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Influence of Triggering Events on the Occurrence of Spontaneous Intracranial Hemorrhage : Comparison of Non-Lesional Spontaneous Intraparenchymal Hemorrhage and Aneurysmal Subarachnoid Hemorrhage

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Objective : Spontaneous intracranial hemorrhage is a life-threatening disease, and non-lesional spontaneous intraparenchymal hemorrhage (nIPH) and aneurysmal subarachnoid hemorrhage (aSAH) are the leading causes of spontaneous intracranial hemorrhage. Only a few studies have assessed the association between prior physical activity or triggering events and the occurrence of nIPH or aSAH. The purpose of this study is to investigate the role of specific physical activities and triggering events in the occurrence of nIPH and aSAH.

Methods : We retrospectively reviewed 824 consecutive patients with spontaneous intracranial hemorrhage between January 2010 and December 2018. Among the 824 patients, 132 patients were excluded due to insufficient clinical data and other etiologies of spontaneous intracranial hemorrhage. The medical records of 692 patients were reviewed, and the following parameters were assessed : age, sex, history of hypertension, smoking, history of stroke, use of antiplatelet or anticoagulation agents, season and time of onset, physical activities performed according to the metabolic equivalents, and triggering event at onset. Events that suddenly raised the blood pressure such as sudden postural changes, defecation or urination, sexual intercourse, unexpected emotional stress, sauna bath, and medical examination were defined as triggering events. These clinical data were compared between the nIPH and aSAH groups.

Results : Both nIPH and aSAH most commonly occurred during non-strenuous physical activity, and there was no significant difference between the two groups (p=0.524). Thirty-two patients (6.6%) in the nIPH group and 39 patients (8.1%) in the aSAH group experienced triggering events at onset, and there was a significant difference between the two groups (p=0.034). The most common triggering events were defecation or urination in both groups.

Conclusion : Specific physical activity dose no affect the incidence of nIPH and aSAH. The relationship between the occurrence of intracranial hemorrhage and triggering events is higher in aSAH than nIPH.

Key Words : Cerebral hemorrhage · Exercise · Precipitating factors · Subarachnoid hemorrhage.

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INTRODUCTION

The causes of spontaneous intracranial hemorrhage include non-lesional spontaneous intraparenchymal hemorrhage (nIPH), aneurysmal subarachnoid hemorrhage (aSAH), arteriovenous malformations, Moyamoya disease, and extra-axial hemorrhage. Both nIPH and aSAH remain leading the causes of spontaneous intracranial hemorrhage[6,11]. Among the risk factors for nIPH and aSAH, chronic hypertension plays an important role in their pathogenesis[12]. On the other hand, a sudden rise in blood pressure on the onset of nIPH and aSAH may be associated with specific physical activities or triggering events, but its contribution to the occurrence of nIPH or aSAH is unclear and controversial.

We hypothesized that the effect of physical activities or triggering events on the onset may be different between nIPH and aSAH patients. In this study, we aimed to elucidate the relationship between specific physical activities or triggering events and the incidence of nIPH and aSAH, and assess the differences between these two groups.

MATERIALS AND METHODS

Study population

The study protocol was approved by the Institutional Review Board of Eulji Medical Center (EMCS 2020-03-018). We reviewed 824 consecutive patients with spontaneous intracranial hemorrhage between January 2010 and December 2018. The diagnosis was confirmed by brain computed tomographic scans, and an angiography was taken to exclude other etiologies of spontaneous intracranial hemorrhage, if needed. The exclusion criteria were as follows : insufficient clinical data and other etiologies except nIPH and aSAH. Finally, 692 patients were included. The following parameters were retrospectively investigated : age, sex, history of hypertension, smoking, history of stroke, use of antiplatelet or anticoagulation agents, season : spring (March to May), summer (June to August), autumn (September to November), and winter (December to February) and time (0–6, 6–12, 12–18, and 18–24 hours) at onset, physical activities performed according to the metabolic equivalents (MET), and triggering events at onset. Physical activities according to MET are shown in Table 1[10]. Physical activities were classified into three categories : 1) inactivity (MET 1), 2) non-strenuous activity (MET 2–5), and 3) strenuous activity (MET ≥6). Events that suddenly raised the blood pressure such as sudden postural changes, defecation or urination, sexual intercourse, unexpected emotional stress, sauna bath, and medical examination were defined as triggering events. The information about physical activities and triggering events at the onset of intracranial hemorrhage was obtained from patients or witnesses when the symptom or sign was first occurred. Of the 692 patients, data on the physical activity or triggering events were available in 484 patients. The above clinical data were statistically analyzed between the nIPH and aSAH groups.

Table 1. Classification of the metabolic equivalents according to the physical activities*

Metabolic equivalents	Type of activity
1	Sleeping, resting
2	Sitting, watching television, eating, reading, desk work, driving on the highway
3	Standing, driving in the city, personal care, office work, strolling
4	Mopping, slow walking, bowling, sweeping, golfing with a cart, gardening with power tools
5	Normal walking, golfing on foot, slow biking, calisthenics, ranking leaves, cleaning windows, hanging wallpaper, hunting, fishing, housekeeping, light restaurant work
6	Slow jogging, speed-walking, tennis, swimming, shoveling snow, fast biking, picking up garbage, heavy household repairs, climbing up and down a ladder, overhead work, hurried heavy restaurant work
7	Running, fast jogging, moving boulders, changing tires, basketball, football, hanging drywall, ladder or stair climbing with a 23-kg load
8	Sprinting, fast running, jogging uphill, aggressive sports, extreme work

*Metabolic equivalents are defined as the ratio of metabolic rate during a specific physical activity to a reference metabolic rate

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Statistical analysis

Data are presented as mean±standard deviation and range for continuous variables, and categorical variables are presented as number of cases (%). The chi-square test and Fisher's exact test were used for categorical variables, and independent Student's t-test was used for continuous variables. A probability value less than 0.05 was considered to be statistically significant.

Table 2. Analysis of clinical data between nIPH and aSAH groups

Variable	nIPH group	aSAH group	*p*-value
No. of patients	395 (57.1)	297 (42.9)	
Age (years)	63.1±14.4	58.9±14.3	0.000
Sex			0.000
Male	219 (30.3)	96 (13.9)	
Female	185 (26.7)	201 (29.0)	
History of hypertension			0.000
Yes	220 (31.8)	111 (16.0)	
No	175 (25.3)	186 (26.9)	
History of DM			0.000
Yes	86 (12.4)	32 (13.2)	
No	309 (44.7)	265 (86.8)	
History of strokes			0.000
Yes	59 (8.5)	15 (2.2)	
No	336 (48.6)	282 (40.8)	
History of smoking			0.423
Yes	49 (7.1)	31 (4.5)	
No	346 (50.0)	266 (38.4)	
AntiPLT/COA			0.001
Yes	61 (8.8)	21 (3.0)	
No	334 (48.3)	276 (39.9)	
Season			0.062
Spring	104 (15.0)	70 (10.1)	
Summer	65 (9.4)	73 (10.5)	
Autumn	109 (15.8)	79 (11.4)	
Winter	117 (16.9)	75 (10.8)	
Time at onset			0.563
0–6 hour	55 (7.9)	32 (4.6)	
6–12 hour	107 (15.5)	90 (13.0)	
12–18 hour	107 (15.5)	83 (12.0)	
18–24 hour	126 (18.2)	92 (13.3)	

Values are presented as mean±standard deviation or number (%). nIPH : non-lesional spontaneous intraparenchymal hemorrhage, aSAH : aneurysmal subarachnoid hemorrhage, DM : diabetes mellitus, AntiPLT/COA : antiplatelet or anticoagulation agents

RESULTS

The mean age of the 692 patients was 61.3±14.5 years (range, 17–102). Three hundred and eighty six patients (55.8%) were women. Three hundred and ninety-five patients (57.1%) had nIPH and 297 (42.9%) aSAH.

An older age (p=0.000), male sex (p=0.000), and history of hypertension (p=0.000), diabetes mellitus (p=0.000), history of stroke (p=0.000), and taking antiplatelet or anticoagulation agents (p=0.001) were more frequently observed in the nIPH group. There were no significant differences in time (p=0.563) and season (p=0.062) at onset, but the incidence of nIPH was lower during the summer, and the incidence of aSAH was distributed evenly across all four seasons. Of the 484 patients, triggering events occurred in 71 patients (14.7%) (Table 2).

Physical activities according to MET and triggering events at onset were shown in Table 3. The mean MET score was 2.67±1.75 in the nIPH group and 2.78±1.87 in the aSAH group (p=0.564). Both nIPH and aSAH most commonly occurred during non-strenuous activity in both groups, and there was

Table 3. Analysis according to physical activity and triggering events at onset between nIPH and aSAH groups

Variable	nIPH (n=274)	aSAH (n=210)	*p*-value
MET	2.67±1.74	2.78±1.87	0.564
MET			0.507
1	56 (13.6)	42 (10.2)	
2	108 (26.2)	66 (16.0)	
3	26 (6.3)	26 (6.3)	
4	1 (0.2)	0 (0.0)	
5	29 (7.0)	16 (3.9)	
6	8 (1.9)	5 (1.2)	
7	12 (2.9)	15 (3.6)	
8	2 (0.5)	1 (0.2)	
Physical activity			0.524
Inactivity (MET 1)	57 (13.8)	42 (10.2)	
Non-strenuous (MET 2–5)	163 (39.5)	108 (26.2)	
Strenuous (MET ≥6)	22 (5.3)	21 (5.1)	
Triggering events			0.034
Yes	32 (6.6)	39 (8.1)	
No	242 (50.0)	171 (35.3)	

Values are presented as mean±standard deviation or number (%). nIPH : nonl-esional spontaneous intraparenchymal hemorrhage, aSAH : aneurysmal subarachnoid hemorrhage, MET : metabolic equivalents

no significant difference between the two groups (p=0.524). Thirty-two patients (6.6%) experienced triggering events at onset in the nIPH group and 39 patients (8.1%) experienced triggering events at onset in the aSAH group, with a significant difference between the two groups (p=0.034). In univariate analysis according to the triggering events, the known risk factors of the occurrence of intracranial hemorrhage were no significant association with the triggering events (Table 4). The most common triggering events were defecation or urination in both groups (Table 5).

In subgroup analysis, nIPH more frequently occurred after triggering events in patients with chronic hypertension than without hypertension (6.9% and 4.7%, respectively). The aSAH more frequently occurred following triggering events in patients without chronic hypertension than with hypertension (13.7% and 5.7%, respectively) (Table 6).

Table 4. Analysis of clinical data according to triggering events at onset

Variable	Triggering events (+)	Triggering events (-)	*p*-value
No. of patients	71 (14.7)	413 (85.3)	
Age (years)	58.0±15.8	60.1±13.8	0.364
Sex			0.550
Male	32 (6.6)	202 (8.1)	
Female	39 (41.7)	211 (43.6)	
History of hypertension			0.481
Yes	31 (6.4)	199 (41.1)	
No	40 (8.3)	214 (44.2)	
History of DM			0.624
Yes	13 (2.7)	66 (13.6)	
No	58 (12.0)	347 (71.7)	
History of strokes			0.569
Yes	9 (1.9)	43 (2.2)	
No	62 (12.8)	370 (76.4)	
History of smoking			0.324
Yes	11 (2.3)	47 (9.7)	
No	60 (12.4)	366 (75.6)	
AntiPLT/COA			0.499
Yes	6 (1.2)	46 (9.5)	
No	65 (13.4)	367 (75.8)	
Season			0.970
Spring	16 (3.3)	104 (21.5)	
Summer	16 (3.3)	91 (18.8)	
Autumn	20 (4.1)	114 (23.6)	
Winter	19 (3.9)	104 (21.5)	
Time at onset			0.118
0–6 hour	4 (0.8)	68 (14.0)	
6–12 hour	23 (4.8)	117 (24.2)	
12–18 hour	22 (4.5)	105 (21.7)	
18–24 hour	22 (4.5)	123 (25.4)	

Values are presented as mean±standard deviation or number (%). DM : diabetes mellitus, AntiPLT/COA : antiplatelet or anticoagulation agents

DISCUSSION

This study compared the relationship between triggering events or physical activities and two types of hemorrhagic strokes. Therefore, this study is unique from other studies which mostly investigated this relationship in patients with only one specific type of hemorrhagic stroke. In this study, we found that triggering events were identified in 14.7% of nIPH and aSAH patients, and was more frequently observed in the aSAH group than in the nIPH group. However, there was no

Table 5. Triggering events between nIPH and aSAH groups

Triggering events	nIPH (n=32)	aSAH (n=39)
Sudden postural changes	2 (2.8)	1 (1.4)
Defecation or urination	9 (12.7)	18 (25.4)
Sexual intercourse	3 (4.2)	2 (2.8)
Unexpected emotional stress	4 (5.6)	4 (5.6)
Sauna bath	6 (8.5)	13 (18.3)
Medical examination	8 (11.3)	1 (1.4)

Values are presented as number (%). nIPH : non-lesional spontaneous intraparenchymal hemorrhage, aSAH : aneurysmal subarachnoid hemorrhage

Table 6. Analysis according to triggering events at onset between nIPH and aSAH groups with or without chronic HTN

Variable	nIPN (n=274)		aSAH (n=210)	
	HTN (+)	HTN (-)	HTN (+)	HTN (-)
Triggering events				
Yes	19 (6.9)	13 (4.7)	12 (5.7)	27 (12.8)
No	136 (49.7)	106 (38.7)	63 (30.0)	108 (51.5)

Values are presented as number (%). nIPH : non-lesional spontaneous intraparenchymal hemorrhage, aSAH : aneurysmal subarachnoid hemorrhage, HTN : hypertension

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significant difference in terms of specific physical activities between the nIPH and aSAH groups. Non-strenuous physical activity was most the common cause of both nIPH and aSAH (MET 2–5). Additionally, in agreement with previous studies, older age, male sex, hypertension, diabetes, history of stroke, and use of antiplatelet or anticoagulation agents were more frequently observed in nIPH patients[1,3]. Although there were no significant differences in the time and season at onset, the incidence of nIPH was lower during the summer and the incidence of aSAH was distributed evenly throughout all seasons.

The association between the occurrence of nIPH or aSAH and physical activities or triggering events is unclear, and only a few studies have assessed this. We did not find any association between strenuous physical activity and the occurrence of nIPH or aSAH. In a retrospective study of 513 patients, aSAH occurred most frequently during inactivity or non-strenuous activity[9]. In a case control study, there was no association between physical activity at work and nIPH[16]. These findings are consistent with our results. On the contrary, a study by Passero et al.[13], which analyzed 848 patients with intracerebral hemorrhage (ICH) showed a significant association between the occurrence of hypertensive ICH and moderate (MET 5) or heavy exertion (MET ≥6). In a multi-center study, Anderson et al.[2] found that moderate to extreme physical exertion tripled the risk of aSAH, and they concluded that heavy physical activity may trigger aSAH. Furthermore, in a review of 149 patients, Fann and colleagues[4] found that the relative risk of sustaining aSAH was 11.6 in patients who engaged in strenuous physical activity compared with patients who engaged in inactivity or non-strenuous physical activity which served as the reference group. However, this association was present in a few patients (2.7%). A recent study of 543 patients with aSAH showed that moderate and high occupational physical activity increased the risk of aSAH[7]. This discrepancy may be attributed to differences in the classification of physical activity. While previous investigators included moderate exertion (MET 5) as strenuous activity, we considered it as non-strenuous activity[2,13]. In terms of the study design, previous studies adopted a case-crossover or case-control design for a single disease (nIPH or aSAH), but we investigated the difference between nIPH and aSAH.

As shown in the subgroup analysis, nIPH occurred more frequently after triggering events in patients with chronic hypertension, in contrast to aSAH patients without hypertension. Although hypertension contributes to the occurrence of nIPH and aSAH to a greater extent, this finding suggests that patients with chronic hypertension had a higher risk of developing nIPH than aSAH after triggering events. According to a retrospective study of 500 patients, aSAH occurred during stressful events such as defecation/urination, sex, sudden postural changes, and emotional strain in 42.8% of patients[15]. In a case-crossover study of 250 patients, drinking coffee or cola, nose-blowing, straining for defecation, startling, anger, sexual intercourse, and vigorous to extreme physical exercise were associated with triggering aSAH[17]. The mechanisms of aneurysm rupture during a Valsalva maneuver such as defecation, urination, and sudden postural change have not been clearly elucidated. Schievink et al.[15] suggested that a sudden rise in the arterial blood pressure with a drop in the intracranial cerebrospinal fluid pressure creates a transmural pressure gradient, and this has been implicated in rupture of an aneurysm. In addition, aSAH or nIPH may be precipitated by sexual intercourse[5,14]. In 2011, Reynolds et al.[14] proposed that coitus may be a cause of aSAH by increasing the mean arterial pressure and/or decreasing the intracranial pressure with hyperventilation at the end of an orgasmic phase based on previous studies[8]. A case series of 16 patients assessed eight patients with aSAH, four with angiogram-negative SAH, two with a ruptured arteriovenous malformation, and two with nIPH, and suggested an association between dramatic increases in the arterial blood pressure and sexual intercourse[5].

This study is limited by its retrospective nature and selection bias. Of the 692 patients included, it was impossible to identify physical activities or triggering events at nIPH or aSAH onset in 208 patients. Furthermore, we did not differentiate between the types of physical activities (i.e., leisure time or occupational).

This study investigated the association between physical activities or triggering events and the incidence of nIPH and aSAH. The physical activities were quantified and categorized by MET and this categorization was helpful to elucidate the incidence of nIPH and aSAH. However, triggering event which we defined was not quantified nor categorized. If triggering event could be quantified and categorized like physical activities by MET, this could help to distinctly explain the relationship between triggering events and spontaneous intracranial hemorrhage. Nevertheless, the understanding of triggering events or specific physical activities in the occurrence

of nIPH or aSAH may help to elucidate the pathophysiology of nIPH or aSAH. Moreover, it may be useful to investigate the triggering events for preventing rupture in patients with unruptured intracranial aneurysm.

CONCLUSION

Although the occurrence of nIPH or aSAH did not differ from the specific physical activities, this study suggests that the occurrence of aSAH may be more influenced by triggering events than that of nIPH.

CONFLICTS OF INTEREST

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

INFORMED CONSENT

This type of study does not require informed consent.

AUTHOR CONTRIBUTIONS

Conceptualization : JHN, JHK
Data curation : JHN
Formal analysis : JHK, ISB
Methodology : JHK, HIK, ISB, DRK
Project administration : JHK
Visualization : JHN, JHK
Writing - original draft : JHN, JHK
Writing - review & editing : JHN, JHK, HIK, ISB, DRK, BGM

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References

1. An SJ, Kim TJ, Yoon BW : Epidemiology, risk factors, and clinical features of intracerebral hemorrhage: an update. **J Stroke 19 :** 3-10, 2017
2. Anderson C, Ni Mhurchu C, Scott D, Bennett D, Jamrozik K, Hankey G, et al. : Triggers of subarachnoid hemorrhage: role of physical exertion, smoking, and alcohol in the Australasian Cooperative Research on Subarachnoid Hemorrhage Study (ACROSS). **Stroke 34 :** 1771-1776, 2003
3. Ariesen MJ, Claus SP, Rinkel GJ, Algra A : Risk factors for intracerebral hemorrhage in the general population: a systematic review. **Stroke 34 :** 2060-2065, 2003
4. Fann JR, Kukull WA, Katon WJ, Longstreth WT Jr : Physical activity and subarachnoid haemorrhage: a population based case-control study. **J Neurol Neurosurg Psychiatry 69 :** 768-772, 2000
5. Foreman PM, Griessenauer CJ, Selim MH, Searls DE, Safdar A, Kasper EM, et al. : Sexual activity as a trigger for intracranial hemorrhage. **Acta Neurochir (Wien) 158 :** 189-195, 2016
6. Hanel RA, Xavier AR, Mohammad Y, Kirmani JF, Yahia AM, Qureshi A : Outcome following intracerebral hemorrhage and subarachnoid hemorrhage. **Neurol Res 24Suppl 1 :** S58-S62, 2002
7. Lindbohm JV, Rautalin I, Jousilahti P, Salomaa V, Kaprio J, Korja M : Physical activity associates with subarachnoid hemorrhage risk- a population-based long-term cohort study. **Sci Rep 9 :** 9219, 2019
8. Masters WH, Johnson VE : **Human sexual response.** Boston : Little, Brown and Co., 1966, pp273-293
9. Matsuda M, Watanabe K, Saito A, Matsumura K, Ichikawa M : Circumstances, activities, and events precipitating aneurysmal subarachnoid hemorrhage. **J Stroke Cerebrovasc Dis 16 :** 25-29, 2007
10. Mittleman MA, Maclure M, Tofler GH, Sherwood JB, Goldberg RJ, Muller JE : Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exertion. Determinants of myocardial infarction onset study investigators. **N Engl J Med 329 :** 1677-1683,1993
11. Mohr JP, Caplan LR, Melski JW, Goldstein RJ, Duncan GW, Kistler JP, et al. : The Harvard Cooperative Stroke Registry: a prospective registry. **Neurology 28 :** 754-762, 1978
12. Park HS, Kang MJ, Huh JT : Recent epidemiological trends of stroke. **J Korean Neurosurg Soc 43 :** 16-20, 2008
13. Passero S, Ciacci G, Reale F : Potential triggering factors of intracerebral hemorrhage. **Cerebrovasc Dis 12 :** 220-227, 2001
14. Reynolds MR, Willie JT, Zipfel GJ, Dacey RG : Sexual intercourse and cerebral aneurysmal rupture: potential mechanisms and precipitants. **J Neurosurg 114 :** 969-977, 2011
15. Schievink WI, Karemaker JM, Hageman LM, van der Werf DJ : Circumstances surrounding aneurysmal subarachnoid hemorrhage. **Surg Neurol 32 :** 266-272, 1989

 https://doi.org/10.3340/jkns.2020.0128

16. Thrift AG, Donnan GA, McNeil JJ : Reduced risk of intracerebral hemorrhage with dynamic recreational exercise but not with heavy work activity. **Stroke 33 :** 559-564, 2002

17. Vlak MH, Rinkel GJ, Greebe P, van der Bom JG, Algra A : Trigger factors and their attributable risk for rupture of intracranial aneurysms: a case-crossover study. **Stroke 42 :** 1878-1882, 2011