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ORIGINAL RESEARCH

Prevalence of Intracranial Aneurysm in Patients With Aortic Disease in Korea: A Nationwide Population-Based Study

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BACKGROUND: Patients with aortic disease (AD) might have a higher prevalence of intracranial aneurysm (IA). The present study evaluated the prevalence of IA in patients with AD and identified potential risk factors of IA using nationwide representative cohort sample data.

METHODS AND RESULTS: We defined AD as both aortic dissections and aortic aneurysms. This study used a nationwide representative cohort sample from the Korea National Health Insurance Service–National Sample Cohort database from 1.1million patients. Using χ^2 or Fisher's exact tests, the prevalence of the IA in patients with AD and potential risk factors for their concurrence were analyzed. The prevalence of IA in patients with AD was 6.8% (155/2285). The adjusted odds ratios (OR) for having concurrent IA in patients with AD was 3.809 (95% CI, 3.191–4.546; $P<0.01$). Patients with AD and hypertension were >19 times more likely to be affected by IA (adjusted OR, 18.679; 95% CI, 16.555–21.076; $P<0.01$). Patients with AD and diabetes mellitus, old age (>60 years), and male sex were >4, 3, and 2 times more likely to be affected by IA, respectively (adjusted OR, 4.291, 3.469, and 1.983, respectively; 95% CI, 3.914–4.704, 3.152–3.878, and 1.779–2.112, respectively). Subgroup analysis with socioeconomic status or disability revealed that the prevalence of IA was significantly higher in all groups.

CONCLUSIONS: In the current population-based study, the prevalence of IA in patients with AD was quadrupled compared with that in the general population. Early IA screening might be considered among patients with AD for appropriate management.

Key Words: aortic aneurysms ■ aortic disease ■ aortic dissections ■ intracranial aneurysms ■ prevalence

The overall prevalence of aortic disease (AD) including aneurysms and dissections is estimated at around 1% to 3% in the general population, with up to 10% prevalence in older age groups.[1–3] A generalized connective tissue disorder also involving the intracranial arteries has been suspected in this patient population. Previous studies have suggested an association between AD and intracranial aneurysms (IAs) with a higher prevalence of IA in patients with AD. IA and AD are different disease entities but have similar pathophysiologic mechanisms, which may be caused by excessive hemodynamic stress to the vessel wall or genetic factors for vascular fragility.[3–11] There have been anecdotal reports concerning the relationship between IAs and other vasculopathies, such as cervicocephalic arteriopathies, bicuspid aortic valve,[12] coarctation of the aorta,[13] aortic aneurysm,[9] and dissection,[8] suggesting a common pathophysiology.[4,12–14] Understanding the prevalence of IAs, which are treatable lesions and cause significant morbidity and mortality, in the setting of concurrent AD is important. For such patients, an IA may rupture during an aortic operation by increased cerebral perfusion pressure. In the present

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CLINICAL PERSPECTIVE

What Is New?

- This is the first population-based study to evaluate the prevalence of intracranial aneurysm (IA) in patients with aortic aneurysms and dissections.
- IA in patients with aortic disease was quadrupled compared with that in the general population.
- Patients with aortic disease with risk factors (hypertension, diabetes mellitus, old age, and male sex) showed a much higher risk of having concurrent IA (19, 4, 3, and 2 times, respectively).

What Are the Clinical Implications?

- In the patients with concurrent IA and aortic disease, IA may rupture during an aortic operation by increased cerebral perfusion pressure.
- IA screening might be considered in patients with aortic disease.

Nonstandard Abbreviations and Acronyms

AD	aortic disease
IA	intracranial aneurysm
KCD	Korean classification of diseases
KNHIS	Korean national health insurance service

study, we aimed to evaluate the prevalence of IAs in patients with AD and to identify potential risk factors for IA using nationwide representative cohort sample data.

METHODS

Database

The data that support the findings of this study are available from the corresponding author upon reasonable request. All aspects of the study adhered to the tenets of the Declaration of Helsinki. This study was conducted using Korean National Health Insurance Service (KNHIS)–National Sample Cohort data (NHIS-2018-2-142), made by the National Health Insurance Service and was approved by the Institutional Review Board of Hallym Medical University Chuncheon Sacred Hospital (Institutional Review Board No. 2019-05-015-002). The need for written informed consent was waived because the KNHIS–National Sample Cohort data set consisted of deidentified secondary data for research purposes.

South Korea has maintained a nationwide health insurance system since 1963 under the KNHIS, and controls all medical costs among beneficiaries, medical facilities, and the government. The KNHIS database holds a vast amount (over 1.5 trillion cases) of inpatient and outpatient data, including diagnostic codes, length of inpatient admission, type of treatment, and prescription records. In the KNHIS, the *Korean Classification of Diseases* (*KCD*), which is a system similar to the *International Classification of Diseases,* is used as a system of diagnostic practice codes. No patient's healthcare records are duplicated or omitted because all South Korean residents receive a unique identification number at birth. The National Health Insurance Service is a compulsory healthcare plan for all Korean nationals; eligible citizens are covered through either a community- or employee-based plan. The healthcare usage database, one of the main databases run by the service, was used in the present study.

Study Cohort and Predictors

We defined AD as both aortic aneurysm and aortic dissection. The criteria we employed for extracting an AD cohort from the database were subjects who had been diagnosed at least once with *KCD* diagnosis code I71.x, including, aneurysm and dissection of aorta, any part (I71.0); thoracic aortic aneurysm, ruptured (I71.1); thoracic aortic aneurysm, without mention of rupture (I71.2); abdominal aortic aneurysm, ruptured (I71.3); abdominal aortic aneurysm, without mention of rupture (I71.4); thoracoabdominal aortic aneurysm, ruptured (I71.5); thoracoabdominal aortic aneurysm, without mention of rupture (I71.6); aortic aneurysm of unspecified site, ruptured (I71.8); and aortic aneurysm of unspecified site, without mention of rupture (I71.9). Likewise, the unruptured IA cohort was defined as those who had been diagnosed at least once with *KCD* diagnosis code I67.1. Individuals with a ruptured IA were defined as those who had been diagnosed at least once with *KCD* diagnosis code I60.x.

Details of patients' age, sex, household income, disabilities, and comorbidities were obtained from the database. For the purpose of subgroup analysis, the cohort was regrouped into younger and older groups. The cutoff used was 60 years, reflecting the peak age of onset for AD.[15,16] The cohort was divided into 10 income brackets (deciles), and then regrouped as *lower* (brackets 1–4), *middle* (brackets 5–7), or *upper* (brackets 8–10) income tiers. The study cohort was also divided from a grade of 0 to 6 according to the extent of their disability, and regrouped as normal (grade 0), moderate (grades 1–2), and severe (grades 3–6), if present. This grading system demonstrates the information from the Disability Registration System, operated by the Ministry of

Health and Welfare in Korea. It provides the presence or absence of disability and categories of disability. We analyzed comorbidities, including hypertension (*KCD* code I10) and diabetes mellitus (*KCD* code E10–E14), which are all known risk factors for AD and IA. We defined the presence of comorbidities as any diagnoses of these codes in 2018.

Statistical Analysis

A summary of demographic and baseline characteristics was constructed using descriptive analysis; the mean, maximum, minimum, and SD for quantitative variables, and the frequency and percentage for qualitative variables. Prevalence of IA with respect to the status of AD was analyzed using χ^2 tests or Fisher's exact test. The logistic regression analyses were performed for IA and confounders (sex, age groups, hypertension, and diabetes mellitus) to calculate the odds ratio (OR) and 95% CI without considering any interactions. One of the co-authors, a medical statistician, was tasked with supervision of the overall analytics procedure. All statistical analyses were performed using SAS Enterprise Guide 6.1 M1 (SAS Institute Inc., Cary, NC) and SPSS software package for Windows version 19.0 (IBM, Armonk, NY). All tests were 2-sided, and *P* values <0.05 were deemed statistically significant.

RESULTS

Baseline Characteristics

Baseline demographic information is summarized in Table 1. The whole cohort consisted of 1 113 656 individuals, with nearly equal sex distribution (M:F=50.1:49.9). For the entire cohort, "baseline" prevalence of AD, unruptured or ruptured IA, unruptured IA, and ruptured IA was computed at 0.2%, 0.6%, 0.4%, and 0.3%, respectively.

Table 1. Baseline Characteristics

Variables	n (%)
Total	1 113 656 (100.0)
Sex	
Female	555 470 (49.9)
Male	558 186 (50.1)
Age	
<60 y	994 001 (89.3)
≥60 y	119 655 (10.7)
Hypertension	
No	1 047 836 (94.1)
Yes	65 820 (5.9)
Diabetes mellitus	
No	1 073 321 (96.4)
Yes	40 335 (3.6)
Household income	
Low income (0–4)	326 695 (29.3)
Middle income (5–7)	356 214 (32.0)
High income (8–10)	430 747 (38.7)
Disability grade	
Normal (Grade 0)	1 086 953 (97.6)
Moderate (Grades 1 and 2)	9038 (0.8)
Severe (Grades 3–6)	17 665 (1.6)
Aortic disease	
No	1 111 371 (99.8)
Yes	2285 (0.2)
Unruptured or ruptured IA	
No	1 106 615 (99.4)
Yes	7041 (0.6)
Unruptured IA	
No	1 109 710 (99.6)
Yes	3946 (0.4)
Ruptured IA	
No	1 109 883 (99.7)
Yes	3773 (0.3)

IA indicates intracranial aneurysm.

Prevalence of All IA and Associated Risk Factors in Relation to AD Status

Of the 2285 individuals with AD, 155 (6.8%) had concurrently been diagnosed with IA. In contrast, the prevalence of all IA in individuals without AD (1 111 371 in total) was 0.6% (6 886 people) (Table 2). After adjustment for all included variables, patients with AD were about 4 times more likely to be affected by IA than individuals without AD (adjusted OR, 3.809; 95% CI, 3.191–4.546; *P*<0.01). Patients with AD and hypertension were roughly 19 times more likely to be affected by IA (adjusted OR, 18.679; 95% CI, 16.555–21.076; *P*<0.01). In addition, individuals with AD who were >60 years of age were roughly 3.5 times more likely to be affected by all IA compared with their younger counterparts (adjusted OR, 3.496; 95% CI, 3.152–3.878; *P*<0.01). Patients with AD and diabetes mellitus and male sex also were >4 and 2 times more likely to be affected by IA (adjusted OR, 4.291 and 1.983, respectively; 95% CI, 3.914–4.704 and 1.779–2.112, respectively). These results are summarized in Table 3.

Prevalence of Unruptured or Ruptured IA and Associated Risk Factors in Relation to AD Status

One hundred ten (4.8%) of the 2285 individuals with AD were affected with unruptured IA and 3 386 (0.3%) of the 1 111 371 individuals without AD were affected with unruptured IA. These findings were statistically

Table 2. Prevalence of Intracranial Aneurysms in Relation to Aortic Disease Status

Variables	Total n=1 111 371	Aortic Disease n=2285	*P* Value
Sex, n (%)			
Female	554 499 (49.9)	971 (42.5)	<0.01
Male	556 872 (50.1)	1314 (57.5)	
Age, n (%)			
<60 y	993 448 (89.4%)	698 (30.5%)	<0.01
≥60 y	117 923 (10.6%)	1587 (69.5%)	
Hypertension			
No	1 047 350 (94.2%)	486 (21.3%)	<0.01
Yes	64 021 (5.8%)	1799 (78.7%)	
Diabetes mellitus			
No	1 072 215 (96.5%)	1106 (48.4%)	<0.01
Yes	39 156 (3.5%)	1179 (51.6%)	
Household income			
Low income (0–4)	325 975 (29.3%)	686 (30.0%)	<0.01
Middle income (5–7)	355 674 (32.0%)	567 (24.8%)	
High income (8–10)	429 722 (38.7%)	1032 (45.2%)	
Disability grade			
Normal (Grade 0)	1 085 110 (97.6)	1933 (84.6)	<0.01
Moderate (Grades 1 and 2)	8896 (0.8)	114 (5.0)	
Severe (Grades 3–6)	17 365 (1.6)	238 (10.4)	
Unruptured or ruptured IA, n (%)			
No	1 104 485 (99.4)	2130 (93.2)	<0.01
Yes	6886 (0.6)	155 (6.8)	
Unruptured IA, n (%)			
No	1 107 535 (99.7)	2175 (95.2)	<0.01
Yes	3836 (0.3)	110 (4.8)	
Ruptured IA, n (%)			
No	1 107 671 (99.7)	2212 (96.8)	<0.01
Yes	3700 (0.3)	73 (3.2)	

IA indicates intracranial aneurysm.

significant (*P*<0.001). The patients with AD were >4 times more likely to be affected by unruptured IA (adjusted OR, 4.84; 95% CI, 3.918–5.979; *P*<0.01). The adjusted OR for unruptured IA in patients with AD and controls in the entire study sample stratified by age, sex, hypertension, and diabetes mellitus are presented in Table 4. Patients with AD and hypertension, diabetes mellitus, old age (>60 years), and male sex were >18, 4, 3, and 2 times more likely to be affected by unruptured IA, respectively.

For ruptured IA, the proportion of ruptured IA was significantly higher in individuals with AD (3.2%; 73/2285) compared with the non-AD group (0.3%; 3 700/1 111 371). The patients with AD were >3 times more likely to be affected by ruptured IA (adjusted OR, 3.23; 95% CI, 2.514–4.150; *P*<0.01). Patients with AD and hypertension, diabetes mellitus, old age (>60 years), and male sex were >19, 4, 3, and 2 times more likely to be affected by ruptured IA, respectively (Table 5).

Subgroup Analysis

Subgroup analysis with χ^2 or Fisher's exact test revealed that the pattern of AD-all IA/unruptured IA/ruptured IA relationship was valid in all household income (*P*<0.01, in all household income groups). The AD-IA relationship was also analyzed by disability status. χ^2 or Fisher's exact analysis yielded virtually the significant high prevalence of IA in all disability groups. These results are summarized in Table 6.

DISCUSSION

IAs are found in approximately 0.4% to 3% of the general population.[8] The present study demonstrated that the prevalence of IA in the general population was 0.6% and, in patients with AD, was estimated at 6.8%. This is about 11 times higher than in the general population. This trend remained 4 times higher, even after adjusting for several risk factors with age, sex, hypertension, and diabetes mellitus.

Several studies found that patients with AD had a higher prevalence of IA than the general population. Lee et al[17] reported a 22.2% net prevalence of IA in 158 patients with aortic dissection or aneurysm, which was at least 7-fold higher than in the general population and about twice as high as in similar diseased groups. Shin et al[5] reported an 11.6% prevalence of IAs in a cohort of 611 patients with aortic aneurysms. In a small study, Kuzmik et al[11] observed a 9.0% prevalence of IA in a series of 212 patients with thoracic aortic aneurysms. Some authors reported 11% of IA concurrence in patients with aortic aneurysm.[5,18] Also, IA showed higher prevalence in patients with other diseases involving the aorta. Curtis et al[14] and Schievink et al[12] evaluated 9.8% in the bicuspid aortic valve. Cook et al[19] reported that the prevalence in patients with coarctation of the aorta was 10.3%. However, there are a limited number of studies[3,17,18,20] showing the association between IA and AD. To the best of our knowledge, this is the first population-based, cross-sectional study about the prevalence of IA in patients with AD.

The reason for the high IA prevalence in patients with AD is unclear; recent studies proposed several potential explanations for the association between IAs and AD. Genetic factors may play a more significant role for IA and AD, as several congenital defects or syndromes involve the ascending aorta.[21] Regalado et al[22] suggested the possibility of a genetic link between IA and thoracic aortic aneurysm,

Table 3. Relationship Between All Intracranial Aneurysms and Aortic Disease

Variables	Aortic Disease					
	Crude			Adjusted*		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Unruptured or ruptured IA						
No						
Yes	11.672	9.899–13.763	<0.01	3.809	3.191–4.546	<0.01
Sex						
Female						
Male				1.938	1.779–2.112	<0.01
Age groups, y						
<60						
≥60				3.496	3.152–3.878	<0.01
Hypertension						
No						
Yes				18.679	16.555–21.076	<0.01
Diabetes mellitus						
No						
Yes				4.291	3.914–4.704	<0.01

IA indicates intracranial aneurysm; and OR, odds ratio.
*Adjusted by sex, age, hypertension, and diabetes mellitus.

and dissection, in a cohort of 514 families in which 29 IAs were found. They found an autosomal dominant inheritance between IA and thoracic aortic aneurysm and dissection. IA and AD may have common pathophysiologic mechanisms for its development.[18] IA and AD are characterized by degeneration of the media, and hypertension was a major risk factor.[23] Fukuda et al[20] demonstrated that both IA and AD were caused by chronic inflammation of the arterial wall in hypertensive rats. The arterial walls are continuously exposed to blood pressure and develop various forms of diseases, such as aortic dissection and IA under

Table 4. Relationship Between Unruptured Intracranial Aneurysm and Aortic Disease

Variables	Aortic Disease					
	Crude			Adjusted*		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Unruptured IA						
No						
Yes	14.602	12.025–17.731	<0.01	4.84	3.918–5.979	<0.01
Sex						
Female						
Male				1.943	1.783–2.117	<0.01
Age groups						
<60, y						
≥60, y				3.508	3.162–3.891	<0.01
Hypertension						
No						
Yes				18.846	16.703–21.264	<0.01
Diabetes mellitus						
No						
Yes				4.282	3.905–4.694	<0.01

IA indicates intracranial aneurysm; and OR, odds ratio.
*Adjusted by sex, age, hypertension, and diabetes mellitus.

Table 5. Relationship Between Ruptured Intracranial Aneurysm and Aortic Disease

	Aortic disease					
	Crude			Adjusted*		
Variables	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Ruptured IA						
No						
Yes	9.88	7.808–12.502	<0.01	3.23	2.514–4.150	<0.01
Sex						
Female						
Male				1.913	1.756–2.085	<0.01
Age groups, y						
<60						
≥60				3.511	3.165–3.894	<0.01
Hypertension						
No						
Yes				19.038	16.872–21.483	<0.01
Diabetes mellitus						
No						
Yes				4.291	3.914–4.705	<0.01

IA indicates intracranial aneurysm; and OR, odds ratio.
*Adjusted by sex, age, hypertension, and diabetes mellitus.

excessive pressure beyond physiological condition.[20] It is assumed that high hemodynamic stress loaded on the arterial walls makes a small tear in the intima of the arterial wall, which leads to IA or AD.[24] However, how the arterial wall becomes fragile to hemodynamic stress has not been fully understood. A potential explanation about vascular fragility is that the aorta and intracranial arteries embryologically originate from the neural crest cells, which comprise the tunica media of the aortic arch and its branches, and some anomalous development of these cells could explain the susceptibility to both AD and IA.[25]

Understanding the prevalence of IA in the setting of concurrent AD is important not just for long-term patient health, but also perioperatively. Clinicians should consider the likelihood of IA rupture during an aortic operation for such patients because cerebral perfusion pressure may increase temporarily by clamping or balloon occlusion of the aorta.[14] Empirical observations by one group have pointed to an increased risk of IA rupture after surgical thoracic aortic aneurysm repair (2 patients).[10] Subarachnoid hemorrhage secondary to IA rupture is a life-threatening event with substantial morbidity and mortality; 40% of hospitalized patients die within 1 month and 30% of survivors have persistent neurologic deficits.[26] In contrast, the rate of adverse outcomes after treatment of unruptured IA has been as low as 1%.[27] Therefore, early identification of IAs and measures, such as strict postoperative blood pressure control to the AD patient population, are likely to confer significant benefits. This is very important and should be taken into account when considering patients with aortic aneurysms for a systematic screening to identify IAs. Indeed, in patients with autosomal dominant polycystic kidney disease, the prevalence of associated IA was around 10% to 12%, with a 4 times higher risk.[28,29] According to this relative risk, some have advised a systematic screening with magnetic resonance angiogram for IA in autosomal dominant polycystic kidney disease.[30] The present study demonstrated that the prevalence of IA in patients with AD was estimated at 6.8%. This is about 11 times higher than in the general population. Despite a high prevalence of IA, no systematic screening for IA is proposed for patients with AD.

The present investigation is not without its limitations. First, the cross-sectional nature of the study meant that these new findings were built on the premise of the IA preceding AD in onset. The validity of this assumption is difficult to ascertain, since the exact prevalence and onset of AD tend to fluctuate from one report to another. This cross-sectional study provides concurrent prevalence of IA and AD at one point. Further studies using longitudinal data might help to reveal whether patients with AD will develop IA. Second, this study did not include all patients. Patients with AD tended to have done systemic imaging examinations including brain imaging examinations which could increase the detection rate of IA. Therefore, the patients with IA who are not evaluated for AD may escape the diagnosis. From a different perspective, the prevalence of IA in patients with AD might also be underestimated. AD

Table 6. Subgroups Analysis by Socioeconomic Status and Disability Grade

			Aortic Disease, n (%)		
Household Income			**No**	**Yes**	***P* Value**
Low (1–4)	Unruptured or ruptured IA	No	323 853 (99.3)	642 (93.6)	<0.01
		Yes	2122 (0.7)	44 (6.4)	
	Unruptured IA	No	324 862 (99.7)	658 (95.9)	<0.01
		Yes	1113 (0.3)	28 (4.1)	
	Ruptured IA	No	324 775 (99.6)	664 (96.8)	<0.01
		Yes	1200 (0.4)	22 (3.2)	
Middle (5–7)	Unruptured or ruptured IA	No	353 742 (99.5)	530 (93.5)	<0.01
		Yes	1932 (0.5)	37 (6.5)	
	Unruptured IA	No	354 663 (99.7)	543 (95.8)	<0.01
		Yes	1011 (0.3)	24 (4.2)	
	Ruptured IA	No	354 555 (99.7)	548 (96.6)	<0.01
		Yes	1119 (0.3)	19 (3.4)	
High (8–10)	Unruptured or ruptured IA	No	426 890 (99.3)	958 (92.8)	<0.01
		Yes	2832 (0.7)	74 (7.2)	
	Unruptured IA	No	428 010 (99.6)	974 (94.4)	<0.01
		Yes	1712 (0.4)	58 (5.6)	
	Ruptured IA	No	428 341 (99.7)	1000 (96.9)	<0.01
		Yes	1381 (0.3)	32 (3.1)	
Disability Grade					
Normal (0)	Unruptured or ruptured IA	No	1 078 624 (99.4)	1806 (93.4)	<0.01
		Yes	6486 (0.6)	127 (6.6)	
	Unruptured IA	No	1 081 444 (99.7)	1841 (95.2)	<0.01
		Yes	3666 (0.3)	92 (4.8)	
	Ruptured IA	No	1 081 663 (99.7)	1875 (97.0)	<0.01
		Yes	3447 (0.3)	58 (3.0)	
Moderate (1–2)	Unruptured or ruptured IA	No	8746 (98.3)	107 (93.9)	0.004
		Yes	150 (1.7)	7 (6.1)	
	Unruptured IA	No	8840 (99.4)	109 (95.6)	0.001
		Yes	56 (0.6)	5 (4.4)	
	Ruptured IA	No	8794 (98.9)	110 (96.5)	0.045
		Yes	102 (1.1)	4 (3.5)	
Severe (3–6)	Unruptured or ruptured IA	No	17 115 (98.6)	217 (91.2)	<0.01
		Yes	250 (1.4)	21 (8.8)	
	Unruptured IA	No	17 251 (99.3)	225 (94.5)	<0.01
		Yes	114 (0.7)	13 (5.5)	
	Ruptured IA	No	17 214 (99.1)	227 (95.4)	<0.01
		Yes	151 (0.9)	11 (4.6)	

IA indicates intracranial aneurysm.

was found in general systemic imaging examinations, and IA was usually diagnosed by computed tomography angiogram or magnetic resonance angiogram, which was not commonly used in general screening. Thus, the patients with IA might escape the diagnosis. The epidemiologic studies, including population with systemic image examinations, would demonstrate more exact odds ratios for having concurrent IA in patients with AD. Third, a lack of information regarding disease severity and subtype impeded a more detailed analysis. Detailed information like Stanford or DeBakey classification system for aortic disease or the exact location of the aortic aneurysm would have allowed the authors to propose a more elaborate disease mechanism. This study used *KCD* codes for disease definitions, in which it is difficult to access to the severity or exact subtype of the disease. Although this study was based on a

1-million-strong, population-based cohort, in which statistical power is hardly an issue, and selection bias less of a concern (ie, in comparison with hospital records), it might not have been completely free from the clutches of "accessibility" bias (only patients with adequate income and leisure could afford to visit the cardiologist or neurosurgeon). Additionally, KNHIS–National Sample Cohort data have been established for medical service claims and reimbursement, not for research. Further population-based studies about their exact prevalence and pathophysiologic investigations are needed to clarify their relationship.

CONCLUSIONS

The present study is the first population-based study about the prevalence of IA in patients with AD and demonstrated the prevalence of IA in patients with AD is quadrupled compared with that in the general population. This study has attempted to elicit a potential common thread between AD and IA, which may cause substantial morbidity and mortality during AD surgery. IA screening might be considered in patients with AD for appropriate management.

ARTICLE INFORMATION

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