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An Analysis of the Determinants of the Health-Related Quality of Life in Asian Patients With Cluster Headaches During Cluster Periods Using the Time Trade-Off Method

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Background and Purpose Patients with cluster headache (CH) exhibit impaired health-related quality of life (HRQoL). However, there have been few studies related to the HRQoL of patients with CH from Asian backgrounds. This study aimed to determine the impact of CH on HRQoL and to identify the factors affecting HRQoL in patients with CH during cluster periods.

Methods This prospective study enrolled patients with CH from 17 headache clinics in South Korea between September 2016 and February 2021. The study aimed to determine HRQoL in patients with CH using the EuroQol 5 Dimensions (EQ-5D) index and the time trade-off (TTO) method. Age- and sex-matched headache-free participants were recruited as a control group.

Results The study included 423 patients with CH who experienced a cluster period at the time. EQ-5D scores were lower in patients with CH (0.88±0.43, mean±standard deviation) than in the controls (0.99±0.33, $p<0.001$). The TTO method indicated that 58 (13.6%) patients with CH exhibited moderate-to-severe HRQoL deterioration. The HRQoL states in patients with CH were associated with current smoking patterns, headache severity, frequency, and duration, and scores on the Generalized Anxiety Disorder 7-item scale (GAD-7), Patient Health Questionnaire 9-item scale (PHQ-9), 6-item Headache Impact Test, and 12-item Allodynia Symptom Checklist. Multivariable logistic regression analyses demonstrated that the HRQoL states in patients with CH were negatively correlated with the daily frequency of headaches, cluster period duration, and GAD-7 and PHQ-9 scores.

Conclusions Patients with CH experienced a worse quality of life during cluster periods compared with the headache-free controls, but the degree of HRQoL deterioration varied among them. The daily frequency of headaches, cluster period duration, anxiety, and depression were factors associated with HRQoL deterioration severity in patients with CH.

Keywords cluster headaches; disability; quality of life; EQ-5D.

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INTRODUCTION

Cluster headaches (CHs) are a disabling neurological condition characterized by severe recurrent unilateral headaches with ipsilateral cranial autonomic symptoms. A higher severity of each bout predicts considerable functional and social disability during the cluster period. Assessing the health-related quality of life (HRQoL) is critical for understanding the effect of CH on the physical, emotional, and functional capabilities of patients.[1,2] Nevertheless, there may be limitations in measuring the overall HRQoL in patients with CH due to the paroxysmal pattern of CH attacks.

Previous studies have found that patients with CH have a worse HRQoL, but most only analyzed small samples, used different assessment tools (e.g., Short Form-20 or 36-Item Short Form Health Survey questionnaires, or the European Quality of Life Visual Analogue Scale) for patients with episodic or chronic CH, and were mostly conducted in Western countries.[3-6]

The present study hypothesized that CH affects physical and social functioning and that the severity of these effects can vary among patients with CH. The study objectives were to compare the degree of HRQoL impairment between patients with CH and headache-free controls, categorize patients with CH according to HRQoL deterioration severity, and identify clinical factors associated with CH-associated HRQoL deterioration severity during cluster periods using the prospective multicenter CH registry of South Korea.

METHODS

Research design

The Korean Cluster Headache Registry (KCHR) is a prospective, multicenter registry of patients with CH (19 years or older) in South Korea. Version 1 of this registry enrolled patients between September 2016 and December 2018 and version 2 commenced enrollment in October 2018, in both cases from 15 university hospitals (9 tertiary and 6 secondary referral centers) and 2 secondary referral general hospitals.

This was a cross-sectional study that was planned as part of the KCHR study. Patients with CHs between September 2016 and February 2021 were recruited from the same 17 headache clinics in South Korea. The detailed protocol of the KCHR study has been published previously.[7-9] The registry protocol was reviewed and approved by the Institutional Review Board of each participating headache center (Dongtan Sacred Heart Hospital, IRB No. 2016-09-396), and written informed consent was obtained from the patients.

Participants

Eligible patients were adults (19 years or older) who were able and willing to provide informed consent and could communicate in the Korean language. All patients were carefully evaluated by KCHR investigators who were experienced board-certified neurologists specializing in headache disorders. CH was diagnosed at each enrollment site based on the history and clinical presentation of the patient according to the third edition of the International Classification of Headache Disorders (ICHD-3), or the beta version when available.[10] Participants who fulfilled the diagnostic criteria for CH were evaluated, and only those who were in a cluster period (frequent attacks lasting for weeks to months at the time of enrollment) were included in the study. These participants stated in the questionnaire that they were experiencing an ongoing cluster period of CH attacks, and the providers confirmed this information after the survey. Patients with CH in a remission period who had not experienced day for months or years at the time of enrollment were excluded. The circadian rhythmicity of the current bout was determined by investigators who asked patients if their attacks tended to occur at the same time of day. Patients with experience of two or more lifetime bouts were asked about seasonal rhythmicity, which was determined by investigators who asked patients if their cluster periods tended to occur in the same season as the previous cluster period. More-detailed information is available in reports on previous KCHR studies.[7-9]

Headache-free volunteers were recruited as control subjects from 3 of the 17 hospitals and were matched with the patient group based on age and sex. Headache-free controls were invited to complete the questionnaires if they were aged 19–65 years and had no history of diabetes, thyroid disorder, severe obesity, severe hepatic or renal illness, malignancy, or primary or secondary headache disorders, and who were headache-free (less than 1 day with headache per month) with the cognitive capacity to participate. Most participants in the control group were friends or relatives of the patients or employees of the hospital who were recruited via a noticeboard. The control subjects were enrolled after providing informed written consents.

Data collection and measurements

Anonymized data were accessed in accordance with the KCHR data access policy. The data included demographics, social habits, headache diagnosis, CH history and characteristics, psychiatric status, suicidal ideation and attempts, and scores on the 12-item Allodynia Symptom Checklist (ASC-12), Korean version of the Generalized Anxiety Disorder 7-item scale (GAD-7), Patient Health Questionnaire

9-item scale (PHQ-9), 6-item Headache Impact Test (HIT-6), and the EuroQoL 5 Dimensions index with 3 levels of impairment (EQ-5D-3L). The ASC-12 is a brief, self-administered questionnaire designed to assess cutaneous allodynia during CH bouts. Anxiety and depression during the cluster period were assessed on the day of study enrollment. Generalized anxiety disorder and major depressive disorder were defined as having scores on the Korean versions of the GAD-7 and PHQ-9 of at least 10. Headache effects were assessed using HIT-6 scores.

The primary outcome scale for assessing the impact of CH on HRQoL was the EQ-5D-3L in this study. The Korean version of the EQ-5D-3L questionnaire was employed, which consists of five dimensions: mobility, self-care, usual activities, pain and/or discomfort, and anxiety and/or depression. Each item in the EQ-5D-3L is rated using a three-point scale: 1, no problems; 2, some problems; and 3, extreme problems. This scale provides a single summary score derived from the responses of the patient to the EQ-5D-3L questionnaire, and it also allows for the description of 243 possible health states that correspond to combinations of five three-level digits (i.e., 3 to the power of 5 is 243).[11]

The quality-weighted EQ-5D scale, which was obtained using the time trade-off (TTO) method, was employed to categorize patients into five groups based on the degree of HRQoL deterioration to provide a more-detailed assessment and allow for comparisons across patient subgroups.[12] The TTO method includes 243 EQ-5D-3L health states along with the baseline states "33333" and "11111" for direct valuations. The 243 health states were grouped into the 5 HRQoL states of no problem, very mild, mild, moderate, and severe after the TTO method was performed. The degree of severity was defined by a standard metric according to EQ-5D-3L score. For example, a mild state can include up to three level-2 problems but no level-3 ones. Accordingly, the states "11121" and "21113" were categorized into the very mild and moderate groups, respectively. Severe states included at least two level-3 problems but none from level 1. States were classified as moderate if they were neither mild nor severe; for example, the state "21113" would be categorized as moderate rather than mild because it includes a level-3 problem. The instruments and protocols used in this study were similar to those used in the Measurement and Valuation of Health study performed in the UK and Taiwan.[11-13]

Statistical analyses

Statistical analyses were performed using SAS software (version 9.4, SAS Institute, Cary, NC, USA) and R software (version 4.1.2, R Core Team, R Foundation for Statistical Computing, Vienna, Austria). The results are expressed as mean± standard-deviation values, median (interquartile range [IQR]) values, or proportions, as appropriate. The Kruskal-Wallis test or Mann-Whitney U-test (Wilcoxon rank-sum test) was used to compare the median and IQR values of the scores for continuous data. EQ-5D scores of HRQoL impairment were categorized as very mild, mild, moderate, and severe according to quality-weighted calculations using the TTO method. Sequential logistic regression analysis was performed to investigate the clinical factors significantly affecting the EQ-5D scores. The R package MASS version 7.3−53 was used for ordinal logistic regression. Results were considered significant when $p<0.05$.

RESULTS

Demographics, headache characteristics, and comorbidities

Initially, 547 subjects comprising 494 patients with CH and

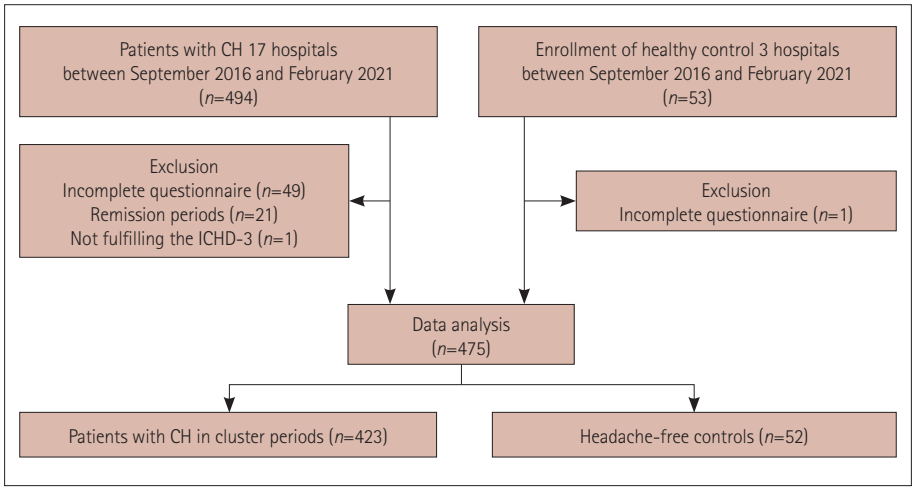

Fig. 1. Flow chart of participating subjects. CH, cluster headache; ICHD-3, third edition of the International Classification of Headache Disorders.

Table 1. Subject demographics and clinical characteristics by group

Variable	CH (*n*=423)	HC (*n*=52)	*p*
Age, years	37.8±9.6	36.2±8.8	0.334
Sex, male	344 (81.3)	43 (82.7)	1.000
Age at CH onset, years	27.0 [20.0–34.0]	NA	NA
Recurrence	344 (80.9)	NA	NA
Total duration of CH, years	7.0 [2.0–14.0]	NA	NA
Average duration of CH per bout, weeks	5.0 [2.0–10.0]	NA	NA
Headache intensity, NRS	9.0 [8.0–10.0]	NA	NA
Attack frequency per day	1.5 [1.0–2.5]	NA	NA
Attack duration, minutes	90.0 [60.0–120.0]	NA	NA
Chronic CH	17 (4.0)	NA	NA
Current smoking	186 (43.8)	16 (30.2)	0.592
Alcohol drinking	198 (46.8)	28 (53.8)	0.061
GAD-7 score	7.0 [4.0–12.0]	1.5 [0.0–3.0]	<0.001
PHQ-9 score	7.0 [3.0–12.0]	2.0 [0.5–4.0]	<0.001
HIT-6 score	70.0 [65.0–76.0]	NA	NA
Suicidal ideation	88 (20.7)	0 (0.0)	<0.001
Allodynia (ASC-12 score ≥3)	75 (17.8)	0 (0.0)	<0.001
EQ-5D	0.88±0.43	0.99±0.33	<0.001
Mobility	1.0 [1.0–1.0]	1.0 [1.0–1.0]	0.089
Self-care	1.0 [1.0–1.0]	1.0 [1.0–1.0]	0.725
Usual activities	1.0 [1.0–2.0]	1.0 [1.0–1.0]	<0.001
Pain/discomfort	2.0 [1.0–2.0]	1.0 [1.0–1.0]	<0.001
Anxiety/depression	1.0 [1.0–2.0]	1.0 [1.0–1.0]	<0.001

Data are median [interquartile range], *n* (%), mean±standard deviation values.
ASC-12, 12-item Allodynia Symptom Checklist; CH, cluster headache; EQ-5D, EuroQol 5 Dimensions index; GAD-7, Generalized Anxiety Disorder 7-item scale; HC, healthy control; HIT-6, 6-item Headache Impact Test; NA, not available due to one group being empty; NRS, numeric rating scale score; PHQ-9, Patient Health Questionnaire 9-item scale.

53 headache-free controls were recruited. Seventy-one patients with CH who did not answer all the questions, were in a remission period, or did not meet the criteria in the ICHD-3 were excluded, and the remaining 423 patients with CH were included in the study (Fig. 1). Table 1 lists the demographic and clinical characteristics of the participants. No significant differences were observed between the patients with CH and headache-free controls in age, sex, current smoking status, or alcohol consumption. Among the patients with CH, 344 (81.3%) were male, and their age at onset was 27.0 (20.0–34.0) years, and 17 (4.0%) had chronic CH with a bout without remission of more than 1 year or with remission periods lasting <3 months. The GAD-7 and PHQ-9 scores were significantly higher in patients with CH than in the controls (GAD-7 score: 7.0 [4.0–12.0] vs. 1.5 [0.0–3.0], $p<0.001$; PHQ-9 score: 7.0 [3.0–12.0] vs. 2.0 [1.0–4.0], $p<0.001$). Suicidal ideation was significantly more common in the CH group ($n=88$, 20.7% vs. 0, 0%; $p<0.001$). Among the patients with CH, 17.8% (75/423) experienced cutaneous allodynia (ASC-12 score ≥3, $p<0.001$).

The weighted EQ-5D score was significantly lower in the CH group (0.88±0.43) than in the controls (0.99±0.33, $p<0.001$). Pairwise comparisons indicated no differences between the groups in the mobility and self-care domains of the EQ-5D. The scores in the domains of usual activities, pain and/or discomfort, and anxiety and/or depression were lower in the CH group ($p<0.001$).

HRQoL deterioration severity according to the EQ-5D using the TTO method

Patients with CH ($n=423$) were categorized into five groups according to the degree of HRQoL deterioration (no problem, very mild, mild, moderate, and severe) using the quality-weighted EQ-5D scores with the TTO method. The patients with CH included 57 (13.5%) with moderate-to-severe HRQoL impairments (Fig. 2).

Among the five HRQoL groups, patients with CH in the severe-impairment group had the highest headache intensity (10.0 [8.0–10.0], $p=0.011$) and the daily headache frequency (2.2 [1.0–4.0], $p=0.001$). Median GAD-7, PHQ-9, and HIT-6 scores were the highest in the severe-impairment group ($p<0.001$, Table 2).

Clinical factors associated with HRQoL deterioration severity

Univariate analyses indicated that headache intensity, daily bout frequency, and bout duration were significantly correlated with the level of HRQoL impairment in the CH group (p<0.001, Table 3). Similarly, the GAD-7, PHQ-9, and HIT-6 scores were significantly correlated with the level of HRQoL impairment (p<0.001). A significant association was also observed between the degree of HRQoL deterioration and current smoking status in patients with CH (p=0.03).

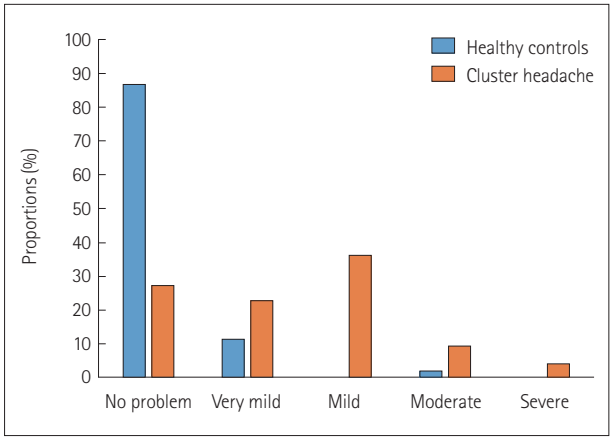

Fig. 2. Degree of health-related quality-of-life impairment according to EuroQol 5 Dimensions score using the time trade-off method.

The regression analysis indicated that daily bout frequency, bout duration, and GAD-7 and PHQ-9 scores were significant predictors of HRQoL impairment level in patients with CH. After adjusting for the confounders of sex, age, bout duration, and GAD-7, PHQ-9, and HIT-6 scores, a 1-unit increase in bout frequency per day in patients with CH corresponded to a 1.166-fold increase in the risk of a worse EQ-5D score (p<0.001), while a 1-point increase in PHQ-9 score corresponded to a 1.117-fold increase in this risk (p<0.001, Table 4).

DISCUSSION

This study found that patients with CH had worse QoL during cluster periods of CHs compared with headache-free

Table 2. Classification of patients with CH (n=25) according to quality weight calculation of EQ-5D using the time trade-off method

Variable	No problem (n=116, 27.4%)	Very mild (n=97, 22.9%)	Mild (n=152, 35.9%)	Moderate (n=40, 9.5%)	Severe (n=18, 4.3%)	Total (n=423)	p
Sex, male	98 (84.5)	78 (80.4)	122 (80.3)	36 (90.0)	10 (55.6)	344 (81.3)	0.046
Age at CH onset, years	28.0 [18.5–34.5]	26.0 [20.0–36.0]	26.0 [19.5–34.0]	29.0 [23.5–34.0]	27.0 [20.0–42.0]	27.0 [20.0–34.0]	0.766
Total period of CH, years	9.0 [4.0–13.0]	5.0 [1.0–11.0]	7.0 [2.0–15.0]	10.0 [1.0–16.0]	5.5 [3.0–14.0]	7.0 [2.0–14.0]	0.024
Average duration of CH bout, weeks	5.5 [3.0–10.0]	3.0 [1.0– 7.5]	6.0 [2.0–10.0]	4.0 [1.0–10.5]	4.0 [2.0–8.0]	5.0 [2.0–10.0]	0.033
Headache intensity, NRS	9.0 [8.0–10.0]	9.0 [8.0–10.0]	9.0 [8.0–10.0]	10.0 [8.0–10.0]	10.0 [9.0–10.0]	9.0 [8.0–10.0]	0.011
Attack frequency, per day	1.0 [1.0–2.0]	1.0 [1.0–2.0]	1.5 [1.0–2.8]	2.0 [1.0–4.0]	2.2 [1.0–4.0]	1.5 [1.0–2.5]	0.001
Attack duration, minutes	85.0 [55.0–120.0]	60.0 [60.0–120.0]	90.0 [60.0–120.0]	120.0 [60.0–150.0]	105.0 [60.0–150.0]	90.0 [60.0–120.0]	0.156
GAD-7 score	5.0 [2.0–8.0]	5.0 [3.0–8.5]	10.0 [6.0–14.0]	12.0 [7.0–16.5]	17.0 [11.0–21.0]	7.0 [4.0–12.0]	<0.001
PHQ-9 score	4.0 [1.0–8.0]	5.0 [3.0–8.0]	9.0 [5.0–14.5]	11.0 [7.5–17.0]	21.0 [11.0–24.0]	7.0 [3.0–12.0]	<0.001
HIT-6 score	67.5 [60.0–74.5]	68.0 [63.0–74.0]	71.0 [66.5–76.0]	72.0 [68.0–78.0]	78.0 [76.0–78.0]	70.0 [65.0–76.0]	<0.001
Circadian rhythmicity in headache attacks	65 (25.0)	61 (23.5)	99 (38.1)	25 (9.6)	10 (3.8)	260 (100.0)	0.678
Seasonal rhythmicity in headache attacks, yes	61 (28.1)	44 (20.3)	82 (37.8)	20 (9.2)	10 (4.6)	217 (100.0)	0.769
Suicidal ideation	19 (16.5)	15 (15.8)	42 (27.6)	8 (20.0)	4 (22.2)	88 (21.0)	0.141
Current smoker	45 (38.8)	38 (39.2)	65 (42.8)	25 (62.5)	11 (61.1)	184 (43.5)	0.206

Data are median [interquartile range], n (%), mean±standard deviation values.
CH, cluster headache; EQ-5D, EuroQol 5 Dimensions index; GAD-7, Generalized Anxiety Disorder 7-item scale; HIT-6, 6-item Headache Impact Test; NRS, numeric rating scale score; PHQ-9, Patient Health Questionnaire 9-item scale.

Table 3. Results of univariate ordinal logistic regression to identify the associations between potential covariates and health-related quality of life deterioration severity

Variable	Odds ratio	95% CI		*p*
		Lower	Upper	
Sex (female vs. male)	1.267	0.814	1.972	0.294
Age at CH onset, years	1.006	0.991	1.021	0.420
Total period of CH, years	1.003	0.981	1.026	0.777
Average duration of CH bout, weeks	0.996	0.981	1.011	0.598
Headache intensity, NRS	1.261	1.098	1.449	<0.001*
Attack frequency, per day	1.149	1.059	1.246	<0.001*
Attack duration, minutes	1.003	1.001	1.006	<0.001*
Average duration of CH bout, weeks	0.993	0.982	1.002	0.123
GAD-7 score	1.167	1.129	1.207	<0.001*
PHQ-9 score	1.167	1.132	1.203	<0.001*
HIT-6 score	1.061	1.037	1.085	<0.001*
Circadian rhythmicity	1.009	0.984	1.036	0.480
Seasonal rhythmicity	1.009	0.696	1.463	0.962
Suicidal ideation	1.476	0.963	2.261	0.074
Smoking (current smoker vs. never smoked)	1.520	1.042	2.217	0.030
Alcohol drinking	0.939	0.838	1.052	0.280
ASC-12 (mild vs. no)	1.558	0.800	3.034	0.193
ASC-12 (moderate vs. no)	2.558	1.276	5.126	0.008
ASC-12 (severe vs. no)	4.127	1.595	10.681	0.004

*p<0.001.
ASC-12, 12-item Allodynia Symptom Checklist; CH, cluster headache; CI, confidence interval; GAD-7, Generalized Anxiety Disorder 7-item scale; HIT-6, 6-item Headache Impact Test; NRS, numeric rating scale score; PHQ-9, Patient Health Questionnaire 9-item scale.

Table 4. Results of multivariable ordinal logistic regression to identify the associations between potential covariates and health-related quality of life deterioration severity

Variable	Coefficients	Standardized coefficient	Odds ratio	95% CI		*p*
				Lower	Upper	
Sex (female vs. male)	-0.122	-0.026	0.886	0.554	1.414	0.601
Age at CH onset, years	0.007	0.044	1.007	0.991	1.023	0.400
Attack frequency, per day	0.154	0.185	1.166	1.072	1.269	<0.001
Attack duration, minutes	0.003	0.165	1.003	1.001	1.110	0.003
GAD-7 score	0.053	0.170	1.054	1.001	1.110	0.045
PHQ-9 score	0.111	0.404	1.117	1.067	1.170	<0.001
HIT-6 score	0.023	0.103	1.024	0.998	1.050	0.072

CH, cluster headache; CI, confidence interval; GAD-7, Generalized Anxiety Disorder 7-item scale; HIT-6, 6-item Headache Impact Test; PHQ-9, Patient Health Questionnaire 9-item scale.

controls. The EQ-5D evaluation scores in the domains of usual activities, pain and/or discomfort, and anxiety and/or depression were lower in the CH group. Moderate-to-severe HRQoL impairments were observed in 13.7% of the patients with CH. HRQoL impairment severity in patients with CH was associated with the number of headaches per day, headache bout duration, and anxiety and depression levels.

While several previous studies have found that patients with CH have impaired HRQoL, HRQoL deterioration is more severe in chronic CH than in episodic CH.[6,14-16] However, only 4% of the patients with CH in the present study experienced chronic CH, reflecting that their HRQoL could be affected by the cluster periods rather than the chronicity of CH. The HRQoL of patients with CH might have been compromised even before they started experiencing chronic CH, so even the HRQoL of patients with episodic CH should receive attention.

The present findings suggest that a higher frequency of headache episodes per day and a longer bout duration in patients with CH are associated with more-severe HRQoL de-

terioration. Severely painful CH bouts during the cluster period may contribute to and exacerbate HRQoL deterioration, even during the interictal state. The frequency of headaches per day and the bout duration should therefore be carefully considered during the active period in order to improve the HRQoL of patients with CH.

The present results also indicate that mood alterations such as depression and anxiety are more frequent among patients with CH, which was consistent with previous studies finding that depression, anxiety, and suicidal symptoms were common among patients with CH.[17,18] Depression was also the strongest predictor of HRQoL deterioration in patients with CH in the present study. Considering the paroxysmal and severity characteristics of CH bouts, depression and anxiety may occur at any period of CH and affect the overall HRQoL of patients. Although the directionality of the association between mood symptoms and HRQoL could not be determined in this study, effective management of mood symptoms can improve patient HRQoL since the control of cluster bouts is the most important determinant of their emotional status.

These results highlight the importance of assessing HRQoL in patients with CH, which might be overlooked if only headache and associated symptoms are considered. Determining the associations among depression, anxiety, daily headache frequency, and bout duration provides relational insights into the HRQoL of patients with CH.

The predictors of worse HRQoL in patients with CH have not been well evaluated using the EQ-5D, which is the most widely used tool to measure HRQoL. It is recommended to weight EQ-5D scores using social preferences in the general population, and the TTO method considers the relative preference of each health state in a specific disease condition. However, the EQ-5D score, which represents a health state between 0 (worst condition) and 1 (perfect health), limits the determination of HRQoL deterioration severity for each patient with CH, and categorizing value sets is necessary to calculate its utility for each possible health state. This study utilized the TTO value set for EQ-5D health states from patients with CH in South Korea, which allows quantification and categorization according to QoL deterioration severity. Patients with CH were divided into five groups using the TTO method to determine the extent of HRQoL impairments, and the factors that affecting the severity of those impairments were analyzed. The patients with CH in the severe-impairment group had the highest headache intensity levels and daily headache frequencies. Furthermore, GAD-7 and PHQ-9 scores among the patients with CH were highest in the severe-impairment group. HRQoL was therefore not uniform among the patients with CH analyzed in this study.

In addition, only 13.7% of patients reported moderate-to-severe impairments and 27.4% reported no problems. These findings were contradictory to the expectation of CH being a suicidal headache. However, in the previous studies that used KCHR data, suicidal ideation was not reported by 35.8% of the subjects, and moderate-to-severe depression and anxiety were not reported by 61.8% and 65.4%, respectively.[17,18] CH is the most-disabling primary headache disorder, but its impact may differ among patients.

To our knowledge, this was the first study to compare HRQoL deterioration severity between patients with CH and headache-free controls in an Asian population. HRQoL deterioration caused by CH has been overlooked since headaches are not recognized as a disease in most Asian countries. In a previous South Korean study, the mean EQ-5D-3L scores for mild-stage Parkinson's disease and for dementia were 0.849 and 0.840, respectively.[19] The study findings indicate that HRQoL levels in patients with CH are comparable to those in patients with other chronic neurological disorders. However, unlike other neurological disorders, the HRQoL of patients with CH has not yet been recognized, and related medical interventions remain inadequate.

This study had several limitations. First, its cross-sectional design made it impossible to determine the direction of causality between QoL and associated mood symptoms. Second, some items in the questionnaires, such as in the PHQ-9 and HIT-6, might be similar to or overlap with those in the EQ-5D questionnaire. The PHQ-9 is a tool that aims to assist clinicians in identifying and diagnosing depression. HIT-6 evaluates the impact of three out of six items on headaches during the 4-week period preceding the assessment, and assessments of the overall QoL of patients with new-onset or episodic CH are restricted if a CH is not experienced during that time. The PHQ-9 and HIT-6 are therefore inadequate tools for assessing the overall QoL in patients with CH. Third, the HRQoL measures and the QoL questionnaire were not specific to patients with CH. The QoL of patients with CH can be evaluated using some questionnaires;[20] however, there is no validated QoL questionnaire for patients with CH available in the Korean language. The EQ-5D also has already been used in previous studies to determine the effectiveness of CH treatment.[21,22] Fourth, QoL questionnaires other than the EQ-5D were not evaluated. Fifth, although age and sex were matched when recruiting the controls, the control group was much smaller than the patient group. Finally, because many patients in the study were recruited from a specialty headache clinic, some selection bias was inevitable due to nonparticipation or exclusion, and the results might not be generalizable to all individuals with CH.

In conclusion, the study found that HRQoL impairment

was more severe in patients with CH than in headache-free controls. However, the degree of HRQoL deterioration varied among those patients. HRQoL impairment severity was associated with the symptoms of depression and anxiety, daily headache frequency, and bout duration. The aforementioned associations also suggested that treatment to alleviate these factors can improve HRQoL associated with CH, although definitive conclusions could not be drawn from this study. Future work is needed to explore the bidirectional associations between HRQoL and CH-related symptoms.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

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Conflicts of Interest

Min Kyung Chu and Byung-Kun Kim, contributing editors of the Journal of Clinical Neurology, were not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

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