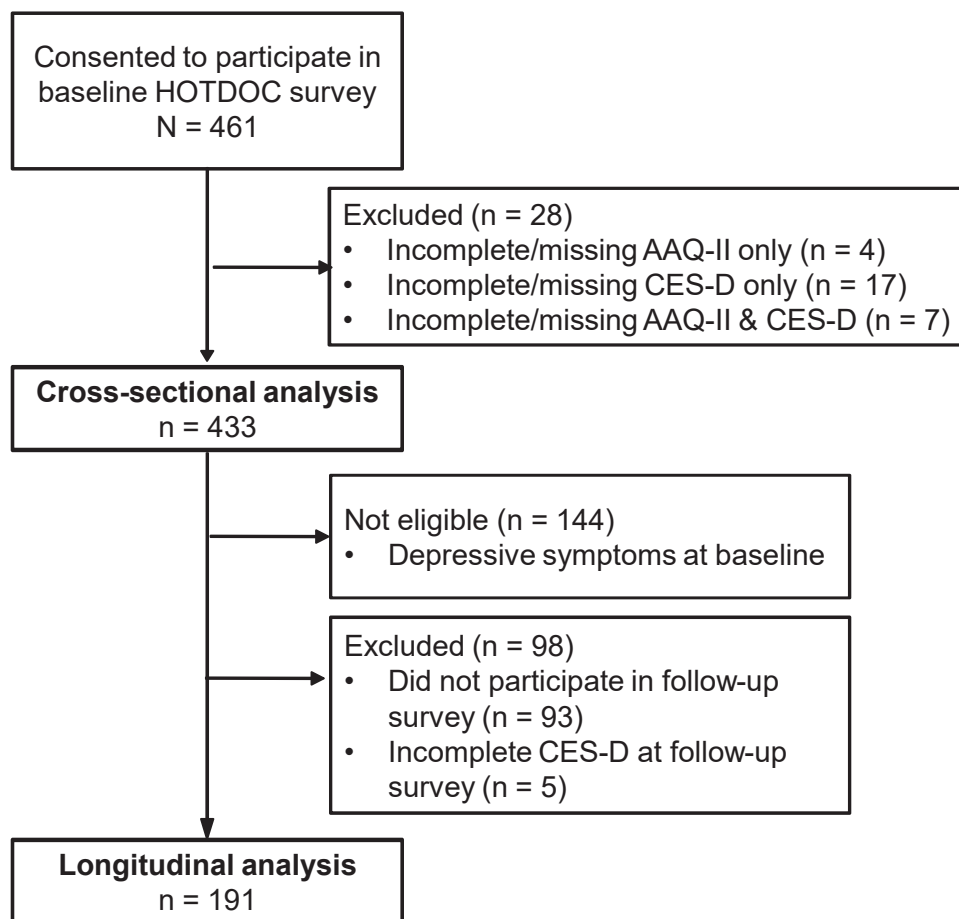


Figure 1. Flow chart of study design. Abbreviations: AAQ-II, Acceptance and Action Questionnaire-II; CES-D, Center for Epidemiologic Studies Depression; HOTDOC, Hope Trajectory and Disease Outcome Consortium.

unknown reasons ($n = 55$). Therefore, 191 patients were included for the longitudinal analysis after exclusion of those with incomplete responses to the CES-D during the 1-year follow-up survey ($n = 5$). Excluding impaired performance status, baseline characteristics were similar between those who completed the follow-up survey and those who did not (Table S2). Thirty-seven (19.4%) patients experienced incident depression. In the covariate-adjusted modified Poisson regression model, a 5-point higher AAQ-II score (after reversal, indicating better psychological flexibility) was associated with lower likelihood of developing depression (adjusted risk ratio, 0.72 [95% CI, 0.61-0.85]; Table 4). Sensitivity analysis of the association between a 5-point higher AAQ-II score and the development of depression showed similar results (Table S3).

DISCUSSION

This cohort study demonstrated that decreased prevalence and incidence of depression were associated with better psychological flexibility among patients with CKD. In addition, patients receiving peritoneal dialysis and

hemodialysis demonstrated worse psychological flexibility than patients with CKD who were not receiving dialysis.

The association between better psychological flexibility and lower prevalence of depression aligns with results of previous studies. In the general population, better psychological flexibility is associated with improvement in depression.^{24,25} Previous research has shown that worse psychological flexibility was associated with greater depression score among patients with chronic cardiovascular disease.²⁶ However, that study exclusively examined simple correlations between the AAQ and depression scores. Longitudinal associations between decreased incidence of depression and better psychological flexibility were examined. In addition, patients with CKD are unique in that they experience disease-specific burdens, such as unpleasant sensations and feelings such as pain, pruritus, and fatigue related to uremia and dialysis treatment,²⁷ all of which potentially affect psychological flexibility. Examination of associations between psychological flexibility and depression in this specific population is therefore of clinical importance.

Apart from the relationship between psychological flexibility and depression, the greater prevalence of

Table 1. Baseline Characteristics of Study Participants

	Treatment Categories			Total (n = 433)
	Nondialyzed (n = 118)	Peritoneal Dialysis (n = 100)	Hemodialysis (n = 215)	
Demographics				
Age, y ^a	72.3 (12.3)	67.0 (13.2)	63.6 (13.9)	66.7 (13.8)
Women	41 (35%)	29 (29%)	69 (32%)	139 (32%)
Vintage, mo ^a	NA	34.2 [15.2-73.7]	52.1 [15.6-121]	45.6 [15.6-99.8]
Kidney disease				
Diabetic nephropathy	16 (14%)	25 (25%)	73 (34%)	114 (26%)
Glomerulonephritis	17 (14%)	38 (38%)	59 (27%)	114 (26%)
Hypertensive disease	37 (31%)	9 (9%)	31 (14%)	77 (18%)
Others	48 (41%)	28 (28%)	52 (24%)	128 (30%)
Impaired performance status	5 (4%)	8 (8%)	30 (14%)	43 (10%)
Have family, yes	108 (92%)	84 (84%)	195 (91%)	387 (89%)
Working, yes	38 (32%)	42 (42%)	63 (29%)	143 (33%)
Comorbid Conditions				
Coronary artery disease	15 (13%)	19 (19%)	31 (14%)	65 (15%)
Cerebrovascular disease	13 (11%)	17 (17%)	27 (13%)	57 (13%)
Malignancy	13 (11%)	8 (8%)	24 (11%)	45 (10%)
Psychological Measurements				
AAQ-II, points ^{a,b}	41.8 (6.5)	39.4 (7.3)	38.4 (8.7)	39.5 (7.9)
	43.0 [37-47]	40.0 [36-46]	40.0 [33-46]	41.0 [35-46]
CES-D, points ^a	11.4 (6.9)	14.0 (9.2)	14.2 (9.0)	13.4 (8.6)
	12.0 [6-15]	13.5 [7-18]	13.0 [8-19]	12.0 [7-18]

Note: n = 433.

Abbreviations: AAQ-II, Acceptance and Action Questionnaire-II; CES-D, Center for Epidemiologic Studies Depression questionnaire; NA, not applicable.

^aValues for continuous data are expressed as mean (standard deviation) and/or median [interquartile range].

^bReversed AAQ-II score (ie, higher score indicates better psychological flexibility).

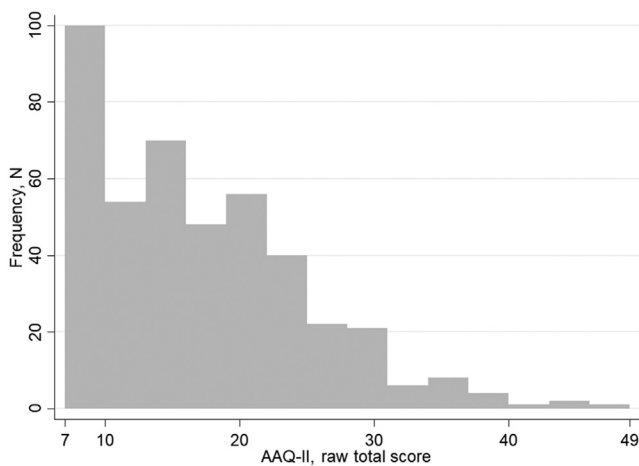


Figure 2. The histogram of Acceptance and Action Questionnaire-II (AAQ-II). Gray bars indicate frequency of the total AAQ-II score (ie, higher score indicates worse psychological flexibility). The left vertical axis illustrates frequency of each bar.

depression associated with women concurs with a previous finding that female sex is a risk factor for depression among patients undergoing dialysis.²⁸ However, the longitudinal analysis failed to demonstrate an association between female sex and incident depression. This can be attributed to 2 reasons. First, the longitudinal study had

fewer than 200 participants and a small number of patients demonstrating incident depression could have resulted in the analysis being underpowered. A previous study of fewer than 300 patients with CKD failed to show an association between female sex and depression.²⁹ Second, because only nondepressed patients were monitored for 1 year, the mechanism underlying the occurrence of incident depression in the female sex could not be evaluated.

These findings have several implications for researchers and physicians. First, psychological flexibility is a modifiable factor and can be a therapeutic target for depression among patients with CKD. In support of this, the efficacy of acceptance and commitment therapy (ACT) in the improvement of psychological flexibility and the treatment of depression has been demonstrated in the general population^{30,31} and patients with chronic diseases such as Crohn disease.^{10,11} Beneficial ACT programs among patients with CKD will: (1) address the approach of being open to the sensation of pain and pruritus, drained feelings associated with dialysis, role changes within the family, and time-restrictions without evaluating them; (2) aid identification of their valued life; and (3) advise proper behavior to achieve goals while living with the disease. Considering the high prevalence and poor clinical outcomes of depression, ACT programs in particular may be appealing for patients with CKD.

Second, lower psychological flexibility without depression at baseline could predict the incidence of

Table 2. Associations Between Baseline Characteristics and Worse Psychological Flexibility

	Adjusted Mean Difference, points ^a	P
	Point Estimates (95% CI)	
Age, per y	-0.02 (-0.09 to 0.04)	0.46
Women vs men	-0.91 (-2.57 to 0.75)	0.28
Diabetic nephropathy	0.01 (-1.73 to 1.74)	0.99
Treatment status		
Nondialyzed	Reference	
Peritoneal dialysis	2.26 (0.23 to 4.28) ^b	0.03 ^b
Hemodialysis	3.16 (1.39 to 4.94) ^b	<0.001 ^b
Impaired performance status	0.85 (-1.70 to 3.40)	0.51
Have family	-0.78 (-3.19 to 1.63)	0.53
Working	-0.59 (-2.38 to 1.20)	0.52
Comorbid conditions		
Coronary artery disease	-0.35 (-2.50 to 1.80)	0.75
Cerebrovascular disease	-1.54 (-3.75 to 0.67)	0.17
Malignancy	1.44 (-1.03 to 3.91)	0.25

Note: n = 433. Adjusted mean differences were estimated from average marginal effects obtained from a generalized linear model (with gamma distribution and log-link function). All variables listed in this table were entered into the single model.

Abbreviation: AAQ-II, Acceptance and Action Questionnaire-II.

^aHigher point estimates indicated worse psychological flexibility (ie, higher total AAQ-II score [before reversal]).

^bStatistically significant differences.

depression. Therefore, an assessment of psychological flexibility enables the provision of early interventions such as ACT to prevent future episodes of depression. In addition, due to the potential mechanisms affecting the incidence of depression, nephrologists should be more aware of low psychological flexibility. In daily clinical settings, nephrologists can counsel patients about their sensations, thoughts, and feelings related to CKD and more appropriately judge the necessity of ACT.

Third, correlates of low psychological flexibility could reflect important clinical factors that influence the inability of patients to embrace personal unpleasant experiences that are associated with CKD. Specifically, results revealed that low psychological flexibility was associated with hemodialysis and peritoneal dialysis. Interestingly, the 3.16-point difference in AAQ-II score observed in patients undergoing hemodialysis is similar to the magnitude of the improvement in the score after implementation of ACT for chronic disease, with simultaneous improvements in depression and fatigue.¹¹ Thus, the observed difference in psychological flexibility among patients with nondialysis CKD and patients with CKD treated by dialysis may be sufficient to affect quality of life. It was speculated that among patients with stage 5D CKD, especially hemodialysis patients, symptoms associated with treatment and/or feeling of “sin” associated with changes in their role within the family due to time restrictions might be

Table 3. Association Between Better Psychological Flexibility Level and the Prevalence of Depression

	Adjusted Prevalence Ratio	
	Point Estimates (95% CI)	P
AAQ-II, per 5 point higher ^a	0.75 (0.70-0.80) ^b	<0.001 ^b
per 1 SD higher ^a	0.63 (0.57-0.70) ^b	
Age, per 1 y	1.00 (0.99-1.01)	0.61
Women vs men	1.43 (1.10-1.85) ^b	0.007 ^b
Diabetic nephropathy	1.15 (0.88-1.52)	0.30
Impaired performance status	1.15 (0.80-1.67)	0.45

Note: n = 433. The data were fit to a modified Poisson regression model. The model was adjusted for treatment status, having family, working, comorbid conditions, and all variables listed in this table.

Abbreviations: AAQ-II, Acceptance and Action Questionnaire-II; SD, standard deviation.

^aHigher AAQ-II score (after reversal) indicates better psychological flexibility.

^bStatistically significant differences.

Table 4. Association Between Better Psychological Flexibility Level and Incident Depression

	Adjusted Risk Ratio	
	Point Estimates (95% CI)	P
AAQ-II, per 5 point higher ^a	0.72 (0.61-0.85) ^b	<0.001 ^b
per 1 SD higher ^a	0.64 (0.51-0.81) ^b	
Age, per 1 y	0.97 (0.96-0.99) ^b	<0.001 ^b
Women vs men	0.73 (0.36-1.51)	0.40
Diabetic nephropathy	1.57 (0.90-2.74)	0.12
Impaired performance status	1.07 (0.40-2.91)	0.89

Note: n = 191. The data were fit to a modified Poisson regression model. The model was adjusted for treatment status, having family, working, comorbid conditions, and all variables listed in this table.

Abbreviations: AAQ-II, Acceptance and Action Questionnaire-II; SD, standard deviation.

^aHigher AAQ-II score (after reversal) indicates better psychological flexibility.

^bStatistically significant differences.

sufficient for patients to perceive enormous somatic and psychological distress and therefore lose psychological flexibility.

This study had several strengths. First, to our knowledge, this is the first study showing an association between psychological flexibility and incidence of depression among patients with CKD with adjustment for potential confounding variables. Second, the multicenter design increases the generalizability of the findings to other Japanese facilities.

This study had several limitations. First, the definition of depression in this study was based on a self-reported scale (ie, CES-D) rather than a structured clinical interview, such as the Structured Clinical Interview for Diagnostic and Statistical Manual Disorders (SCID). However, the CES-D is often used in clinical and research settings for screening depression. In addition, the CES-D scale was validated against the SCID for diagnosing depressive disorders in hemodialysis patients.³²

Second, the non-negligible dropout of patients due to unknown reasons (n = 55) before the follow-up survey

might limit the applicability of the observed association between better psychological flexibility and reduced incident depression. However, baseline characteristics, including treatment modality, of patients who could not participate in the follow-up survey were similar to those of patients who could participate (Table S2). Therefore, the observed association applies to patients in different stages of CKD.

Third, some potential predictors of depression among patients with CKD, such as education level and detailed measures of socioeconomic status, were not collected. However, working status was adjusted as a proxy for socioeconomic status. In addition, patients' medical costs related to dialysis treatment are almost entirely covered by the Japanese health insurance system; therefore, socioeconomic status would presumably not confound the observed associations.

Fourth, the findings may not be generalizable to other countries because psychological flexibility may not be similarly interpreted by patients in Western countries like those in Asian countries.

Fifth, despite the multicenter study design and increased possibility of generalizability, the cohort was not representative of the total CKD population because patients were limited to those who could respond to the questionnaire and provided consent. For example, mean age among dialysis patients was slightly lower than that reported by the Japanese Society for Dialysis Therapy in 2016 (68.2 years).³³ In addition, the exclusion of patients with dementia could be challenging in that the generalizability of the present findings depends on the prevalence of dementia. For example, the prevalence of severe cognitive impairment among patients with advanced CKD is reported to be 25% in the United States.³⁴ The prevalence of dementia in patients undergoing dialysis was reported to be 10% in Japan.³⁵ However, we believe the exclusion of dementia has the merit of maintaining the validity of the observed associations because dementia renders the patients incapable of perceiving psychological flexibility similar to patients without dementia.

In summary, acceptance, as captured by psychological flexibility using the AAQ-II, was associated with lower prevalence and incidence of depression among patients with different stages of CKD. In addition, patients receiving hemodialysis and peritoneal dialysis exhibited worse psychological flexibility than patients with non-dialysis CKD. Vigilance against poor psychological flexibility before a depressive state and the development of nonpharmacologic interventions such as ACT to improve psychological flexibility are critical for preventing and treating depression among patients with CKD.

SUPPLEMENTARY MATERIAL

[Supplementary File \(PDF\)](#)

Table S1: Japanese version of the Acceptance and Action Questionnaire-II (AAQ-II).

Table S2: Baseline characteristics of study patients who did not exhibit depressive symptoms at baseline, stratified by completeness of follow-up.

Table S3: Sensitivity analysis of the association between better psychological flexibility level and incident depression (n = 191).

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Does psychological flexibility influence prevalence and incidence of depression in patients with CKD?



Multicenter Cohort Study



Multicenter
Five Hospitals
Japan



n = 433



CKD stage 3-5

or



CKD stage 5D
treated with
hemodialysis or
peritoneal dialysis

Predictor



Psychological
flexibility



Measured using the
Acceptance and Action
questionnaire (AAQ-II)

Each 5-point increase in AAQ-II

Cross-sectional Analysis



n = 433

Associated with
lower prevalence of
depression in
patients with CKD.



PR – 0.75
(Prevalence Ratio)

Longitudinal Analysis



n = 191

Associated with
lower incidence of
depression at 1 year.



RR – 0.72
(Risk Ratio)

Conclusion: Better psychological flexibility is associated with lower prevalence and incidence of depression in patients with CKD.

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