



# Characteristics of Elderly-Onset ( $\geq 65$ years) Headache Diagnosed Using the International Classification of Headache Disorders, Third Edition Beta Version

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**Background and Purpose** New-onset headache in elderly patients is generally suggestive of a high probability of secondary headache, and the subtypes of primary headache diagnoses are still unclear in the elderly. This study investigated the characteristics of headache with an older age at onset ( $\geq 65$  years) and compared the characteristics between younger and older age groups.

**Methods** We prospectively collected demographic and clinical data of 1,627 patients who first visited 11 tertiary hospitals in Korea due to headache between August 2014 and February 2015. Headache subtype was categorized according to the International Classification of Headache Disorders, Third Edition Beta Version.

**Results** In total, 152 patients (9.3%, 106 women and 46 men) experienced headache that began from 65 years of age [elderly-onset group (EOG)], while the remaining 1,475 patients who first experienced headache before the age of 65 years were classified as the younger-age-at-onset group (YOG). Among the primary headache types, tension-type headache (55.6% vs. 28.8%) and other primary headache disorders (OPH, 31.0% vs. 17.3%) were more common in the EOG than in the YOG, while migraine was less frequent (13.5% vs. 52.2%) ( $p=0.001$ ) in the EOG. Among OPH, primary stabbing headache (87.2%) was more frequent in the EOG than in the YOG ( $p=0.032$ ). The pain was significantly less severe ( $p=0.026$ ) and the frequency of medication overuse headache was higher in EOG than in YOG (23.5% vs. 7.6%,  $p=0.040$ ).

**Conclusions** Tension-type headache and OPH headaches, primarily stabbing headache, were more common in EOG patients than in YOG patients. The pain intensity, distribution of headache diagnoses, and frequency of medication overuse differed according to the age at headache onset.

**Key Words** old age, International Classification of Headache Disorders, Third Edition Beta Version, tension-type headache, medication-overuse headache, other primary headache disorders.

## INTRODUCTION

Headache is one of the most common neurological complaints of elderly patients,<sup>1</sup> and about 52% of patients with headache are elderly ( $\geq 65$  years).<sup>2</sup> Accordingly, careful and prudent consideration of the diagnosis is important in elderly patients with headache, and investigating the general features of headache in the elderly is mandatory for providing the correct treatment.<sup>3</sup> However, there is a lack of detailed information about headache in elderly patients, particularly new-onset headache in the elderly. Studies of the prevalence of headache have usually included only younger patients ( $<65$  years)<sup>4</sup> or only a few elderly pa-

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tients.<sup>5</sup> Moreover, studies that did include relatively large populations of elderly patients with headache did not use the updated the International Classification of Headache Disorders, Third Edition Beta Version (ICHD-3 $\beta$ ).<sup>2,6,7</sup>

The characteristics of headache differ between elderly and younger patients.<sup>8</sup> Headache in elderly patients more frequently have typical aura without headache, hypnic headache, facial pain syndrome, and secondary headache, which may be caused by hormonal or metabolic changes, concomitant diseases, and various medications.<sup>8</sup> Therefore, investigations of headache should consider the age of the patients. In addition, ICHD-3 $\beta$  expanded the subtypes of primary headache disorders and the probable diagnostic entities, and changed the criteria for chronic migraine compared to previous versions, and so applying ICHD-3 $\beta$  may be helpful when investigating headache in elderly patients.<sup>9</sup>

We conducted a prospective cross-sectional multicenter headache registry study to evaluate characteristics of first-visit patients with elderly-onset ( $\geq 65$  years) headache based on the ICHD-3 $\beta$  criteria in a Korean population.

## METHODS

### Standard protocol approval, registration, and patient consent

This study was a substudy of a prospective, cross-sectional, multicenter study based on the Headache Registry Using CHD-3 $\beta$  for First-Visit Patients (HEREIN) study.<sup>10</sup> Data were obtained from consecutive first-visit patients with headache treated at the neurology outpatient departments of 11 hospitals (9 university hospitals, comprising 6 tertiary and 3 secondary referral hospitals, plus 2 general secondary referral hospitals) in Korea between August 2014 and February 2015.<sup>10</sup> The information, history, and diagnosis of patients with headache were performed by board-certified neurologists with headache expertise. The participants were Koreans aged 19–100 years who had complained of headache as the main reason for their outpatient visit, and they had no communication disability that would interfere with history-taking. Patients with impaired cognitive function or language problems or any other serious medical or psychiatric condition based on a physician's evaluation were excluded, as well as those who visited the hospital for major symptoms other than headache. This study protocol was reviewed and approved by the ethics committee of each participating hospital. All patients gave informed consent to participate in this study or waived informed consent in accordance with the decision of the ethics committee of each hospital.<sup>10</sup>

### Headache assessment and diagnosis

All enrolled patients completed a self-administered questionnaire and were examined by a headache specialist at each center. If secondary headache was suspected, the blood and/or cerebrospinal fluid (obtained via lumbar puncture) were/was sampled. Brain imaging including the vasculature was also conducted if necessary based on the recommendation of the headache specialist. The questionnaire was designed to obtain information about the medical history and characteristics of headache including routes of access to the hospital, aura, frequency and severity using a visual analog scale (VAS), pain characteristics, attack location and duration, presence or absence of aggravation after routine physical activity, accompanying symptoms, and autonomic features including vertigo.

The detailed method for reaching the final diagnosis was described in a previous study and was supplemented (Supplementary Material in the online-only Data Supplement).<sup>6</sup> In brief, the confirmative diagnosis was made based on the ICHD-3 $\beta$  criteria after considering the questionnaire results, medical records, neurological examination, appropriate testing, and treatment response. Controversial cases were reviewed by researchers in case-analysis meetings. The patients were classified according to the age at the onset of the presenting headache. Those who first experienced the headache from the age of 65 years were classified as the elderly onset group (EOG), while those with a first headache before the age of 65 years were classified as the younger-age-at-onset group (YOG).

Thirty-one patients were assigned randomly using the R-program (<https://www.r-project.org>), which was also used to evaluate the interrater agreement. Each investigator independently reviewed the structured clinical data and subsequently reported the diagnosis by e-mail, and levels of agreement for the headache classification were calculated.

### Statistical analysis

Statistical analyses were performed using the Windows SPSS software package (version 20.0, SPSS Inc., Chicago, IL, USA). Continuous variables are presented as mean  $\pm$  standard deviation values, and categorical variables are presented as frequencies and percentages. Continuous or interval-scaled variables were compared using Student's *t*-test or the Mann-Whitney test, and categorical variables were compared using the chi-square test or Fisher's exact test. The interrater agreement was assessed by calculating the Fleiss' kappa coefficient among the researchers, which was 0.61. A two-tailed probability value of  $p < 0.05$  was considered to be indicative of statistical significance.

## RESULTS

### Demographic data of the study population

The 1,627 patients in the HEREIN study were aged  $47.3 \pm 14.6$  years, with a higher proportion of female patients [605 males (37.2%) vs. 1,022 females (62.8%)]. The EOG included 152 (9.3%) patients aged  $72.6 \pm 5.8$  years. Brain imaging was performed in 1,080 patients [total 66.4%: 30.1% received brain computed tomography (CT) and 36.3% received magnetic resonance imaging (MRI)], and the rate of brain imaging did not differ between the EOG (27.6% received brain CT and 39.5% received brain MRI) and the YOG (30.3% vs. 36.0%) ( $p=0.666$ ). The most common abnormalities associated with headache were as follows: sinusitis ( $n=6$ ), non-traumatic intracranial hemorrhage ( $n=4$ ), spontaneous intracranial hypotension ( $n=4$ ), cerebral arterial dissection ( $n=3$ ), reversible cerebral vasoconstriction syndrome ( $n=3$ ), and intracranial malignancy ( $n=2$ ).<sup>11</sup> Brain imaging in cases of primary stabbing headache were conducted with CT ( $n=44$ , 24.6%) or MRI ( $n=42$ , 23.4%). No neurovascular compression was found in patients with primary stabbing headache in our study.

Of the 1,627 patients, 1,429 (87.8%) were diagnosed with primary headache, 135 (8.3%) with secondary headache, 28 (1.7%) with facial pain syndrome, and 35 (2.2%) as other headache disorder. The frequencies of secondary headache (11.2% vs. 8.0%), facial pain syndrome (2.0% vs. 1.7%), and other headache disorders (3.9% vs. 2.0%) tended to be higher in the EOG than in the YOG, while primary headache (82.9% vs. 88.3%) tended to be less frequently diagnosed in the EOG, but there were no statistically significant differences ( $p=0.193$ ) (Table 1).

### Comparisons of primary headache, secondary headache, and facial pain syndrome

The 1,429 patients with primary headache were aged  $47.1 \pm 14.4$  years, with a higher proportion of female patients ( $n=922$ ,

64.5%). Tension-type headache (55.6% vs. 28.8%) and other primary headache disorders (31.0% vs. 17.3%) were more frequent in the EOG than in the YOG, and migraine (13.5% vs. 52.2%) was less frequent in the EOG ( $p<0.001$ ). No case of cluster headache was detected in the EOG.

Migraine was more frequent in female patients (63.8%) than in male patients (31.6%,  $p=0.001$ ) in the YOG, but its frequency did not differ with sex in the EOG (13.3% of females vs. 13.9% of males,  $p=0.996$ ).

Marginal significance ( $p=0.062$ ) was noted between the EOG and YOG for the migraine subgroup, particularly chronic migraine (41.2% EOG vs. 20.0% YOG) after excluding the probable migraine subtype. This result was not significant when probable migraine was included ( $p=0.139$ ) (Table 2). The VAS score was lower in the EOG than that in the YOG ( $6.2 \pm 1.3$  vs.  $7.3 \pm 1.4$ ,  $p=0.026$ ). Episodic tension-type headache tended to be less frequent in the EOG than in the YOG ( $p=0.297$ ) regardless of whether or not probable tension-type headache was excluded ( $p=0.199$ ) (Table 2). The VAS score for patients with tension-type headache did not differ between the EOG and the YOG ( $5.2 \pm 1.1$  vs.  $5.1 \pm 1.2$ ,  $p=0.121$ ).

Regarding other primary headache disorders, primary stabbing headache (87.2%) was the most common diagnosis in the EOG, whereas primary exercise headache, primary headache associated with sexual-activity, and primary thunderclap headache were more frequently noted in the YOG ( $p=0.032$ ) (Table 3). The frequency of medication overuse headache (MOH) was higher in EOG than in YOG (23.5% vs. 7.6%,  $p=0.040$ ) but did not differ significantly in those with tension-type headache (5.7% vs. 2.9%,  $p=0.271$ ) (Table 4). Moreover, the following main causes of MOH did not differ between the EOG and YOG ( $p=0.551$ ): combination analgesics (36.4% vs. 42.9%), nonsteroidal anti-inflammatory drugs (27.3% vs. 28.6%), and triptan (0.0% vs. 7.1%) use.

The distribution of secondary headache subtypes ( $p=0.239$ )

**Table 1.** Comparison\* between aged ( $\geq 65$ ) onset group and younger age onset ( $< 65$ ) group

	Age $< 65$ ( $n=1,475$ )	Age $\geq 65$ ( $n=152$ )	Total ( $n=1,627$ )
Primary headache	1,303 (88.3)	126 (82.9)	1,429 (87.8)
Migraine <sup>†</sup>	680 (52.2)	17 (13.4)	697 (48.8)
Tension type headache <sup>†</sup>	375 (28.8)	70 (55.6)	445 (31.1)
Cluster headache <sup>†</sup>	22 (1.7)	0 (0.0)	22 (1.5)
Other primary headache <sup>†</sup>	226 (17.3)	39 (31.0)	265 (18.5)
Secondary headache	118 (8.0)	17 (11.2)	135 (8.3)
Facial pain syndrome	25 (1.7)	3 (2.0)	28 (1.7)
Other headache disorders	29 (2.0)	6 (3.9)	35 (2.2)

Values are number (%).

\* $p=0.193$  by chi-square test with frequency of primary headache, secondary headache, facial pain syndrome, and other headache disorders, <sup>†</sup>Including diagnosed as probable type, <sup>‡</sup>The percent (%) represents ratio of each headaches in primary headache.

did not differ between the EOG and YOG. The most common secondary headache diagnosis was headache attributed to infection in both of the study groups (Table 5).

### Comparison aged ( $\geq 65$ years) onset with the younger age ( $< 65$ years) onset group in elderly ( $\geq 65$ years) patients

Among the 210 elderly ( $\geq 65$  years) patients with headache, 152 (72.4%) were defined as EOG and 58 (27.6%) had headache before the age of 65-years. Older age ( $72.6 \pm 5.8$  vs.  $70.1 \pm 5.2$ ,  $p=0.001$ ) and proportion of different types of headache, particularly migraine (11.2% vs. 36.2%) and other primary headache disorders (25.7% vs. 8.6%), differ between EOG and YOG among elderly ( $\geq 65$  years) patients ( $p=0.003$ ) (Supplementary Table 1 in the online-only Data Supplement).

## DISCUSSION

This prospective, first-visit, outpatient-based, multicenter study using ICHD-3 $\beta$  has demonstrated the following features of elderly-onset headache compared with younger-age-at-onset headache. First, tension-type headache and other primary headache disorders were more common, whereas

migraine was less common in patients with headache that began from the age of 65 years in a Korean population. Second, ICHD-3 $\beta$  was useful for diagnosing elderly patients with first-onset headache.

Tension-type headache was the most frequent diagnosis in previous studies, with prevalence rates ranging from 11% in Singapore to 20–40% in the USA and  $>80\%$  in Denmark in a general population-based study.<sup>12</sup> Moreover, Spanish tertiary hospital data show that the frequency of tension headache in older patients (age  $\geq 65$  years) is about 30%.<sup>2</sup> Other studies have found annual prevalence rates of tension-type headache of 16–44% in elderly patients.<sup>13–16</sup> In the present study we assessed the frequency of tension headache among elderly-onset patients with primary headache, and the increased frequency of tension-type headache we detected in older patients was in line with these previous studies.

In this study, the second most common primary headache diagnosis in the EOG was other primary headache disorders, particularly primary stabbing headache. In contrast, new daily persistent headache, primary exercise headache, primary headache associated with sexual-activity, and primary thunderclap headache were relatively common diagnoses in the YOG. This intergroup difference may be associated with

**Table 2.** Comparison of migraine and tension type headache between aged ( $\geq 65$ ) onset group and younger age onset ( $< 65$ ) group

Migraine*	Age $< 65$ (n=680)	Age $\geq 65$ (n=17)	Total (n=697)
Migraine without aura	393 (57.8)	7 (41.2)	400 (57.4)
Migraine with aura	42 (6.2)	0 (0.0)	42 (6.0)
Chronic migraine	136 (20.0)	7 (41.2)	143 (20.5)
Probable migraine	109 (16.0)	3 (17.6)	112 (16.1)
Tension type headache†	Age $< 65$ (n=375)	Age $\geq 65$ (n=70)	Total (n=445)
Infrequent episodic tension-type headache	60 (16.0)	12 (17.1)	72 (16.2)
Frequent episodic tension-type headache	112 (29.9)	16 (22.9)	128 (28.8)
Chronic tension type headache	77 (20.5)	21 (30.0)	98 (22.0)
Probable tension type headache	126 (33.6)	21 (30.0)	147 (33.0)

Values are number (%).

\* $p=0.062$  after excluding probable migraine and  $p=0.139$  after including probable migraine, † $p=0.199$  after excluding probable tension type headache and  $p=0.297$  after including probable tension type headache.

**Table 3.** Comparison\* of other primary headache disorder between aged ( $\geq 65$ ) onset group and younger age onset ( $< 65$ ) group

Type of other primary headache disorders	Age $< 65$ (n=226)	Age $\geq 65$ (n=39)	Total (n=265)
Primary cough headache	8 (3.5)	0 (0.0)	8 (3.0)
Primary exercise headache	19 (8.4)	1 (2.6)	20 (7.5)
Primary headache associated with sexual activity	10 (4.4)	0 (0.0)	10 (3.8)
Primary thunderclap headache	19 (8.4)	0 (0.0)	19 (7.2)
Cold-stimulus headache	1 (0.4)	0 (0.0)	1 (0.4)
Primary stabbing headache	145 (64.2)	34 (87.2)	179 (67.5)
Nummular headache	1 (0.4)	0 (0.0)	1 (0.4)
Hypnic headache	0 (0.0)	1 (2.6)	1 (0.4)
New daily persistent headache	23 (10.3)	3 (7.6)	26 (9.8)

Values are number (%).

\* $p=0.032$  by chi-square test.

the characteristics of the headache (attack frequency, duration, and/or potency), physical activity, combined vascular risk factors, hormonal changes, and concomitant drug usage.<sup>6</sup> It is uncertain why the frequency of primary stabbing headache was higher in the EOG than in the YOG in our study. However, there are several possible causes that could explain our results. First, increased cervicogenic headache, nerve inflammation, or vascular tortuosity are often noted in elderly populations, and these problems could result in an association between primary stabbing headache and the findings in our EOG.<sup>17,18</sup> Second, even though the rate of brain imaging was higher (48.0%) in our study than in a previous study<sup>19</sup> (5%) investigating primary stabbing headache, there is a possibility of existing secondary causes for primary stabbing headache in patients in whom brain imaging was not conducted. Third, the mean age at onset has varied from 28 to 47 years in studies based on the Second Edition of the International Classification of Headache Disorders (ICHD-2), but the mean age for patients with primary stabbing headache was 53–74 years in a recent study from Asia, and so primary stabbing headache may be common among the elderly.<sup>2,19</sup> Fourth, our study applied ICHD-3 $\beta$  rather than ICHD-2 for classifying headache. The diagnostic yield of chronic migraine and other primary headaches is more favorable for ICHD-3 $\beta$  than for ICHD-2. In particular, the primary stabbing headache diagnostic criteria that limited the pain distribution to the first division of the trigeminal nerve were deleted from ICHD-3 $\beta$ .<sup>9</sup> Therefore, our results may be more explainable than those obtained in previous studies.

Migraine was the third most frequent diagnosis in the EOG.

The annual incidence of migraine in the elderly population has been reported to range from 10% to 25%.<sup>6,20</sup> Previous studies found that the migraine prevalence decreases progressively during ageing.<sup>21,22</sup> Moreover, in our study migraine with aura was rare in the EOG, which is consistent with the findings of a previous epidemiological study.<sup>2</sup> Late-life migraine accompaniment is not rare in the elderly, but we enrolled elderly patients with their first presentation of headache, and so aura without headache was not detected.<sup>23</sup> Furthermore, we found that chronic migraine tended to be more common in the EOG. Migraine transforms into chronic headache and changes over time, particularly in elderly patients.<sup>24–26</sup> Chronic daily headache is a neurological condition that reportedly affects 1–4% of the general population.<sup>27,28</sup> Patients with chronic daily headache have initially suffered from episodic headache that subsequently develops into chronic daily headache.<sup>27</sup> Therefore, physicians should consider the characteristics of these primary headaches, including their chronicity, when diagnosing and/or treating migraine and tension-type headache in the elderly.

The patients in the EOG with migraine had less-severe pain, which is compatible with the results in a previous cross-sectional study involving outpatients aged  $\geq 60$  years.<sup>29</sup> Although the exact mechanism underlying the decreased intensity of headache with ageing is still unclear, increased somatosensory pain thresholds and decreased estrogen-withdrawal-related migraine in elderly headache patients might account for our results.<sup>30,31</sup>

Female dominance was noted in the YOG but not in the EOG among our migraineurs. Migraine generally begins af-

**Table 4.** Comparison of frequency of medication overuse headache between aged ( $\geq 65$ ) onset group and younger age onset ( $< 65$ ) group

	Age $< 65$ N <sub>case</sub> /N <sub>total</sub> (%)	Age $\geq 65$ N <sub>case</sub> /N <sub>total</sub> (%)	<i>p</i> value*
Migraine	52/680 (7.6)	4/17 (23.5)	0.040
Tension-type headache	11/375 (2.9)	4/70 (5.7)	0.271
Other primary headache disorders	1/226 (0.4)	0/39 (0.0)	Not available

Values are number of case/total number of each headache (%).

\**p* value were acquired by Fisher's exact test according to each headaches.

**Table 5.** Comparison\* of secondary headache between aged ( $\geq 65$ ) onset group and younger age onset ( $< 65$ ) group

Type of secondary headache	Age $< 65$ ( <i>n</i> =118)	Age $\geq 65$ ( <i>n</i> =17)	Total ( <i>n</i> =135)
Trauma or injury to the head and/or neck	12 (10.2)	1 (5.8)	13 (9.6)
Cranial or cervical vascular disorder	16 (13.6)	2 (11.8)	18 (13.3)
Non-vascular intracranial disorder	23 (19.5)	0 (0.0)	23 (17.0)
Substance or its withdrawal	10 (8.5)	2 (11.8)	12 (8.9)
Infection	31 (26.2)	5 (29.4)	36 (26.8)
Homeostasis	3 (2.5)	2 (11.8)	5 (3.7)
Cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure	23 (19.5)	5 (29.4)	28 (20.7)

Values are number (%).

\**p*=0.239 by chi-square test.

ter menarche, is more common during menstruation, and often improves during pregnancy and after menopause.<sup>32</sup> The estrogen-withdrawal hypothesis is the most commonly used to explain the female preponderance in migraine.<sup>33</sup> If the opposing roles of estrogen (increases neural activity) and progesterone (decreases neural activity) within the brain become unbalanced, these conditions may alter the susceptibility to migraine.<sup>34</sup> Furthermore, because increased estrogen is related to the up-regulation of serotonin in the brain, consequent menstruation-related cyclical changes in serotonin levels in the trigeminal nerve ganglia could contribute to the selective response to estrogen withdrawal and may increase the likelihood of migraine developing.<sup>35</sup>

The frequency of MOH was higher in EOG migraineurs than in YOG migraineurs, which is consistent with a previous study finding that patients with MOH more frequently transformed from migraine than those with chronic tension-type headache (69.2% vs. 23.8%).<sup>6</sup> Our results suggest that the characteristics or underlying headache for MOH may have differed between the EOG and YOG. Further large population studies of whether the features of MOH are influenced by the age at headache onset are needed.

Our study had some limitations that should be considered. First, it was a cross-sectional study with no long-term longitudinal follow-up. Moreover, this prospective multicenter study did not determine headaches diagnosed as “probable,” which could cause bias. Therefore, a long-term longitudinal study should be performed in the future. Second, our data involved subjective descriptions of current symptoms and recall of previous events, and so recall or selection bias could have affected the obtained results. Third, the smallness of the EOG sample may have resulted in type II errors, while the relatively large YOG sample may have caused type I errors, such as no or only marginal differences in migraine frequency. Caution is therefore needed when interpreting our findings. Lastly, our study did not investigate important factors that could be associated with or contribute to headache, such as sociodemographic, family, psychological, or life-event factors. Further studies of whether these factors are related to headache are still needed.

In conclusion, tension-type headache and other primary headache disorders were more common in patients with headache that began from an age of 65 years in a Korean population. The frequency of headache differed according to the age of the patients at the headache onset.

### Supplementary Materials

The online-only Data Supplement is available with this article at <http://dx.doi.org/10.3988/jcn.2016.12.4.419>.

### Conflicts of Interest

The authors have no financial conflicts of interest.

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