Patient Factors Influencing Outpatient Retention in Patients with Affective and Anxiety Disorders: A Retrospective Study

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Objective: The aim of the present study is to identify the factors that affect retention in outpatients with psychiatric disorders as indicators of treatment adherence, including Minnesota Multiphasic Personality Inventory (MMPI) scores. **Methods:** The medical records of 146 patients diagnosed with major depressive disorder, bipolar disorder, or anxiety disorder for at least 10 years and discharged were retrospectively reviewed in the present study. The subjects were categorized based on the duration of outpatient treatment as < 6 months (L6) or ≥ 6 months (M6) groups and reclassified as < 36 months (L36) and ≥ 36 months (M36) groups. The demographic, clinical, and personality characteristics of the groups were compared.

Results: Patients in M6 and M36 groups were more likely to have a higher educational level compared with those in the L6 and L36 groups, respectively. Patients in the M6 group showed significantly lower hypomania (Ma) scores on the MMPI test than did patients in the L6 group.

Conclusion: The association between high Ma score on the MMPI test and early discontinuation of treatment suggests that impulsivity, hostility, and disinhibition confer higher risk of nonadherence.

KEY WORDS: Nonadherence; Psychiatric patients; Outpatient retention; MMPI.

INTRODUCTION

In treating psychiatric disorders, poor adherence can be an obstacle to the optimal outcome of treatment, and nonadherence to medication is often a cause of recurrence or re-hospitalization [1,2]. However, patients with psychiatric illnesses typically have difficulty following a medication regimen for various reasons and have a tendency to discontinue their medications by self-withdrawal [3].

As with other chronic conditions, high discontinuation rates are a frequent and recurring problem among patients with major psychiatric disorders. The discontinuation rate for oral antipsychotics in schizophrenia ranges from 26%

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to 44%, and as many as two-thirds of patients are at least partially nonadherent, resulting in increased risk of hospitalization [4]. In patients with bipolar disorder (BD), the nonadherence prevalence ranged from 20% to 60% in several studies [5-7]. In addition, the adherence to initial antidepressant medication by depressed patients decreased over time; nonadherence rates of 41% by 3 months, 31% by 6 months, 24% by 9 months, and 21% by 12 months were reported in a previous study [8].

Many studies have been conducted to identify the predictors of nonadherence in psychiatric patients to provide clinicians with a guide regarding how to recognize when patients are at risk of nonadherence [9-11]. Haddad *et al.* [12] categorized factors associated with nonadherence into illness factors, medication factors, patient factors, caregiver factors, and physician/service-provider factors. Several illness, medication, and physician/service factors have been identified that consistently predict nonadherence, including poor insight, cognitive impairment, poor effectiveness, high cost burden, and complex regimen. Conversely, many patient factors, including demographic var-

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iables such as age, sex, socioeconomic status, and ethnicity, are not consistently associated with adherence [12].

Regarding patient factors, personality profiles can be a factor influencing adherence among psychiatric patients. Patients suffering from chronic physical or mental health conditions must manage various steps toward modifying their behavior to follow their physician's prescribed treatment regimen. Accordingly, their coping response to these tasks, which reflect the patient's personality, often have substantial implications for treatment success and disease progression [13]. Although comorbid personality disorders, poor insight, a poor therapeutic alliance, and negative beliefs regarding treatment have negative effects on adherence [9,14], minimal research has been conducted on the association between personality characteristics and treatment adherence in psychiatric patients. Therefore, patient factors associated with adherence in patients with psychiatric disorders, including depressive disorder (DD), BD, and anxiety disorder (AD), were identified in the present study. In addition, personality profile were assessed using the Minnesota Multiphasic Personality Inventory (MMPI), reflects understanding of personality and psychopathology [15].

METHODS

Subjects

The medical records of all subjects included in the present study were retrospectively reviewed at Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea. All patients hospitalized in this institution from June 2005 to May 2015 were investigated by board-certified psychiatrists to determine the Diagnostic and Statistical Manual of Mental Disorders 4th edition, text revision (DSM-IV-TR) diagnosis. Subjects 20 years of age or older at discharge who were diagnosed with DD, BD, or AD and who completed the MMPI within 6 months before discharge from the index hospitalization were included in the study. Patients hospitalized for other than therapeutic reasons, including social or legal reasons or for diagnostic purposes, and those who were diagnosed with other DSM-IV-TR Axis I or II disorders were excluded. Patients who died, who were transferred, or whose treatment was terminated by recovery during the follow-up period were also excluded from the study.

Assessments

The subjects were categorized based on their treatment persistence [16], which was defined as the time from the index date (the date of discharge) to the discontinuation of outpatient visits (i.e., time to discontinuation [TTD]); this is a modified definition of treatment persistence [16], which was originally defined as discontinuation 30 days or more after discharge. The gap was modified to longer than 90 days because this period better represents true non-persistence in a chronic condition [17]. The subjects were classified as TTD < 6 months (L6) or TTD \ge 6 months (M6). The subjects were then reclassified as ≤ 36 months (L36) or \geq 36 months (M36). If the patient was followed up continuously to the time of the present study, the date of the last outpatient visit was estimated to be May 31, 2018. Visits for non-treatment-related reasons, such as issuance of medical record copies or medical certificates, were not included as outpatient visits.

Socioeconomic characteristics including sex, age, marital status, occupation, socioeconomic status, cohabiting status, educational level, and residence location at the index hospitalization were included. Therapeutic and clinical characteristics included DSM-IV-TR diagnosis, age at onset, number of past psychiatric hospitalizations, type of hospitalization (voluntary or involuntary), comorbid physical conditions and treatment, family history of psychiatric illness, past history of suicidal attempts, and type of discharge from hospital (planned or against medical advice). Personality profile was assessed using the MMPI-2, administered by a psychologist as part of a routine admission examination. The MMPI-2 is a questionnaire widely used to assess psychopathological functioning [18,19]. The MMPI-2, a restandardization of the MMPI, is a guestionnaire include 567 items of true-false response format. The inventory includes 1) 3 validity scales: Lie (L), Infrequency (F), and Correction (K); 2) 10 clinical scales: Hypochondriasis (Hs), Depression (D), Hysteria (Hy), Psychopathic Deviate (Pd), Masculinity/Femininity (Mf), Paranoia (Pa), Psychasthenia (Pt), Schizophrenia (Sc), Hypomania (Ma), and Social Introversion (Si). Intellectual efficiency was measured using the Korean-Wechsler Adult Intelligence Scale (K-WAIS) at hospitalization.

Statistical Analysis

The characteristics were compared between the L6 and M6 and between the L36 and M36 groups using a chi-square

test or Fisher's exact test for categorical variables and independent t test or Mann — Whitney U test for continuous variables. In addition, multivariate logistic regression analysis was used to identify the factors predictive of premature discontinuation of follow-up. Comparisons of the L6 and M6 groups and of the L36 and M36 groups in age, sex, and variables that were statistically significant or showed a trend toward significance (p < 0.10) on univariate comparison were included in the multivariate models. All statistical tests were two tailed, and statistical significance was set at 0.05. Statistical analysis was performed using SAS for Windows, version 9.3 (SAS Institute, Cary, NC, USA).

Ethics

The Institutional Review Board (IRB) of Yeouido St.

Table 1. Comparison of characteristics between patients who discontinued outpatient visits before 6 months versus after 6 months

Variable	Less than 6 months $(n = 41)$	More than 6 months ($n = 105$)	p value
Age at onset (yr)	34.7 ± 16.2	33.9 ± 13.4	0.768
Age at index hospitalization (yr)	41.0 ± 15.1	41.5 ± 13.6	0.851
Educational level (yr)	12.5 ± 3.7	13.5 ± 3.1	0.095
Intelligence (FSIQ)	104.9 ± 9.9	107.8 ± 11.1	0.645
Number of total hospitalizations	1.6 ± 1.6	2.3 ± 2.5	0.081
Male	16 (39.0)	48 (45.7)	0.578
Married	20 (48.8)	51 (48.6)	0.982
Employed	19 (46.3)	46 (43.8)	0.782
Socioeconomic status			0.474
High	7 (17.1)	11 (10.5)	
Middle	33 (80.5)	89 (84.8)	
Low	1 (2.4)	5 (4.8)	
Living alone	4 (9.8)	10 (9.5)	> 0.999
Living within the metropolitan area	34 (82.9)	90 (85.7)	0.797
Family history of anxiety or mood disorder	21 (51.2)	39 (37.1)	0.120
Past history of suicide attempt	11 (26.8)	22 (21.0)	0.290
Hospitalization against will	14 (34.1)	39 (37.1)	0.735
Discharge against medical advice	4 (9.8)	1 (1.0)	0.022
Physical comorbidity	20 (48.8)	41 (39.0)	0.188
Treatment of physical comorbidity in the same hospital	6 (14.6)	10 (9.5)	0.270
Diagnosis			
Major depression/depressive disorders	28 (68.3)	60 (57.1)	0.216
Bipolar disorder, manic episode	4 (9.8)	23 (21.9)	0.089
Bipolar disorder, depressive episode	6 (14.6)	16 (15.2)	0.927
Anxiety disorder	9 (22.0)	17 (16.2)	0.414
Comorbid two or more disorders	6 (14.6)	11 (10.5)	0.567
MMPI			
L	55.5 ± 16.1	52.9 ± 11.9	0.280
F	57.7 ± 13.5	53.7 ± 11.1	0.090
K	52.4 ± 12.7	54.3 ± 12.5	0.407
Hs	64.1 ± 11.1	61.8 ± 11.6	0.270
D	61.9 ± 13.6	63.6 ± 13.1	0.476
Ну	63.9 ± 10.0	63.0 ± 10.6	0.672
Pd	60.5 ± 11.0	59.1 ± 9.0	0.439
Mf	49.5 ± 12.1	50.2 ± 9.3	0.699
Pa	63.0 ± 13.3	58.9 ± 10.8	0.054
Pt	62.4 ± 13.3	63.8 ± 13.4	0.576
Sc	62.9 ± 13.7	60.6 ± 10.5	0.340
Ma	55.0 ± 9.1	49.2 ± 11.4	0.004
Si	54.6 ± 13.8	54.1 ± 12.6	0.829

Values are presented as mean ± standard deviation or number (%).

FSIQ, full scale intelligence quotient; MMPI, Minnesota Multiphasic Personality Inventory; L, lie; F, infrequency; K, correction; Hs, hypochondriasis; D, depression; Hy, hysteria; Pd, psychopathic deviate; Mf, masculinity/femininity; Pa, paranoia; Pt, psychasthenia; Sc, schizophrenia; Ma, hypomania; Si, social introversion.

Mary's Hospital in Seoul, Korea (SC18RESI0054) reviewed and approved the protocol, and the study was conducted in accordance with good clinical practices and the Helsinki Declaration. The IRB waived patient-specific informed consent for this confidential chart review and anonymous reporting of aggregate data.

RESULTS

During the study period (June 2005 to May 2015), 844 patients were discharged with a diagnosis of DD, BD, or AD. Among these patients, 146 (17.3%) fulfilled the eligibility criteria for the study.

Comparisons of Demographic and Clinical Characteristics

The results from univariate comparisons between the L6 and M6 groups are presented in Table 1. The number of patients discharged against medical advice after the index hospitalization was significantly greater in the L6 (n = 4, 9.8%) than in the M6 group (n = 1, 1.0%; ρ = 0.022). The mean number of years of education in the L6 group (12.5 ± 3.7) was lower than that in the M6 group $(13.5 \pm$ 3.1), and the number of hospitalizations in the M6 group (2.3 ± 2.5) was greater than that in the L6 group $(1.6 \pm$ 1.6); however, these differences were not statistically significant (p = 0.095 and 0.081, respectively). As shown in Table 2, in the L36 and M36 groups, the mean years of education (12.6 \pm 3.7 and 14.0 \pm 2.6, respectively; p =0.007) and number of hospitalizations (1.7 \pm 1.6 and 2.7 \pm 2.8, respectively; p = 0.018) differed significantly between the two groups. Furthermore, the number of patients hospitalized against their will (45.5%, n = 30) was significantly higher in the M36 than in the L36 group (28.7%, n = 23; p = 0.037). The diagnosis at discharge from the index hospitalization also differed significantly between the L36 and M36 groups. Bipolar mania was significantly more frequent in the M36 group (27.3%, n = 18)than in the L36 group (11.3%, n = 9; p = 0.013); conversely, patients diagnosed with DD or AD were significantly more frequent in the L36 group (70.0%, n = 56for DD and 23.8%, n = 19 for AD) than in the M36 group (48.5%, n = 32 for DD; p = 0.008 and 10.6%, n = 7; p = 0.039 for AD). However, there was no significant difference in intelligence quotient (IQ) between L6 group (104.9 ± 9.9) and M6 group $(107.8 \pm 11.1; p = 0.645)$, and also between L36 group (106.6 \pm 10.0) and M36 group (107.4 \pm 11.8; ρ = 0.081).

MMPI Results

A comparison of MMPI test scores (Table 1) revealed significantly higher Ma scores in the L6 (55.0 \pm 9.1) than in the M6 group (49.2 \pm 11.4; p = 0.004), and the Hs score was significantly higher in the L36 (64.1 \pm 11.3) than in the M36 group (60.3 \pm 11.5; p = 0.046). Other MMPI scores did not differ significantly between the groups, although numerical differences in the F scores were found between the L6 and M6 groups and between the L36 and M36 groups, as well as differences in Pa scores between L6 and M6 groups (Table 2).

Factors Associated with Longer Treatment Retention

Based on logistic regression analysis, age, sex, educational level, number of hospitalizations, discharge against medical advice, diagnosis of bipolar mania, and lower Ma scores were associated with low risk of treatment discontinuation before 6 months (p=0.034, odds ratio [OR] = 0.958, 95% confidence intervals [CI] = 0.921 – 0.997). Higher educational level showed a non-significant trend toward a higher probability of treatment retention at 6 months or more (p=0.089, OR=1.112, 95% CI=0.984 – 1.257). Higher educational level was a significant predictor of treatment retention for 36 months or more (p=0.024, OR=1.161, 95% CI=1.020 – 1.322). No other significant predictors of treatment retention for 36 months or more was found, including in MMPI scores and other clinical and demographic variables.

DISCUSSION

In the present study, treatment retention based on short-term criteria (6 months or more) was associated with Ma scores on the MMPI, and long-term (36 months or more) treatment retention was associated with educational level. Other variables including sex, age, and diagnosis with mood or AD were not significantly associated with short-term or long-term treatment retention.

There are several possible explanations for the association between high Ma scores on the MMPI and early discontinuation of treatment. First, manic patients with more severe symptoms had higher Ma scores on MMPI [20]. Many researchers have shown that greater severity of psy-

Table 2. Comparison of characteristics between patients who discontinued outpatient visits before 36 months versus after 36 months

Variable	Less than 36 months (n = 80)	More than 36 months (n = 66)	p value
Age at onset (yr)	36.0 ± 15.0	32.0 ± 12.8	0.089
Age at index hospitalization (yr)	41.9 ± 14.8	40.7 ± 13.0	0.594
Educational level (yr)	12.6 ± 3.7	14.0 ± 2.6	0.007
Intelligence (FSIQ)	106.6 ± 10.0	107.4 ± 11.8	0.081
Number of total hospitalizations	1.7 ± 1.6	2.7 ± 2.8	0.018
Male	33 (41.3)	31 (47.0)	0.299
Married	37 (46.3)	34 (51.5)	0.526
Employed	35 (43.8)	30 (45.5)	0.837
Socioeconomic status;			0.282
High	13 (16.3)	5 (7.6)	
Middle	64 (80.0)	58 (87.9)	
Low	3 (3.8)	3 (4.5)	
Living alone	10 (12.5)	4 (6.1)	0.151
Living within the metropolitan area	65 (81.3)	59 (89.4)	0.127
Family history of anxiety or mood disorder	37 (46.3)	23 (34.8)	0.11
Past history of suicide attempt	16 (20.0)	17 (25.8)	0.264
Hospitalization against will	23 (28.8)	30 (45.5)	0.037
Discharge against medical advice	4 (5.0)	1 (1.5)	0.249
Physical comorbidity	46 (57.5)	39 (59.1)	0.846
Treatment of physical comorbidity in the same hospital	9 (11.3)	7 (10.6)	0.559
Diagnosis			
Major depression/depressive disorders	56 (70.0)	32 (48.5)	0.008
Bipolar disorder, manic episode	9 (11.3)	18 (27.3)	0.013
Bipolar disorder, depressive episode	9 (11.3)	13 (19.7)	0.156
Anxiety disorder	19 (23.8)	7 (10.6)	0.039
Comorbid two or more disorders	13 (16.3)	4 (6.1)	0.056
MMPI	,,,,,,	, , , , ,	
L	54.4 ± 13.6	52.7 ± 12.8	0.438
F	56.3 ± 11.7	52.9 ± 11.9	0.087
K	52.9 ± 13.0	54.9 ± 12.0	0.322
Hs	64.1 ± 11.3	60.3 ± 11.5	0.046
D	64.0 ± 12.4	62.0 ± 14.1	0.367
Hy	63.7 ± 10.0	62.8 ± 11.0	0.603
Pd	60.4 ± 10.3	58.5 ± 8.6	0.233
Mf	49.9 ± 10.9	50.2 ± 9.3	0.887
Pa	61.3 ± 11.9	58.6 ± 11.2	0.173
Pt	64.0 ± 12.5	62.7 ± 14.4	0.58
Sc	62.1 ± 12.0	60.2 ± 10.8	0.328
Ma	51.9 ± 10.0	49.4 ± 12.2	0.171
Si	54.7 ± 13.1	53.7 ± 12.6	0.644

Values are presented as mean ± standard deviation or number (%).

FSIQ, full scale intelligence quotient; MMPI, Minnesota Multiphasic Personality Inventory; L, lie; F, infrequency; K, correction; Hs, hypochondriasis; D, depression; Hy, hysteria; Pd, psychopathic deviate; Mf, masculinity/femininity; Pa, paranoia; Pt, psychasthenia; Sc, schizophrenia; Ma, hypomania; Si, social introversion.

chopathology is a predictor of nonadherence in BD [9]. Second, elevated Ma could be associated with impulsivity, irritability, hostility, overactivity, and aggressive outbursts [21]. Therefore, the personality profiles associated with a high Ma score may negatively affect adherence. For example, greater sensation seeking, disinhibition, and susceptibility to boredom may confer higher risk of nonadherence [9,22]. Although the two constructs are not completely independent, the high Ma score suggests that both disease severity and the personality tendency could affect poor adherence in BD.

In a long-term study, a higher educational level was associated with better treatment retention, possibly because more educated patients can better understand the beneficial effects of medication, which might enhance treatment adherence. Fleischhacker et al. [23] investigated the influ-

ence of patient attitudes on actual compliance and found that the most important factor was whether the patient thought the drug had a positive effect on the illness. These findings are in agreement with a study by Misdrahi and colleagues [24], in which awareness of the effects of medication was more closely linked to adherence than was the awareness of any individual symptom. Elsewhere, the correlation between educational level and better adherence has been attributed to greater awareness of the illness and of the beneficial effects of medication [25-27]. And also in schizophrenia patients, there has been a study that sharing decision-making with their physicians in selection of the antipsychotic medications has a positive effect on improving patient satisfaction and adherence [28,29]. It might increase the chances of finding an effective treatment that is novel and has a positive effect on adherence [30]. As our data suggested, patients with BD who have a lower educational level appear to be at increased risk of medication nonadherence [31].

However, the correlation between these variables and adherence has not been consistently demonstrated among patients with other psychiatric diagnoses, and some opposing views persist. For example, ten Doesschate and colleagues [2] found that a higher educational level was associated with nonadherence. These authors suggested that remitted recurrently depressed patients with more education do not follow their doctor's advice if they believe that the disadvantages of antidepressants outweigh the advantages in this phase of treatment [2]. Therefore, concerns regarding the disadvantages of medication could be associated with nonadherence in some depressed patients. Collectively, as suggested in our research, these findings indicate that it is important to educate patients on the benefits of treatment in order to promote positive feelings regarding treatment and thus improve adherence. In particular, patients who have lower educational levels require more attention.

Educational level could also be associated with the stigma of mental illness. In previous studies, a higher educational level was associated with reduced bias against mental illness [32], in contrast to lower educational levels [33]. The stigma associated with mental illness and medication may be very important for schizophrenia and BD patients [34]. Patients may internalize society's stigmatization, diminishing their sense of worth and self-esteem. In addition, the stigma may be an impediment to recov-

ery, serving as a barrier to seeking help for mental health problems [35,36]. Compared with Caucasians, Asians perceive people with mental illness as more dangerous [37]. Many people of Asian descent view people with mental illnesses as dangerous, aggressive, and unpredictable. Furthermore, a person's mental illness is viewed as the family's mental illness, making it difficult for those with mental health issues to achieve or to feel that they are worthy of recognition, academic and occupational success, or marriage [35,38,39]. In Asian countries such as Korea, the stigma associated with mental illness is deeply rooted and may have a negative effect on treatment adherence. In particular, this tendency is more evident when the educational level is low. Similarly, based on our study results, patients with more education are more likely to overcome the effects of stigma, which could result in higher treatment retention.

The issue of adherence has been addressed in numerous systematic reviews, and various factors have been reported in a wide range of studies. In a previous study, comorbidity with substance use disorder and treatment side effects were predictors of nonadherence [9]. In addition, poor insight, denial of illness, and negative attitude toward medication were reported as patient-related psychological risk factors for medication nonadherence [31]. Based on the results of the present study, awareness of the illness and of the beneficial effects of treatment were associated with educational level. However, the relationship of adherence with comorbid disease could not be determined because this study was designed to exclude the effects of comorbid substance use disorder or personality disorder on adherence. In addition, sociodemographic characteristics affecting treatment adherence have been reported in previous reviews. In general, younger age, unmarried status, living alone, and living in a rural area appear to be associated with increased risk of nonadherence [9,31,40-44]. However, no significant associations were found between sociodemographic and clinical factors and adherence in the present study: sex, age at onset, age at index hospitalization, total number of hospitalizations, and socioeconomic status did not predict nonadherence. Our study results may differ from previous reports for two reasons. First, substance use disorder and personality disorder were intentionally excluded from our study; we included only mood disorders and personality profiles that were expected to affect other factors on the MMPI.

Second, multiple methods have been used in other studies to quantify adherence including plasma level evaluation, clinical interviews, self-reported questionnaires, pill count, and prescription records, and the choice of method significantly affected the findings [12]. Unlike previous studies, the main method used to assess adherence in the present study was duration of treatment compliance. Treatment retention was considered a more accurate objective measure to assess nonadherence because maintaining treatment continuously for a period of time reflects favorable therapeutic compliance. Therefore, using adherence predictors could be advantageous.

The present study has several limitations. The personality factors that affect the duration of treatment retention were identified using MMPI scores without classifying the type of diagnosis. Therefore, combining MMPI scores that reflect characteristics of various diseases and applying them to different diagnoses was disadvantageous. In addition, the factors specific to each diagnosis that were associated with adherence could not be separated. Thus, the relationship between MMPI scores and adherence factors classified based on each diagnosis will be investigated in future studies. Another limitation pertains to the severity of patients' conditions. Because the patients in this study were hospitalized in an acute phase with severe symptoms, disease-specific factors were more clearly reflected in the MMPI test results than were the patient's specific personality profiles. Therefore, conducting follow-up MMPI tests after the acute symptoms were improved and comparing these with the MMPI scores from the time of admission to determine the correlation between personality profiles and treatment retention in the absence of acute symptoms may be a limitation. Finally, drug side effects were not considered in the results due to lack of adequate information from inpatient records regarding such effects in relation to the different diagnoses. Future research including information regarding patients' subjective feelings about the effectiveness of their prescribed medication or reflecting patients' perception of the stigma of psychiatric illness and drug side effects could help to elucidate the factors associated with adherence to psychiatric treatment. In addition, participants were limited to patients discharged from a tertiary hospital, so individuals with more severe illness and relatively better socioeconomic status may be over-represented. Thus, studies of patients from different medical institutions are necessary.

In the present study, characteristics of patients with symptoms sufficiently severe for admission to a psychiatric hospital and who remained in outpatient treatment after discharge were identified. Understanding the characteristics of patients who maintain long-term outpatient treatment would be useful for mental health professionals to plan adequate strategies for clinically managing patients. Patient's educational level should be considered in treatment planning, and ensuring that patients are aware of the disease and the benefits of treatment could be an important component of treatment guidelines.

■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions-

Seyeon Chang, Young Sup Woo, and Won-Myong Bahk designed the study. Sheng-Min Wang and Hyun Kook Lim acquired data. Seyeon Chang, Young Sup Woo, and Won-Myong Bahk analysed the data. Finally, Seyeon Chang and Young Sup Woo wrote the article, which all authors reviewed and approved for publication.

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