INTRODUCTION

Vestibular schwannomas (VS) are benign tumors arising from the Schwann cells of the vestibular nerve. While vestibular symptoms are expected from the nerve of origin, auditory symptoms such as hearing loss and tinnitus are most common symptoms presenting at the time of diagnosis [1]. Patients with VS may present with vestibular symptoms of significant variability in severity and progression; symptoms include vertigo and dizziness, and sometimes postural instability [1-7]. The onset of the symptoms is variable because the central compensation may mask the development of slowly ongoing peripheral vestibular hypofunction with slow-growing tumors. Gradual deterioration of vestibular function eventually leads to postural instability, which poses significant impact on patients’ quality of life [8,9].

Many researches have focused on the relationship of objective parameters such as vestibular function tests and tumor characteristics to explain the wide spectrum of vertigo in VS patients. Caloric testing has been the most common method to evaluate vestibular function in VS patients, and more recently vestibular myogenic evoked potentials (VEMP) and video head impulse test (vHIT) have been employed [1,10-14]. Larger tumors have been associated with more severe caloric paresis [12,13].
The vestibular symptoms to the objective CDP findings in this patient population. We hypothesized that the acute vertigo symptoms the patients experience might reflect current change in vestibular nerve function, while patients who report vestibular symptoms with insidious progression reflect increased postural instability. In this study, we analyzed vestibular function tests and CDP results in VS patients and their correlation with subjective vertigo symptoms.

MATERIALS AND METHODS

The Review Board of the Gangnam Severance Hospital approved this study (IRB No. IRB3-2016-0317). All the procedures performed in the studies involving human participants were performed in accordance with the ethical standards of our institutional and/or national research committees and those of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Since this is a retrospective study, no informed consent was obtained. The medical records of 49 patients newly diagnosed with unilateral VS from magnetic resonance imaging (MRI) findings between 2014 and 2015 were retrospectively reviewed. Twenty-two of the patients presented with vertigo symptoms, and vestibular function tests including CDP were performed in 18 patients (male:female = 8:10; mean age, 57.4 ± 15.0 years). Acute onset group included 6 patients (33.3%) who had a history of acute episodes of vertigo within recent 3 months, and insidious onset group included 12 patients (66.7%) who complained of vertigo/imbalance but without an acute episode. The audiovestibular evaluation included pure-tone audiometry, videonystagmography with bithermal caloric tests, and CDP. Subjective symptoms were evaluated using self-report questionnaires.

Subjective measurements of vertigo

The patients indicated their feeling of dizziness on a vertigo visual analogue scale (VAS). The VAS is a 10-cm scale ranging from 0 (no dizziness) to 10 (maximum dizziness). Dizziness related handicaps in daily activities was measured using the Korean version of the Dizziness Handicap Inventory (DHI), which measures self-perceived handicaps resulting from the functional, emotional, and physical aspects of dizziness, using a 25-item questionnaire. The DHI-total score ranges from 0 (no dizziness handicap) to 100 (maximum dizziness handicap). The DHI scores are subcategorized as functional (DHI-F, 36 points), emotional (DHI-E, 36 points), and physical (DHI-P, 28 points).

MRI and tumor grading

MRI scans were reviewed and the tumor size was measured on contrast-enhanced T1-weighted axial or coronal images. In each case, a maximum diameter was measured, and separate measurements for the internal auditory canal (IAC) and cerebello-
Table 1. Clinical characteristics of patients with vestibular schwannoma presenting with vertigo symptoms

| Variable                        | All patients (n=18) | Acute onset (n=6) | Insidious onset (n=12) | P-value |
|---------------------------------|---------------------|-------------------|------------------------|---------|
| Age (yr)                        | 57.4±15.0           | 66.7±14.3         | 52.8±13.7              | 0.062   |
| Sex (male:female)               | 8:10                | 5:1               | 3:9                    | -       |
| Site (right:left)               | 3:9                 | 3:3               | 6:6                    | -       |
| Tumor size                      |                     |                   |                        |         |
| Maximum size of tumor (mm)      | 25.3±18.0           | 15.9±12.4         | 34.3±15.0              | 0.020   |
| IAC extension (no. of patients) | 16 (88.9)           | 4 (66.7)          | 12 (100)               | -       |
| IAC portion size                | 7.3±4.3             | 4.7±4.7           | 8.6±3.5                | 0.065   |
| CPA portion size                | 23.3±16.3           | 10.3±10.2         | 29.8±15.1              | 0.012   |
| Koos classification             |                     |                   |                        |         |
| I                               | 3 (16.7)            | 2 (33.3)          | 1 (8.3)                |         |
| II                              | 1 (5.6)             | 1 (16.7)          | 0                      |         |
| III                             | 11 (61.1)           | 3 (50.0)          | 8 (66.7)               |         |
| IV                              | 3 (16.7)            | 0                 | 3 (25.0)               |         |
| Associated symptom              |                     |                   |                        |         |
| Hearing loss in ipsilateral ear | 11 (61.1)           | 4 (66.7)          | 7 (58.3)               |         |
| Tinnitus                        | 7 (38.9)            | 3 (50.0)          | 4 (33.3)               |         |
| Facial palsy                    | 5 (27.8)            | 1 (16.7)          | 4 (33.3)               |         |
| PTA (dB HL)                     |                     |                   |                        |         |
| Ipsilateral ear                 | 66.3±34.3           | 51.5±31.8         | 73.8±34.3              | 0.202   |
| Contralateral ear               | 24.8±26.9           | 33.5±27.1         | 20.3±26.9              | 0.330   |

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

IAC, internal auditory canal; CPA, cerebellopontine angle; PTA, pure-tone audiometry; HL, hearing level.
Jongkees’ formula was used to determine canal weakness. Canal weakness greater than 25% was defined as abnormal.

Data analyses
All statistical analyses were performed using SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). The difference in variables between the acute onset and insidious onset groups of VS patients was tested using Pearson’s chi-square test. Spearman correlation analysis was used to identify linear associations between two variables. All data are presented as mean ± standard deviation. A P-value <0.05 was considered to reflect statistically significance.

RESULTS
The clinical characteristics of patients in the acute and chronic onset groups are described in Table 1. The tumor size was significantly larger for the insidious onset group (mean, 34.3±15.0 mm) compared to the acute onset group (mean, 15.9±12.4 mm; P=0.020). Tumor extended into the IAC in four patients (66.7%) of acute onset group and all patients of insidious onset group. Although the tumor size for the IAC portion appeared larger for the insidious onset group, the difference was not statistically significant. The tumor size for the CPA portion was larger for the insidious onset group (P=0.012). Acute onset group included grade I, II and III, and insidious onset included one case of grade I and others were graded III and IV according to Koos classifications. Most commonly associated symptom was hearing loss, followed by tinnitus and facial palsy. Hearing thresholds in the ipsilateral ears were worse in the insidious onset group, but the difference was not statistically significant.

Subjective perception of symptoms severity as measured by VAS ranged from mild to severe (1–10), and did not show significant difference between the acute onset and insidious onset groups (P=0.318). Likewise, the DHI total score or subscale scores (DHI-P, E, and F) did not differ between two groups (P>0.05). Caloric weakness was noted in 13 of all patients (72.2%). All patients showed decreased ES for C5 and C6, and resulting VEST and COMP scores were also decreased, supporting that postural instability is prevalent in these patients. When the acute onset and insidious onset groups were compared, the VAS and DHI scores did not show significant difference. The insidious onset group had higher rate of caloric weakness (100%), and caloric weakness was greater (P=0.014) than the acute onset group (Table 2).

Correlation between postural instability measured as COMP score and other associated factors was examined (Table 3). The COMP scores were not correlated with VAS or DHI scores. Tumor sizes (the maximum diameter, IAC or CPA portion sizes) did not show significant correlation with COMP scores. Fig. 1 shows the box-plots to compare variables related to postural instability between the acute onset and insidious onset groups. The ES for C5 and C6, VEST and COMP scores were generally lower for the insidious onset group compared to acute onset group, but the difference was not statistically significant (Fig. 1).

DISCUSSION
Vestibular symptoms in VS patients are widely variable. Although the VS is a slowly-growing tumor, some patients may experience acute onset of severe vertigo, while others develop subtle or no symptoms. Maximum tumor size, nerve of origin,
associated cochlear symptoms and objective vestibular function test results have been investigated for their correlation of symptom severity of vertigo and imbalance. However, little is known about acute onset of symptoms in VS patients. It has been surmised that acute change in tumor size, such as tumor growth or intratumoral hemorrhage or cystic change would compress the vestibular nerves or cerebellum leading to acute vestibular symptoms. Direct compression of the vestibular nerves would lead to demyelination, and also decreased microcirculation would damage the neural structures. In addition, metabolic changes caused by tumoral secretions from VS have been related to cochlear damage causing sensorineural hearing loss, and similar effects on vestibular organs may contribute to their abrupt or gradual loss of function [20].

In this study, we aimed to investigate whether tumor characteristics and vestibular functional status of vestibular system and postural control are related to acute onset or insidious onset of vertigo. Our results showed that the maximum size of tumor and the IAC and CPA portion sizes were larger, hearing impairment was more common, and canal weakness was greater in patients with insidious onset of vestibular symptoms. It can be suggested that acute onset of vertigo is not related to tumor size. Sudden change in vestibular sensory input, possibly by mechanical or biochemical damage can be postulated as possible explanation for acute bouts of vertigo. Considering that caloric weakness was more evident in the insidious onset group, acute onset of symptoms may reflect acute deterioration of residual vestibular function. While the insidious onset group showed greater caloric weakness, gradual vestibular compensation in these patients might explain the lack of difference in SOT parameters compared to acute onset vertigo group. However, it remains a question whether the direct compression of the nerves can be deduced from tumor size measurements, and a longitudinal follow-up study of VS patients with IAC involvement to correlate changes in tumor dimensions in the IAC and development of acute vertigo symptoms would be informative. Another explanation is that the proximity of the tumor to the inner ear in VS patients with IAC involvement would facilitate diffusion of metabolites that cause cochlear and vestibular damage. However, VS-secreted metabolites have been identified only recently, and their possible effect on vestibular organs are still unknown.

The CDP is widely employed, and the SOT paradigm provides essential information regarding a patient’s ability to maintain stable posture. While static balance tests such as the Rom-
berg test or standing on a foam are simpler to perform in a clinical setting, the CDP offers the obvious advantage to assess sensory integration in sensory conflict situations, by altering the visual and proprioceptive inputs in six different conditions. Previous studies have reported that the ES for SOT conditions C5 and C6 are related to canal paresis as measured by caloric or rotational chair tests in the VS patients [6] and whether they complain of vertigo symptoms [16]. Gait disturbance was noted in patients with small tumors, especially while walking with eyes closed [21]. Postural instability impacts daily activities, and it has been shown that the vestibular symptoms correlate with prospective working disability in VS patients [8]. These findings support the use of CDP in vestibular function evaluation of VS patients. In our analysis, we focused on ES for C5 and 6, COMP and VEST scores: the C5 and C6 conditions test the patients’ ability to maintain posture relying on vestibular sensory inputs, and VEST and COMP scores takes ES for C5 and/or C6 into consideration. Dynamic postural instability measured by these parameters did not differ between patients with acute or insidious symptoms. Interestingly, there was a tendency of increased postural instability in patients with insidious onset, but the difference was not statistically significant. With slow growth of tumors and gradual deterioration of vestibular inputs, central compensation would take place and alleviate expected acute symptoms, and it is plausible that some patients would experience intermittent or subtle imbalance. Indeed, many patients would vaguely describe their symptoms as vertigo or imbalance that occurs “sometimes, but not always” over some period of time. Since many are referred after diagnosis of VS, the patients were already apprehensive about their conditions and sometimes they would not bring up subtle vertigo complaints unless asked. During initial interviews with patients who visited our tertiary-referral clinic, we asked specific questions regarding hearing status and vertigo symptoms. Our results show even these nonspecific symptoms should alert the clinician to suspect postural instability and consider CDP testing.

Evaluation of vestibular function and posture control in VS patients is important because their prominent effect on patients’ quality of life. In patients with untreated VS, vertigo symptoms negatively affected quality of life, while hearing symptoms were less damaging [22]. Also, vertigo symptoms were more associated with disability affecting VS patients’ working status after treatment than hearing problems [8]. While hearing loss and facial nerve dysfunction can be measured easily, vestibular tests often require more expertise and attention. Furthermore, clinicians may be focused to utilize vestibular function tests as tools to estimate tumor size, nerve of origin and treatment outcomes, which are essential in treatment planning. In addition to these pertinent information, patients’ performance in posture control should also be considered as an important index of their general well-being.

Limitations of this study include that only VS patients with subjective vertigo symptoms were evaluated for postural instability. About half of the newly diagnosed VS patients did not have vestibular symptoms and CDP was not tested, and further vestibular evaluation would have been valuable to confirm subclinical vestibular dysfunction. In addition to the conventional caloric test, VEMP and vHIT would have provided more comprehensive description of vestibular function status, and their correlation with postural instability remains to be explored. Prospective longitudinal studies on larger groups of VS patients would provide more detailed information regarding postural instability and their symptom correlation.

This study was aimed to examine factors associated with subjective vestibular symptoms and postural instability in VS patients. The patients with insidious onset of vertigo symptoms tended to show increased canal weakness and postural instability. Thus, clinicians should consider that postural instability is likely present even in patients who do not complain of acute vertigo, and appropriate counseling should be discussed with the patients.

**CONFLICT OF INTEREST**

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

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