Research Article

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High pillow and spontaneous vertebral artery dissection: A case-control study implicating "Shogun pillow syndrome"

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Abstract

Introduction: The underlying causes of spontaneous vertebral artery dissection (sVAD) remain insufficiently understood. This study aimed to determine whether high-pillow usage is associated with an increased risk of sVAD and evaluate the frequency of sVAD attributable to high-pillow usage.

Patients and Methods: This case-control study identified patients with sVAD and age- and sex-matched non-sVAD controls (case-to-control ratio: 1:1) treated at a certified comprehensive stroke center in Japan between 2018 and 2023. The pillow height used at the onset of the index disease was measured and classified into three categories between 12 and 15 cm boundaries. Univariable logistic regression was performed to assess the odds ratio (OR) with a 95% confidence interval (CI) of high-pillow usage for sVAD development. A subgroup of sVAD attributable to high-pillow usage was defined with the following three conditions: high-pillow usage ($\geq$12 or $\geq$15 cm); no minor preceding trauma; and wake-up onset.

Results: Fifty-three patients with sVAD and 53 non-sVAD controls (42% women, median age: 49 years) were identified. High-pillow usage ($\geq$12 and $\geq$15 cm) was more common in the sVAD group than in the non-sVAD group (34 vs 15%; OR = 2.89; 95%CI = 1.13–7.43 and 17 vs 1.9%; OR = 10.6; 95%CI = 1.30–87.3, respectively). The subgroup of sVAD attributed to high-pillow usage ($\geq$12 and $\geq$15 cm) was found in 11.3% (95%CI = 2.7%–19.8%) and 9.4% (95%CI = 1.5%–17.3%), respectively.

Conclusion: High-pillow usage was associated with an increased risk of sVAD and accounted for approximately 10% of all sVAD cases. This tentative subgroup of sVAD may represent a distinct spectrum of disease—Shogun pillow syndrome.

Keywords

Spontaneous vertebral artery dissection, high pillow, case-control study

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Introduction

Spontaneous vertebral artery dissection (sVAD) is a leading cause of ischemic stroke in young and middle-aged individuals, accounting for 8%–11% of all ischemic stroke cases in these age groups.[1,2] With no curative treatment and approximately 18% patients experiencing poor functional outcomes, the underlying mechanism of sVAD needs to be elucidated to prevent its occurrence.[3,4]

Genetic and environmental factors have been investigated; however, few promising candidates have been found. While extracranial internal carotid artery dissection is the most common form of cervicocephalic artery dissection in the populations in Europe and the United States, vertebral artery dissection (VAD) is the dominating form in East-Asian populations, more frequently affecting the intracranial portion of the artery.[5–8] Inherited connective tissue disorders are estimated to account for no more than 5% of sVAD cases, although precise estimates in East-Asian populations are lacking.[9–11] Genetic predisposition to sporadic VAD has been investigated in genome-wide association studies in European ancestry patients, suggesting an association with few common genetic polymorphisms.[12–14] Among environmental factors, extreme neck and head movements such as coughing, vomiting, sneezing, yoga practice, and chiropractic manipulations have been noted.[15–22] However, these minor preceding traumas are found only in approximately one-third of cases.[23,24] Given the striking preponderance of this dissection site in East-Asian populations, particularly in the two-thirds of patients with no obvious trigger, cultural behaviors varying in different geographic regions may be interesting potential risk factors to explore for sVAD.

We encountered several patients with sVAD who have a habit of using a high pillow, which may serve as a possible triggering factor (Supplemental Figure 1). Most patients experience symptom onset when they wake up and do not report any other preceding traumas. Therefore, we hypothesized that some cases might be attributable to high-pillow usage. This study aimed to determine whether high-pillow usage is associated with an increased risk of sVAD and evaluate the proportion of sVAD attributable to this behavior.

Patients and methods

Anonymized data that support the findings of this study are available from the corresponding author upon reasonable request and after permission has been granted by the ethics committee. This study complies with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (see the checklist in the Supplemental Material).[25]

Study design and setting

This single-center age- and sex-matched case-control study was performed at the National Cerebral and Cardiovascular Center (NCVC), a certified comprehensive stroke center in Osaka, Japan.

Study participants

Study participants were identified from the NCVC Stroke Registry, a database of consecutive patients admitted to the Department of Neurology and Cerebrovascular Medicine of our hospital (clinicaltrials.gov: NCT02251665) between March 2018 and January 2023. Patients who initially presented with subarachnoid hemorrhage (SAH) were not included in the registry because they were admitted to the neurosurgical unit. The case group comprised consecutive patients with sVAD, and age- and sex-matched control patients were selected from the NCVC Stroke Registry within the same period. The non-sVAD control group comprised individuals with acute neurological events consistent with stroke symptoms, other than cervicocephalic artery dissection. Two neurologists (SE and TT) confirmed by chart and imaging reviews the exclusion of patients with cervicocephalic artery dissection from the control group. The non-sVAD controls were selected from the patients admitted within 6 months before or after the time the corresponding sVAD cases were admitted. Age-matching was allowed within 1 year of age. If there was more than one non-VAD candidate meeting these conditions, a random number generator was used to determine the control included in the analysis. Individuals with sVAD who could not be contacted or whose information was unavailable were excluded, as were matched controls. If a control individual could not be contacted or information was unavailable, another age- and sex-matched individual was randomly selected to maintain a 1:1 case-to-control ratio.

Diagnosis of sVAD

The radiological findings of all patients diagnosed with VAD by their treating physician were re-evaluated and regraded by the two neurologists. Only those VAD cases that fulfilled the 2021 European Stroke Organization diagnostic criteria for definite extracranial and intracranial artery dissection were included.[26] Intracranial VAD was defined as definite if it met any of the following criteria: stenosis or occlusion secondary to the development of aneurysmal dilation at a non-branching site, intramural hematoma, intimal flap, or double lumen. Extracranial VAD was classified as definite, if it met any of the following criteria: mural hematoma, dissecting aneurysm, long tapering stenosis, intimal flap, double lumen, or occlusion revealing a dissecting aneurysm or long tapering stenosis after recanalization.[26] The following cases were excluded as non-spontaneous VAD: (i) due to a major trauma (for example, patients with preceding contusions or traffic accidents); (ii) iatrogenic (such as complications of diagnostic or therapeutic interventions); (iii) hereditary (for example, patients with Ehlers-Danlos syndrome, Marfan's syndrome,

osteogenesis imperfecta, polycystic kidney disease, or other hereditary connective tissue diseases); and (iv) underlying fibromuscular dysplasia.

Clinical data collection

Demographic data and clinical information were collected, including age, sex, potential risk factors for high pillow usage (body mass index (BMI), congestive heart failure, chronic obstructive pulmonary disease, and gastroesophageal reflux disease), and vascular risk factors (hypertension, dyslipidemia, diabetes mellitus, migraine, and current smoking status). For the sVAD group, we also collected clinical data on the index sVAD, including whether the patient had a minor preceding trauma, whether the patient had wake-up onset, National Institutes of Health Stroke Scale score at admission, type of onset (head or neck pain alone/ischemic stroke/SAH/transient ischemic attack), and head or neck pain at onset. Radiological features were also investigated, including the dissected segment (V1–4), side of dissection (right/left/bilateral), basilar artery involvement, and diagnostic rationale subitems based on the radiological diagnostic criteria.

Minor preceding trauma was defined as "any event that triggered sudden movements of the neck or head before the index sVAD." Wake-up onset was defined as "recognizing symptoms only after waking up that were not present before falling asleep." Minor preceding trauma and wake-up onset were reconfirmed during the measurement process because this information was considered crucial in attributing the index sVAD to high-pillow usage.

Measurement

The study participants measured the pillow they used at the onset of the index disease at home in terms of the pillow height, hardness, and neck angle (Supplemental Figure 2). Because the measurement was performed over a certain time after the onset of the index diseases in some study participants, those who had discarded the pillows used at the onset of the index diseases were excluded from the analysis. They reported the measurement results to one of the two neurologists (SE or TT) in an outpatient setting or via telephone.

Pillow height was measured at the highest point before the head was placed. When a study participant did not use a pillow, the pillow height was measured to be 0 cm. The pillow height measurement included additional items placed on the pillow, such as towels or blankets. We defined the pillow as "soft" if it sunk more than half as much as before the head was placed and "hard" if it did not sink half as much. Neck angles were measured using "the facial plane," passing through the bilateral lateral canthi and the chin.[27] When the facial plane was parallel to the ground, the neck angle was classified as "straight"; when the facial plane was tilted caudally, the neck angle was classified as "flexion"; and when the facial plane was tilted cranially, the neck angle was classified as "extension."

To minimize measurement bias, dummy questions about miscellaneous sleep practices were asked at the same time as the report of the measurement results to mask the risk factors of interest to the study participants. We also investigated whether the patients had the habit of sleeping on their sides to assess the impact of the sleeping posture. The data was based on self-reported posture at the point at which they started sleeping. However, it was difficult to confirm all the postures the participants had during their time asleep. The questions were manually standardized between the assessors (Supplemental Table 1).

Definition of the high pillow

We formed a two-member working group, consisting of one representative each, from the Japan Bedding Products Association and the Japan Research Laboratory of Sleep Science, to determine the pillow height boundaries defining "high-pillow usage." This working group was blinded to the study data. The responses of the working group were integrated as follows. (i) There are generally three different pillow-height design standards based on customer preferences: 3–5, 6–8, and 9–11 cm, although no accurate statistics are available. (ii) Pillows with a height $\geq$12 cm are the highest among the commonly distributed pillows. (iii) Pillows with a height $\geq$15 cm are extraordinarily high and are generally not recommended for use. Therefore, based on the recommendations of the working group, pillow heights were classified into three categories between the 12 and 15 cm boundaries ($<$12, $\geq$12 and $<$15, and $\geq$15 cm).

Statistical analyses

Baseline characteristics. Descriptive statistics were calculated for baseline characteristics by comparing the sVAD and non-sVAD groups. Continuous variables are presented as medians (interquartile range). Categorical variables are presented as frequencies and percentages. Group comparisons were performed using the Wilcoxon rank-sum test or the Chi-square test.

Association between high-pillow usage and sVAD. Univariable logistic regression was applied to the age- and sex-matched dataset to calculate the odds ratios (OR) of high-pillow usage, with a height of $\geq$12 and $\geq$15 cm, for assessing the risk of sVAD. The Cochran–Armitage trend test was performed to evaluate the trend of the proportion of sVAD in the study population according to the pillow height categories: $<$12, $\geq$12 and $<$15, and $\geq$15 cm. We assumed no factors other than age and sex to be associated with both high-pillow usage and the occurrence of sVAD, and therefore did not consider additional adjustment in the main

Table 1. Baseline characteristics of the cases and controls.

Characteristics	sVAD (n = 53)	Non-sVAD (n = 53)	p-Value
Age, y	49 (45–56)	49 (45–56)	—
Female	22 (42)	22 (42)	—
Potential risk factors for high-pillow usage			
Body height, cm	166 (160–170)	165 (160–173)	0.68
Body weight, kg	66 (58–71)	66 (56–75)	0.43
Body mass index, kg/m^2	23.9 (21.7–25.8)	23.7 (21.2–27.6)	0.72
Congestive heart failure	0 (0)	1 (2)	0.32
Chronic obstructive pulmonary disease	0 (0)	1 (2)	0.32
Gastroesophageal reflux disease	6 (11)	7 (13)	0.77
Sleep conditions (including dummy questions)			
Watching television at bedtime	13 (25)	14 (26)	0.82
Using a smartphone at bedtime	30 (57)	34 (64)	0.43
Sleeping on one's side	4 (8)	6 (11)	0.75
Bed height, cm	15 (10–42)	15 (8–42)	0.69
Listening to music at bedtime	9 (17)	4 (8)	0.14
Vascular risk factors			
Hypertension	21 (40)	39 (74)	<0.001
Dyslipidemia	16 (30)	30 (57)	0.006
Diabetes mellitus	3 (6)	13 (25)	0.007
Migraine	7 (13)	2 (4)	0.081
Current smoking	11 (21)	8 (17)	0.62

sVAD: spontaneous vertebral artery dissection.
Data are presented as medians (interquartile ranges) or numbers (%).

analysis. Instead, we evaluated the ORs as sensitivity analyses (i) after excluding individuals who slept on their sides, (ii) after adjusting BMI, or (iii) after adjusting hypertension, dyslipidemia, and diabetes mellitus.

Exploring a subgroup of sVAD attributable to high-pillow usage. A subgroup of sVAD attributable to high-pillow usage was defined with the following conditions: (i) high pillow usage (≥12 or ≥15 cm); (ii) no minor preceding trauma; and (iii) wake-up onset. The proportion of patients who fulfilled these three conditions was evaluated in the sVAD group.

Modification and mediation analyses. In the exploratory analyses, the transition states of the study participants in terms of pillow height, pillow hardness, and neck angle were illustrated in an alluvial plot. A subgroup analyses was performed to investigate whether pillow hardness modified the association between high-pillow usage (≥12 cm) and sVAD. Thereafter, we used mediation analysis for case-control studies to further investigate the extent to which the association between high-pillow usage and sVAD is mediated by neck flexion. We used the publicly available Stata module *paramed* to calculate the proportion of the association between high-pillow usage (≥12 cm) and sVAD due to neck flexion.[28]

Two-sided values of p < 0.05 were considered significant. All statistical analyses were conducted using StataSE16 software (StataCorp, College Station, Texas, USA).

Results

Baseline characteristics

The clinical characteristics of the sVAD and non-sVAD groups are presented in Table 1. Fifty-three sVAD cases and 53 age- and sex-matched non-sVAD controls (42% women, median age: 49 years) were identified (Supplemental Figure 3). The onset type in the sVAD group was headache alone in 62% of the participants and cerebral infarction in 34%. In 81% of the patients, the dissection was located in the V4 segment, whereas 11% had it in the V3–4 segment. In the non-sVAD group, 58% of patients had a cerebral infarction (large artery atherosclerosis, cardioembolism, or small vessel occlusion), 26% had an intraparenchymal hemorrhage, and 6% had a transient ischemic attack (Supplemental Table 2). The distribution of potential risk factors for high-pillow usage did not vary between the sVAD and non-sVAD groups. The non-sVAD group had a higher frequency of vascular risk factors compared with the sVAD group, most likely due to the high percentage of patients with stroke.

## Association between high-pillow usage and sVAD

A high pillow with a height ≥12 cm was more common in the sVAD group than in the non-sVAD group (34% vs 15%; OR = 2.89; 95% confidence interval (CI) = 1.13–7.43). Similarly, a high pillow with a height ≥15 cm was more

Table 2. Association between high-pillow usage and sVAD.

	sVAD (*n* = 53)	Non-sVAD (*n* = 53)	Odds ratio	95% confidence interval
Pillow-usage status				
High-pillow usage, (≥12 vs <12 cm)	18 (34)	8 (15)	2.89	1.13–7.43
High-pillow usage, (≥15 vs <15 cm)	9 (17)	1 (1.9)	10.6	1.30–87.3

sVAD: spontaneous vertebral artery dissection.
Data are presented as medians (interquartile ranges) or numbers (%).
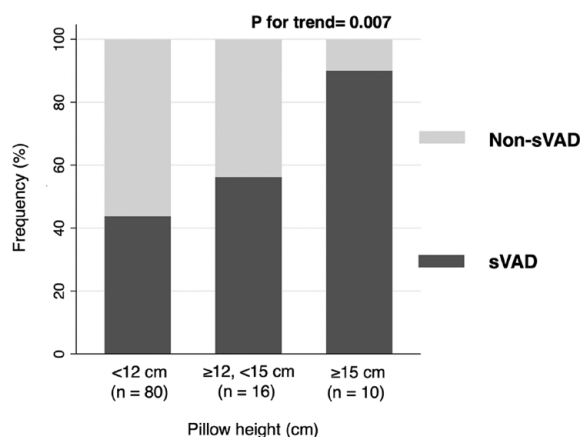
Figure 1. Prevalence of sVAD among the study participants in different pillow height categories.
Study participants were divided into three categories according to their pillow heights (<12, ≥12 and <15, and ≥15 cm). The proportion of sVAD cases increased as the pillow height increased (44 vs 56 vs 90%, respectively). The *p*-value for the trend was 0.007, using the Cochran–Armitage trend test.

common in the sVAD group than in the non-sVAD group (17% vs 1.9%; OR = 10.6; 95%CI = 1.30–87.3) (Table 2). Higher pillows tended to be associated with a higher frequency of sVADs (*p* for trend = 0.007; Figure 1). The sensitivity analyses consistently demonstrated similar or higher ORs, excluding 10 participants (four patients with sVAD and six with non-sVAD) who slept on their sides or adjusting BMI or vascular risk factors (Supplemental Table 3).

Exploring a subgroup of sVAD attributable to high-pillow usage

In the sVAD group, minor preceding trauma was identified in 42% of patients (details are shown in Table S4) and wake-up onset was identified in 25% of patients. The three conditions for high-pillow (≥12 and ≥15 cm) usage, no minor preceding trauma, and wake-up onset were met in 11.3% (95%CI = 2.7%–19.8%) and 9.4% (95%CI = 1.5%–17.3%) of all sVAD cases, respectively (Figure 2).

Modification and mediation analyses

The transition states of the study participants are shown as alluvial plots (Figure 3). Among the high-pillow (≥15 cm)

users, 80% were classified into the neck-flexion group, regardless of whether they used a hard or soft pillow. In contrast, most (78%) lower height pillow (<12 cm) users were in the straight-neck group, 16% were in the neck-flexion group, and 6.3% were in the extension group. The neck-extension group (4.7%) consisted only of individuals who used pillows <12 cm in height.

In the exploratory modification analysis, a heterogeneity was observed in the association between high-pillow (≥12 cm) usage and sVAD, with the association being more pronounced in hard pillow users (Supplemental Figure 4, *p* for interaction = 0.032). In the mediation analysis, the natural direct and indirect effects of high-pillow (≥12 cm) usage on risk of sVAD were 2.43 (95%CI = 0.89–6.62), and 1.06 (95%CI = 0.94–1.83), respectively. The proportion explained by the mediating effect of neck flexion was 30.4%.

Discussion

In a consecutive series of 53 patients with sVAD and 53 age- and sex-matched non-sVAD controls, all with East Asian ancestry, we found that high-pillow usage was associated with an increased risk of sVAD and may account for approximately 10% of sVAD cases.

This study suggested that high-pillow usage is an independent risk factor for sVAD. Moreover, the strength of the association between high-pillow usage and sVAD was comparable to that with the other established risk factors and triggers of sVAD (such as migraine, aortic enlargement, and infection).[15,29,30] Based on the trend test, the level of pillow height showed a dose-dependent association with the incidence of sVAD. These results indicate that high-pillow usage may cause sVAD. Because high-pillow usage is easily modifiable, avoiding high-pillow usage alone may prevent the development of sVAD.

Our exploratory analyses showed that the impact of high-pillow usage on sVAD may be modified by pillow hardness and partially mediated by neck flexion. Previous case reports have implicated neck overflexion in the development of sVAD by stressing the vertebral arterial wall.[31,32] However, sVAD has rarely been reported in patients with drop head due to Parkinson's disease or other neurological disorders, who may be prone to strong neck flexion, suggesting that lack of dynamics in different directions does
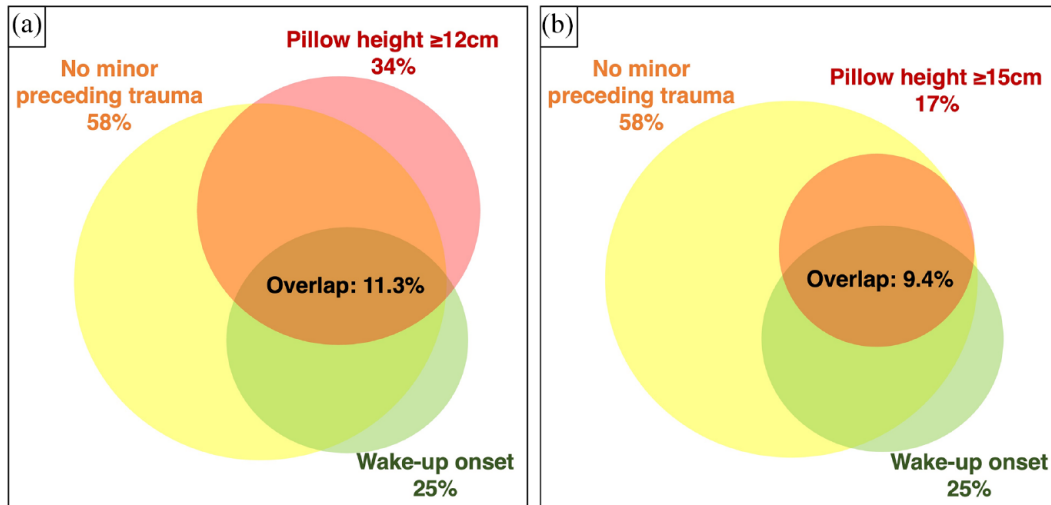
Figure 2. Area-proportional venn diagrams among the sVAD cases.
The size of the circle is expressed in proportion to the percentage size of the subgroup among the sVAD cases. Red, green, and yellow circles indicate high-pillow usage, wake-up onset, and no minor preceding trauma, respectively. The proportion meeting the three requirements was 11.3% (95%CI = 2.7%–19.8%) for high-pillow usage with a height ≥12 cm (a) and 9.4% (95%CI = 1.5%–17.3%) for ≥15 cm (b).
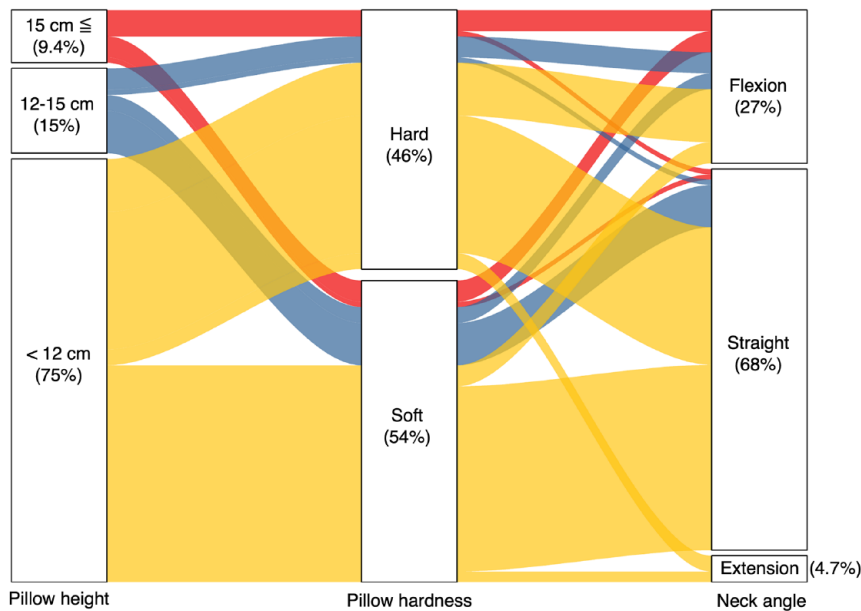

Figure 3. Alluvial plot between pillow height, pillow hardness, and neck angle.
Transition states of the study participants are shown according to their pillow height, pillow hardness, and neck angle. The study participants are classified into three categories according to their pillow height (yellow band, <12 cm; blue band, ≥12 and <15 cm; and red band, ≥15 cm).

not lead to the development of sVAD.[33] Cadaveric studies reported that the stress on the vertebral arterial wall was greatest when contralateral rotation was added to neck flexion.[34] Furthermore, soft pillows may mitigate the effects of neck flexion caused by high-pillow usage and reduce the impact on sVAD. In our dataset, the dissection sites were mostly intracranial (V4) and rare in the extracranial neck region (V1–3). This may be related to the contact of the vertebral artery with the cranium at the dural entry point, as the neck is flexed and rotated, even in pillow-related sVAD.[35] One possible explanation is that neck flexion due to high-pillow usage, potentially together with neck rotation due to tossing and turning during sleep, could cause cumulative mechanical damage to the vertebral arterial wall and intimal rupture due to the contacts with the surrounding bone or dura.

Pillow usage and other sleeping habits largely depend on cultural contexts. In Japan, between the 17th and 19th centuries, pillows as high as 12–16 cm, called Shogun pillow, were widely used to maintain the traditional laborious hairstyle in Shogun, Samurai (warriors), and Geisha (Supplemental Figure 2).[36] Several essays published in the mid-19th century indicate that it was widely believed that "a high pillow of approximately 12 cm is comfortable for living; however, a low pillow of approximately 9 cm is better for longevity" (Supplemental Figure 5).[37,38] People in those days may have been aware of this hidden association between high-pillow usage and stroke. The present study also suggests that cultural factors may partly explain the geographic disparity in sVAD occurrence.[5–8] Although there are no clear reports of regional differences in pillow height, East-Asian people generally of smaller stature than Europeans and the Americans, and thus pillows may be relatively higher for the East-Asian population. This tentative subtype of sVAD may represent a new spectrum of disease, the Shogun pillow syndrome, and further studies are needed to establish a disease concept for this subtype.

Our study has several limitations. First, the small sample size underpowered our results. Moreover, patients with less severe VAD and no SAH cases, a known characteristic of the neurology unit studies, were included.[39] Second, the pillow characteristics were not measured immediately after the onset of the index diseases, and the deformation of the pillow over time was not considered. Third, the retrospective design might have caused reporting bias. However, the pillow height being measured as an objective height and masking the risk factors of interest to the participants may have reduced this bias. Since the annual incidence of sVAD in general population is extremely low, ranging from 1 to 1.5 per 100,000 persons, a prospective study may not be feasible for our research question.[40] Fourth, the control group had a higher frequency of risk factors than the sVAD group, which may have led to an underestimation of the OR. Conversely, using hospital-based controls which originated from the same region as the cases may have reduced regional and cultural biases for pillow usage. Fifth, the definition of neck flexion based on the facial plane did not reflect the degree of tilting, potentially underestimating the effect of neck flexion. Furthermore, we did not measure other variables such as neck rotation, sleeping posture across the entire period of sleep, or mattress hardness. Finally, our sample was restricted to a specific region in Japan; therefore, extrapolation of our findings to other regions and ethnic groups remains unknown.

Conclusion

In this study, high-pillow usage was associated with an increased risk of sVAD and accounted for approximately 10% of all sVAD cases. This tentative subgroup of sVAD may represent a distinct spectrum of disease—the Shogun pillow syndrome.

Declaration of conflicting interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: MI reports lecturer fees from Otsuka and grants support from Panasonic, GE Precision Healthcare, Kyocera Corporation, Towa Pharmaceutical, and Pharma Foods International, all of which are outside the scope of the submitted work. KT reports lecturer fees from Daiichi-Sankyo, Bayer, Otsuka, Bristol-Myers-Squibb, and Novartis, all of which are outside the scope of the submitted work. MK reports lecturer fees from Bayer Yakuhin, Daiichi-Sankyo, Mitsubishi Tanabe Pharma Corporation, BMS/Pfizer, BMS/Janssen Pharmaceuticals, and Otsuka Pharmaceutical and grants support from Daiichi-Sankyo, and Nippon Boehringer Ingelheim, all of which are outside the scope of the submitted work. The other authors report no conflicts of interest for this work.

Guarantor

TT and MI.

Contributorship

Study conception: SE, TT, and MI. Acquisition of data: SE, TY, and TT. Analysis and interpretation of data and drafting of the manuscript: SE, TT, SO, KN, and MI. Editing of the manuscript for intellectual content: SE, TT, SS, SA, TY, KF, HI, EY, YH, MK, KT, SD, and MI. Supervision and funding: MI. Revising the manuscript critically for important intellectual content, final approval of the version to be published, and agreement to be accountable for all aspects of the work and ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: All authors.

Ethical approval

The institutional review board of NCVC approved the study protocol (M23-073-4) and waived the requirement for written consent based on the "opt-out" principle.

Informed consent

Written informed consent was obtained from all subjects for disclosure of any recognizable persons in photographs that may be published in the journal, in derivative works, or on the journal's website.

Trial registration

URL: https://www.clinicaltrials.gov. Unique identifier: NCT 02251665.

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Supplemental material

Supplemental material for this article is available online.

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