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REVIEW

Prevalence of cerebral aneurysms in autopsy studies: a review of the literature

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Abstract

Cerebral aneurysms (CAs) are one of the most important causes of stroke, but details of their prevalence remain under-researched. Autopsy data for CAs were reviewed using standard search engines. Based on previously published autopsy and clinical studies, the prevalence of CAs with respect to age, gender, and aneurysm site, size, and multiplicity was investigated, and the natural course of CA prevalence was estimated. In autopsy studies, the prevalence of CAs across all age groups was 0.3–4.0% for unruptured cerebral aneurysms (UCAs) and 1.3–7.6% for CAs including UCAs and ruptured cerebral aneurysms (RCAs). Patients with UCAs were generally older than those with RCAs. Middle cerebral artery aneurysms were more predominant in autopsy studies than in clinical studies. UCAs tended to be smaller than RCAs, and minute UCAs (< 2 mm), diagnosed microscopically at autopsy and thought to be in the very early stages of formation, were present in 10–20% of the general population. Taking into consideration the clinical data for UCAs and RCAs, 10% of minute UCAs enlarge to major UCAs (≥ 2 mm) detectable by conventional imaging techniques, and 10% of major UCAs eventually rupture within 10 years. The high prevalence of UCAs and RCAs in the elderly and women can be attributed to the more frequent occurrence of minute UCAs in these populations. Minute UCAs occur at a high rate, but only a few enlarge to become major UCAs and rupture. Further advances in diagnostic technology are essential for revealing the true natural course of CA prevalence.

Keywords Autopsy · Cerebral aneurysm · Literature review · Natural history · Prevalence · Subarachnoid hemorrhage

Introduction

Among all subtypes of stroke, subarachnoid hemorrhage (SAH) resulting from a ruptured cerebral aneurysm (RCA) is the most serious. Despite recent diagnostic, medical, and surgical advances, the prognosis of aneurysmal SAH remains poor [34, 36, 39, 48, 49, 52, 53, 62, 68]. Previously, autopsy was an important tool for investigating cerebral aneurysms (CAs). However, advances in imaging technologies such as magnetic resonance angiography (MRA), computed tomography angiography (CTA), and digital subtraction angiography (DSA) have significantly reduced the opportunity for autopsy. Nevertheless, some of the key data from autopsy studies are still invaluable and should be kept in mind. The present review of previous autopsy studies was conducted to reaffirm the important knowledge that can be gained from them. The prevalence of CAs in autopsy studies was investigated in terms of age, gender and aneurysm site, size, and multiplicity and compared with clinical data for CAs. One of the main purposes was to provide clues as to the natural course of CA prevalence, i.e., from development of an unruptured cerebral aneurysm (UCA) to enlargement and finally to CA rupture.

Materials and methods

A comprehensive literature review of CAs investigated in autopsy studies was performed using standard search engines, including PubMed, Web of Science, and Cochrane Library. The search terms "autopsy", "cerebral aneurysm," "formation," "prevalence," and "subarachnoid hemorrhage" and their corresponding synonyms were combined with the "AND" operator. References were reviewed to identify further articles for inclusion. There were no limits with regard to dates. In this study, autopsy data for UCAs and RCAs were compared with clinical data obtained mainly

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from hospital-based and community-based studies (CBSs), respectively. Hospitalized patients with CAs are not truly representative of patients in the community because of inevitable case selection, while CBSs include all incident cases of disease, regardless of the patient's age or clinical condition. With regard to CBSs, if a large geographic area is studied, a number of patients, especially those in outlying areas, may be missed [47, 48, 82]. In such populations, many patients in poor condition, especially the elderly, may not be picked up, with the consequence that the observed incidence might be considerably lower than the actual incidence. The best understanding of CAs can be obtained from CBSs of small geographical areas that include all incident cases of disease, regardless of the age and clinical condition of the patients. Among CBSs cited in this study, the geographic areas covered by 13 of them were small with populations of less than 100,000 [34, 36–40, 42, 43, 47–49, 53, 64], and 5 covered large areas with populations of over 100,000 [41, 52, 55, 62, 68]. The Izumo Study was conducted in a small city in Japan with an area of approximately 175 km^2 and a population of 80,000 [34, 36–40, 42, 43, 47–49].

Results

Aneurysm formation and rupture

The pathogenesis of CAs is unclear and has been debated for many years. In previous autopsy studies, two basic theories concerning the etiology of aneurysm formation have been discussed: the congenital or medial defect theory [20, 26], and the acquired degenerative theory [13, 24, 72, 73]. In 1859, Gul [26] stated that aneurysms were due to a congenital developmental error or an inborn mural defect. This congenital theory became widespread. In 1930, Forbus [20] first described defects in the media of cerebral arteries. He assumed that such defects were congenital and that aneurysms arose at such sites. However, the tunica media defect theory has since been refuted by many studies. In 1940, Glynn [24] considered that tunica media defects have doubtful etiological significance in the formation of CAs, and that instead, degenerative changes in the internal elastic lamina play an essential role. It is well known that tunica media defects are prevalent in the posterior part of the normal cerebral circulation system and at the bifurcations of external and internal cranial arteries in different animals, whereas aneurysms are much less common in those areas [16, 70]. In 1963, Hassler [28] suggested that gaps in the media — or so-called medial defects — were important for aneurysm formation, whereas gaps were frequently observed even in the normal bifurcations of cerebral arteries [70]. In 1963, Stehbens [72] reported that histological changes in the aneurysm wall were similar to those in the arterial wall, and that the architectural differences between the arterial wall and the sac wall could be explained by the enormous wall expansion that occurs during aneurysm formation. On this basis, Stehbens [72, 73] concluded that CAs were acquired degenerative lesions induced by the effect of hemodynamic stress. Some authors believed that aneurysm formation could involve a combination of both congenital and acquired factors [7, 13, 80]. In 1950, Carmichael [7] theorized that defects of both the tunica media and the internal elastic lamina must be present before an aneurysm forms. Tunica media defects were usually congenital whereas internal elastic lamina defects might be due to atheroma formation, although both could occur independently. In 1954, Walker and Allegre [80] reported that atheromatous lesions were found at the sites of CAs, and that such degenerative vascular changes precipitated vascular dilatation. In 1959, Crawford [13] described three main factors that contributed to the pathogenesis of CAs; developmental faults in the media, atherosclerosis, and hypertension were considered to play roles of varying importance according to the age at which an aneurysm developed. In 1966, Crompton [15, 16] suggested that infiltration of leukocytes and fibrin into the aneurysm wall preceded expansion or rupture of the aneurysm, and that this was due to endothelial damage arising through pulsation, turbulent flow, or ischemia as a result of mural thrombosis. In 1985, an autopsy study by Anim [2] showed that hypertension increased the formation and development of CAs, whereas severe atherosclerosis of cerebral vessels was not the main pathogenetic factor in CA formation. In 1994, Kosierkiewiz [54] performed immunocytochemical studies of human saccular aneurysms and concluded that progression of atherosclerosis within the aneurysmal sac was correlated positively with aneurysm growth and might contribute to rupture. In 1999, Chyatte [11] stated that extensive inflammatory and immunological reactions were common in UCAs and might be related to aneurysm formation and rupture. These aforementioned hypotheses were based primarily on pathological findings in human autopsy cases or during surgery.

Recent clinical, experimental, and animal studies have suggested that disruption of the internal elastic lamina is the most important factor in the creation of CAs, and that hemodynamic stress and hypertension may be auxiliary factors [22, 86].

In a postmortem series of 163 RCAs by Crawford [13] in 1959, the rupture occurred at the fundus or apex of the sac in 105 cases (64%), the lateral segment in 17 (10%), the neck or proximal third of the sac in 3 (2%), and was undetermined in 38 (24%). In 1966, Crompton [15] examined the brains of 289 patients who had died of RCA, and among 271 of them, the rupture had occurred through the apex in 227 (84%), the body in 38 (14%), and the neck in only 6 (2%). When an aneurysm ruptures, hemorrhage is arrested by thrombus

formation within the sac [35, 72]. The critical size for rupture of UCAs based on autopsy studies has been estimated to be 4 mm [15, 75], 5 mm [59, 71], and 6–15 mm [13]. In any event, the critical size may differ according to patient age and aneurysm site.

Prevalence of cerebral aneurysms at autopsy

Table 1 shows the percentages of brains with aneurysms based on the number of brain examinations and the percentages of brain examinations relative to total autopsy series. In 1918, Turnbull [76] found 42 brains (0.9%) having 48 aneurysms among 4547 patients subjected to head opening. The reported prevalence of UCAs varied from 0.3 to 4.0% of total brain examinations across all age groups [3, 10, 17, 45, 58]. In a planned study of 2786 consecutive autopsies across all age groups by Chason and Hindman [10] in 1958, 137 patients (4.9%) were found to have berry aneurysms, comprising 80 (2.9%) UCAs and 57 (2.0%) RCAs. According to Berry et al. [3] in 1966, incidental asymptomatic UCAs were found in 39 (1.0%) of 3871 brains examined among a series of 6686 autopsies across all age groups. In a prospective and consecutive autopsy series performed by McCormick [58] in 1973, patients with UCAs accounted for 4.0% (114) of 2831 patients of all ages, 5.0% (114) of 2276 patients aged ≥ 1 year, and 5.9% (114) of 1945 patients aged ≥ 20 years, but no aneurysms were found in 331 patients aged 1–19 years. The reported prevalence of CAs including UCAs and RCAs has varied from 1.3 to 7.6% of total brain examinations across all age groups [3, 10, 17, 29, 45, 46, 51, 58, 71], the highest reported prevalences being 4.6% [51], 4.9% [10], 6.5% [58], and 7.6% [71]. One important aspect of CA prevalence was that women were affected more frequently than men. This trend was noted in patients with UCAs [45], RCAs [17, 25, 46], and CAs including UCAs and RCAs [10, 45, 46, 51]. The only exception was a more recent forensic autopsy study by Ronkainen [69] in 1998, in which the prevalence of UCAs in men relative to women was 27:2. The autopsy rate for men was four times higher than that for women. One explanation is that forensic autopsy material differs from the general population in having a male preponderance and a higher age, the number of autopsies increasing in older age groups.

In clinical studies, the reported prevalence of UCAs, mostly diagnosed by conventional imaging techniques, was estimated to be 1–2%, with higher detection rates for women [1, 78, 84]. The prevalence of UCAs also varies according to the assessment modality employed, i.e., MRA, CTA, or DSA. Two recent studies using 3-T MRA have reported higher prevalences of 4.3% [31] and 8.4% [30] than those reported previously. This can be explained by an increased detection rate of UCAs smaller than 3 mm due to the higher resolution of the 3-T MRA system. A systematic review of the literature on autopsy and angiography studies showed that the prevalence of UCAs in adults of the general population was approximately 2–3% [67, 79]. In a review analysis based on 51 CBSs, the overall incidence of SAH was approximately 9 per 100,000 people per year [18]. Some CBSs reported that the annual incidence of SAH was higher in men, but most other studies reported the incidence to be higher in women [36, 49, 53, 55, 64]. The incidence of aneurysmal SAH was higher in Japan than in Western countries [18, 34, 36, 47, 49, 53, 55, 64]. Nevertheless, a recent review analysis showed that the prevalence of UCAs did not differ between Japan and other Western countries [79]. In the Izumo Study [36], the crude and age- and sex-adjusted incidence rates of aneurysmal SAH were both 23 per 100,000 people per year for all ages. Furthermore, when including in the incidence calculations patients whose death certificates indicated that they might have died of aneurysmal SAH, but who had not been formally examined, the rates increased to 32 and 29 per 100,000 people per year for all ages, respectively [34]. In Izumo, patients with suspected SAH were immediately referred to a hospital irrespective of age or condition, and CT scans were performed as far as practicable to confirm SAH. Some patients who died before arrival at hospital still underwent a CT scan. One of the reasons for the high incidence of SAH in Izumo is a more aggressive diagnostic strategy employed for SAH in this small city, even in older patients with poor clinical status. These factors make it unlikely that many patients have been missed in Japanese studies, even if they are elderly. In addition, Japan has the longest life expectancy in the world, and the number of elderly patients is increasing. From CBSs [18, 36, 47], assuming that the incidence of aneurysmal SAH is 10–20 per 100,000 people per year, RCAs will occur in 0.1–0.2% of the general population in 10 years.

Age distribution of patients with cerebral aneurysms

Table 2 shows the age distributions of patients with CAs in autopsy studies. The age distributions of UCAs and RCAs were different. Namely, patients with UCAs were generally older than those with RCAs [10, 17, 45, 46, 51, 58]. Six studies have reported the age distributions of patients with UCAs and RCAs. Patients aged ≥ 70 years who had UCAs and RCAs accounted for 29% and 4% (33 of 114 and 3 of 71) [58], 39% and 13% (33 of 84, and 17 of 133) [17], 23% and 5% (9 of 39, and 7 of 131) [45, 46], 81% and 34% (22 of 27, and 10 of 29) [51], and 26% and 4% (21 of 80, and 2 of 57) [10], respectively. In autopsy studies, the peak prevalence of incidental UCAs was observed in the seventh decade [10, 17, 45, 58], whereas that of RCAs was recorded in the sixth decade [14, 17, 46, 58, 74]. According to Iwamoto et al. [51], the prevalence of UCAs increased with age, whereas

Table 1 Percentages of brains with cerebral aneurysms based on the number of brain examinations

CA/author	Year	Study Period	Country	Age	CA, *n*	Brains with CAs, *n* (%) Gender F	Gender M	Total	Brain examinations, *n* (%) Gender F	Gender M	Total	Total autopsies, *n*
UCA												
Turnbull [76]	1918	1908–1913	UK		48			42 (0.9)			4547 (66.6)	6829
Cohen [12]	1955	1951–1952	USA					9 (1.5)			593 (97.2)	610
McCaughey [57]	1956	1937–1956	UK		15			15 (0.1)			11200	
Chason and Hindman [10]	1958		USA	All ages				80 (2.9)			2786 (97.0)	2870
Berry et al. [3]	1966	1940–1960	USA	All ages				39 (1.0)			3871 (57.9)	6686
McCormick [58]	1973		USA	≥20 years				114 (5.9)			1945	
				≥1 year				114 (5.0)			2276	
				All ages				114 (4.0)			2831	
de la Monte et al. [17]	1985	1959–1984	USA	All ages	103	20	19	39 (0.3)			13042	
Inagawa and Hirano [45]	1990	1951–1987	USA	30–89 years	102	53	31	84 (0.9)			9232	
				All ages	102	53	31	84 (0.8)			10259	
Ronkainen et al. [69]	1998[a]	1994–1995	Finland	30–70 years	33	2 (1.6)	27 (5.5)	29 (4.7)	125	487	612	
Iwamoto et al. [51]	1999	1962–1991	Japan	All ages	44			27 (2.2)			1230 (98.2)	1252
Mostafazadeh et al. [63]	2008	2005–2007	Iran	≥10 years	18	6 (4.1)	8 (2.9)	14 (3.3)	148	277	425	
RCA												
Cohen [12]	1955	1951–1952	USA		13			13 (2.2)			593 (97.2)	610
McCaughey [57]	1956	1937–1956	UK		102			102 (0.9)			11200	
Chason and Hindman [10]	1958		USA	All ages				57 (2.0)			2786 (97.0)	2870
Berry et al. [3]	1966	1940–1960	USA	All ages	67			67 (1.7)			3871 (57.9)	6686
McCormick [58]	1973		USA	≥20 years				71 (3.7)			1945	
				≥1 year				71 (3.1)			2276	
				All ages				71 (2.5)			2831	
de la Monte et al. [17]	1985	1959–1984	USA	All ages	131	83	48	131 (1.0)			13042	
Inagawa and Hirano [46]	1990	1951–1987	USA	All ages	133	92	41	133 (1.3)			10259	
Iwamoto et al. [51]	1999	1962–1991	Japan	All ages	29			29 (2.4)			1230 (98.2)	1252
Gonsoulin et al. [25]	2002[a]	1977–1997	USA	All ages	221	122	97	219 (1.5)			15033	
UCA and RCA												
Garland [23]	1932	1910–1930	UK			12	20	32 (1.0)			3347 (27.9)	12000
Cohen [12]	1955	1951–1952	USA					22 (3.7)			593 (97.2)	610
McCaughey [57]	1956	1937–1956	UK		117			117 (1.0)			11200	
Chason and Hindman [10]	1958		USA	All ages		77 (7.2)	60 (3.5)	137 (4.9)	1068	1718	2786 (97.0)	2870
Housepian and Pool [29]	1958	1914–1956	USA	0–9 years				0 (0)			3000 (78.7)	3811
				≥10 years				113 (2.0)			5762 (58.2)	9893

Table 1 (continued)

CA/author	Study				CA, *n*	Brains with CAs, *n* (%)			Brain examinations, *n* (%)			Total autopsies, *n*
	Year	Period	Country	Age		Gender		Total	Gender		Total	
						F	M		F	M		
				All ages	115			113 (1.3)			8762 (63.9)	13704
Stehbens [71]	1963	1952–1954	Australia	All ages				77 (7.6)			1013 (74.3)	1364
Berry et al. [3]	1966	1940–1960	USA	All ages				106 (2.7)			3871 (57.9)	6686
McCormick [58]	1973		USA	≥ 0 years				185 (9.5)			1945	
				≥ 1 year				185 (8.1)			2276	
				All ages				185 (6.5)			2831	
Char and Persaud [9]	1984	1973–1982	Jamaica	> 10 years	84			70 (1.9)			3650	
de la Monte et al. [17]	1985	1959–1984	USA	All ages	234	103	67	170 (1.3)			13042	
Inagawa and Hirano [45, 46]	1990	1951–1987	USA	All ages	235	145	72	217 (2.1)			10259	
Iwamoto et al. [51]	1999	1962–1991	Japan	All ages	73	38 (6.7)	19 (2.9)	57 (4.6)	567	663	1230 (98.2)	1252

[a]Forensic autopsies

CA cerebral aneurysm, *F* female, *M* male, *RCA* ruptured cerebral aneurysm, *UCA* unruptured cerebral aneurysm

that of RCAs decreased with age; the mean age of patients with unruptured CAs (80.0 years) was higher than that of patients with ruptured CAs (63.5 years). The age difference between patients with UCAs and those with RCAs suggests that middle age is an important risk factor for aneurysm rupture and that most UCAs are less likely to rupture.

In clinical studies, UCAs were predominantly diagnosed in the middle-aged and older general population [1, 31, 78, 84]. CBSs showed that the incidence of aneurysmal SAH increased almost linearly with age [34, 36, 49, 53, 55, 64]. In Izumo Study, although hypertension and cigarette smoking were independent positive risk factors for aneurysmal SAH, age was not associated with an increased risk of aneurysmal SAH [37, 38, 41].

Site of cerebral aneurysms

Table 3 shows the sites of CAs reported in autopsy studies. This review study revealed that the sites of UCA in patients without SAH were the anterior cerebral artery (ACA), including the anterior communicating artery (ACoA) and distal ACA, in 27–50% of cases; the internal carotid artery (ICA) in 9–28%; the middle cerebral artery (MCA) in 25–45%; and the vertebrobasilar artery (VBA) in 0–8% [9, 45, 51, 63]. Similarly, excluding the forensic data [19, 21], RCA occurred in the ACA in 22–55% of cases, the ICA in 14–49%, the MCA in 10–38%, and the VBA in 0–21% [3, 9, 13, 14, 46, 51, 57, 83], whereas UCAs and RCAs occurred at CA sites in 16–45%, 11–50%, 15–44%, and 8–22% of cases, respectively [3, 9, 10, 23, 29, 45, 46, 51, 58, 60, 66, 71, 74, 83]. Comparing the sites of RCAs and UCAs in four studies of SAH patients with multiple aneurysms, the proportion of ACA aneurysms was higher in the RCA series (22–37%) than in the UCA series (18–23%), and the proportion of ACoA aneurysms was 30–34% for RCAs and 13–20% for UCAs [3, 9, 46, 83]. These findings suggest that ACoA aneurysms are prone to rupture [15, 32, 61]. In general, MCA aneurysms are usually encountered more often at autopsy than in clinical studies [45]. McKissock et al. [61] found that 27 UCAs had not been diagnosed during the lives of 20 of 100 complete necropsy patients who had SAH, and that the most common site for these was the MCA. Therefore, the rate of rupture of UCAs seems to be lower for MCA aneurysms than for ACA or ICA aneurysms [45]. The frequency of ruptured VBA aneurysms is higher in autopsy studies than in CBSs [42]. The difference is attributable to a higher case of fatality rate in patients with VBA aneurysms compared to patients with aneurysms at other sites. In both of two forensic studies, the proportion of ruptured VBA aneurysms was 14% [4, 21], and in one study of patients who had died immediately, the figure reached 18% (27 of 149) [21].

Table 2 Age distribution of patients with cerebral aneurysms in autopsy series

CA/author	Year	Gender	Category	Age (years)													
				–20	–29	21–30	30–39	31–40	40–49	41–50	50–59	51–60	60–69	61–70	70–79	71–	80–	Total
UCA																		
Chason and Hindman [10]	1958	Total	CA Pts, *n*	0		1		6		12		16		24		21		80
McCormick [58]	1973	Total	CA Pts, *n*		1		2		9		24		45		19		14	114
de la Monte et al. [17]	1985	Total	CA Pts, *n*		0		0		4		10		16		6		3	39
Inagawa and Hirano [45]	1990	Total	CA Pts, *n* (%)		0		2 (0.5)		3 (0.3)		13 (1)		33 (1)		22 (1)		11 (1)	84 (1)
			Autopsies, *n*		903		438		921		1868		2663		2290		1176	10,259
Iwamoto et al. [51]	1999	Total	CA Pts, *n* (%)		0		0		0		0		5 (2)		6 (2)		16 (4)	27 (2)
			Autopsies, *n*		23		34		64		111		205		379		414	1230
Ronkainen et al. [69]	1998[a]	F	CA Pts, *n* (%)				0		0		1 (5)		1 (2)					2 (2)
			Autopsies, *n*				22		24		20		59					125
		M	CA Pts, *n* (%)				1 (1)		4 (3)		12 (10)		10 (7)					27 (6)
			Autopsies, *n*				83		137		118		149					487
		Total	CA Pts, *n* (%)				1 (1)		4 (2)		13 (9)		11 (5)					29 (5)
			Autopsies, *n*				105		161		138		208					612
Mostafazadeh et al. [63]	2008	F	CA Pts, *n*	1		2		1		1		1		0				6
		M	CA Pts, *n*	0		3		3		1		0		1				8
		Total	CA Pts, *n*	1		5		4		2		1		1				14
RCA																		
Dinning and Falconer [19]	1953[a]	F	CA Pts, *n*		5		7		18		36		50		36		7	159
		M	CA Pts, *n*		7		14		16		21		21		9		3	91
		Total	CA Pts, *n*		12		21		34		57		71		45		10	250
McCaughey [57]	1956	F	CA Pts, *n*		9		11		16		11		11		4			62
		M	CA Pts, *n*		6		4		10		13		4					37
		Total	CA Pts, *n*		15		15		26		24		15		4			99
Chason and Hindman [10]	1958	Total	CA Pts, *n*	0		2		11		11		14		17		2		57
Housepian and Pool [29]	1958	F	CA Pts, *n*		8		7		18		11		5		3		2	54
		M	CA Pts, *n*		5		14		13		20		5		2		0	59
		Total	CA Pts, *n*		13		21		31		31		10		5		2	113
Crompton [14]	1962	F	CA Pts, *n*			1		6		12		19		19				60
		M	CA Pts, *n*			2		8		11		18		4				43
		Total	CA Pts, *n*			3		14		23		37		23				103
Freytag [21]	1966[a]	F	CA Pts, *n*		8		28		41		27		15		6			125
		M	CA Pts, *n*		12		30		28		38		15		2			125
		Total	CA Pts, *n*		20		58		69		65		30		8			250
Sugai and Shoji [74]	1968[b]	Total	CA Pts, *n*		5		6		25		37		16					100
McCormick [58]	1973	Total	CA Pts, *n*		5		11		19		22		11		3		0	71
Char and Persaud [9]	1984	F	CA Pts, *n*	0		3		8		11		6		7		2		37
		M	CA Pts, *n*	1		7		1		5		9		4		2		29
		Total	CA Pts, *n*	1		10		9		16		15		11		4		66
de la Monte et al. [17]	1985	Total	CA Pts, *n*		11		19		34		36		24		6		1	131
Inagawa and Hirano [46]	1990	F	CA Pts, *n*		5		10		18		24		22		10		3	92

Table 2 (continued)

CA/author	Year	Gender	Category	Age (years)													
				–20	–29	21–30	30–39	31–40	40–49	41–50	50–59	51–60	60–69	61–70	70–79	71–	80–	Total
		M	CA Pts, *n*		2		8		10		11		6		4		0	41
		Total	CA Pts, *n*		7		18		28		35		28		14		3	133
Iwamoto et al. [51]	1999	Total	CA Pts, *n* (%)		0		2 (6)		4 (6)		3 (3)		10 (5)		9 (2)		1 (0.2)	29 (2)
			Autopsies, *n*		23		34		64		111		205		379		414	1230
Gonsoulin et al.[25]	2002[a]	F	CA Pts, *n*	1		9		30		36		25		15		6		122
		M	CA Pts, *n*	2		9		23		27		28		7		1		97
		Total	CA Pts, *n*	3		18		53		63		53		22		7		219
UCA and RCA																		
Chason and Hindman [10]	1958	Total	CA Pts, *n*	0		3		17		23		30		41		23		137
Stehbens [71]	1963	F	CA Pts, *n*		13		13		31		30		34		7		2	130
		M	CA Pts, *n*		10		20		30		28		26		4		1	119
		Total	CA Pts, *n*		23		33		61		58		60		11		3	249
Berry et al. [3]	1966	F	CA Pts, *n*		3		3		14		21		16		8		4	69
		M	CA Pts, *n*		4		2		10		16		11		5		0	48
		Total	CA Pts, *n*		7		5		24		37		27		13		4	117
Sugai and Shoji [74]	1968[b]	Total	CA Pts, *n*		11		15		41		56		32					182
McCormick [58]	1973	Total	CA Pts, *n* (%)		6 (4)		13 (9)		28 (11)		46 (10)		56 (10)		22 (8)		14(10)	185 (8)
			Autopsies, *n*		474		139		259		448		540		277		139	2276
de la Monte et al. [17]	1985	Total	CA Pts, *n*		11		19		38		46		40		12		4	170
Inagawa and Hirano [45, 46]	1990	Total	CA Pts, *n*		7		20		31		48		61		36		14	217
Iwamoto et al. [51]	1999	F	CA Pts, *n* (%)		0		1 (9)		3 (14)		2 (6)		11 (14)		9 (5)		12 (5)	38 (7)
			Autopsies, *n*		12		11		21		36		76		165		246	567
		M	CA Pts, *n* (%)		0		1 (4)		1 (2)		1 (1)		4 (3)		6 (3)		6 (4)	19 (3)
			Autopsies, *n*		11		23		43		75		129		214		168	663
		Total	CA Pts, *n* (%)		0		2 (6)		4 (6)		3 (3)		15 (7)		15 (4)		18 (4)	57 (5)
			Autopsies, *n*		23		34		64		111		205		379		414	1230

CA cerebral aneurysm, *F* female, *M* male, *Pts* patients, *RCA* ruptured cerebral aneurysm, *UCA* unruptured cerebral aneurysm

[a]Forensic autopsies

[b]Studies of patients with major aneurysms measuring ≥ 2 mm

In a systematic review of UCAs found at autopsy and by angiography by Vlak et al. [79], those in the ACA accounted for 18%, those in the ICA 42%, those in the MCA 35%, and those in the VBA 5%. In the Unruptured Cerebral Aneurysm Study of Japan (UCAS Japan) [77], which was based on a large number of UCAs, the ACoA accounted for 16% of UCA sites, the ICA for 34%, the MCA for 36%, the VBA for 9%, and other sites for 6%. In CBSs, the frequency of RCAs was highest in the ACA (24–43%) and lowest in the VBA (5–14%) [42]. The frequencies of ICA aneurysms (19–29%) and MCA aneurysms (21–28%) were intermediate between them [42]. Inagawa [42] roughly estimated that the proportions of RCA sites based on CBSs were 40% for the ACA, including the ACoA and distal ACA, 25% for the ICA, 25% for the MCA, and 10% for the VBA. Therefore, in clinical studies, ACA aneurysms appear to be more common in RCA series than in UCA series, whereas ICA and MCA aneurysms are more common in UCA series.

Two autopsy studies have analyzed the site of aneurysms separately for men and women: one focused on patients with UCAs [63] and the other on patients with UCAs and RCAs [74]. Both studies found that ACoA aneurysms were more frequent in men, whereas ICA aneurysms were more common in women.

Similarly, two CBSs showed that regardless of age, ruptured ACoA aneurysms were found more frequently in men, whereas ICA aneurysms were encountered more commonly in women [42, 55].

Size of cerebral aneurysms

At autopsy, it is often extremely difficult to find a small aneurysm located within a blood clot [23]. For this reason, the presence of small aneurysms is often overlooked, which can reduce the apparent prevalence. McCormick and Acosta-Rua [59] demonstrated that the unfixed size of UCAs was 30–60% greater in maximal diameter during infusion of the cerebral arteries with a 0.9% saline solution under 70 mmHg pressure. Accordingly, they considered that an aneurysm measuring 1 cm in a living patient would measure only about 6–7 mm at autopsy. The same authors also demonstrated that there was a decrease in size of 6–12% following formalin fixation. Allowing for all these factors, the size of aneurysms 10 mm in diameter during life would decrease to 5.5–7.2 mm in autopsy material [45]. Therefore, even in autopsy examinations, CAs may be overlooked, and there is a possibility that the actual prevalence would be higher than those reported so far. Careful examination of the brain is very important to determine the exact prevalence of CAs. In clinical studies, the potential accuracy of angiography in demonstrating CAs has been investigated in a number of studies. However, in a significant number of patients who show clinical symptoms and signs of SAH, the causative lesion cannot be found. In patients in whom angiography is negative, the cause may be a small aneurysm that undergoes thrombosis within the sac, which is sometimes quite extensive [35, 72].

Table 4 shows the size of CAs in autopsy studies. Smaller aneurysms tended to be more common in UCAs than in RCAs, while larger aneurysms showed an opposite tendency [21, 45, 46, 58]. Whether or not the size of CAs differs with patient age has been a controversial issue. In autopsy studies, McCormick and Acosta-Rua [59] reported that small UCAs were more common in patients over 45 years of age, whereas larger RCAs occurred more often in patients under 50. In contrast, dealing primarily with RCAs, Sugai and Shoji [74] suggested that large aneurysms were more common in older age groups. However, Crompton [14] found no tendency for the diameter of 278 RCAs to increase with age, and Inagawa and Hirano [45] found no relationship between UCA size and patient age.

In two large clinical studies of UCAs, older patients had larger UCAs, and the size of the UCAs increased with age [8, 77]. For RCAs, some hospital-based studies have shown that the size was not related to patient age [8, 44, 50, 65, 81]. However, in the Izumo Study [43], RCAs tended to be larger in older age groups, and age (≥ 60 years of age) and cigarette smoking were independently associated with aneurysms ≥ 5 mm in diameter. Considering that the incidence of aneurysmal SAH increases with age [34, 36, 49], and atherosclerosis of the circle of Willis is more prominent in older patients [46], UCAs in the elderly may not rupture as easily as those in younger patients [43]. This may be one of the reasons why a relationship between aneurysm size and age has been suggested [43].

Regarding the relationship between aneurysm site and size, ACoA aneurysms were smaller than ICA and MCA aneurysms (Table 5) [45, 74], similar to the results of the Izumo Study [42, 43].

Multiple cerebral aneurysms

Table 6 gives details of multiple CAs found at autopsy. In this study, the proportion of multiple aneurysms was 14–19% in patients without a history of SAH [45, 63], 6–31% in patients with SAH [9, 13, 15, 19, 21, 25, 46, 57, 74, 83], and 12–36% in patients with and without SAH [3, 10, 12, 29, 45, 46, 51, 58, 60, 66, 71]. In 1958, Housepian and Pool [29] found that arteriosclerosis was more frequent in patients with multiple aneurysms than in those with single aneurysms. Regarding the relationship between age and the multiplicity of aneurysms, Sugai and Shoji [74] showed that all patients aged ≤ 29 years had a solitary aneurysm, and that after the fourth decade, the frequency of multiple aneurysms increased with age. In 1966, Crompton [15] reported that in 90 patients with multiple

Table 3 Sites of cerebral aneurysms in autopsy series

			Site, *n* (%)											
			ACA			ICA			MCA		VBA			
CA/author	Year	Gender	ACoA	Others	Total	IC-PCoA	Others	Total		VA	BA	Total	Unknown	Total
UCA in patients without SAH														
Char and Persaud [9]	1984				2 (50)		1 (25)	1 (25)	1 (25)			0 (0)		4
Inagawa and Hirano [45]	1990				28 (27)			29 (28)	37 (36)			8 (8)		102
Iwamoto et al. [51]	1999		9 (20)	8 (18)	17 (39)			4 (9)	20 (45)			3 (7)		44
Mostafazadeh et al. [63]	2008	F	2 (18)	3 (27)	5 (45)	1 (9)	1 (9)	2 (18)	4 (36)			0 (0)		11
		M	3 (43)		3 (43)			0 (0))	4 (57)			0 (0)		7
		Total	5 (28)	3 (17)	8 (44)	1 (6)	1 (6)	2 (11)	8 (44)			0 (0)		18
UCA in SAH patients with multiple CAs														
Wilson et al. [83]	1954		5 (13)	2 (5)	7 (18)	7 (18)	3 (8)	10 (26)	15 (38)			7 (18)		39
Berry et al. [3]	1966				15 (19)			24 (31)	20 (26)			18 (23)		77
Char and Persaud [9]	1984				3 (21)		2 (14)	2 (14)	5 (36)			4 (29)		14
Inagawa and Hirano [46]	1990		6 (20)	1 (3)	7 (23)			12 (40)	8 (27)		3 (10)	3 (10)		30
RCA														
Wilson et al. [83]	1954		48 (34)	5 (3)	53 (37)	48 (34)	3 (2)	51 (36)	24 (17)			15 (10)		143
McCaughey [57]	1956				36 (35)	11 (11)	13 (13)	24 (24)	37 (36)			5 (5)		102
Crawford [13]	1959		46 (28)	20 (12)	66 (40)	30 (18)		30 (18)	54 (33)			12 (7)	1 (1)	163
Crompton [14]	1962		35 (34)	6 (6)	41 (40)	21 (21)	6 (6)	27 (26)	34 (33)			0 (0)		102
Berry et al. [3]	1966				16 (22)			36 (49)	16 (22)			6 (8)		74
Freytag [21]	1966[a]		59 (24)	22 (9)	81 (32)	4 (2)	62 (25)	66 (26)	68 (27)			35 (14)		250
	1966[a,b]		31 (21)	12 (8)	43 (29)	3 (2)	43 (29)	46 (31)	33 (22)			27 (18)		149
Char and Persaud [9]	1984				21 (32)	6 (9)	1 (17)	17 (26)	25 (38)			3 (5)		66
Inagawa and Hirano [46]	1990		40 (30)	2 (2)	42 (32)			53 (40)	28 (21)	5 (4)	5 (4)	10 (8)		133
Iwamoto et al. [51]	1999		13 (45)	3 (10)	16 (55)			4 (14)	3 (10)			6 (21)		29
UCA and RCA														
Garland [23]	1932		2 (6)	3 (9)	5 (16)	2 (6)	2 (6)	4 (13)	14 (44)			7 (22)	2 (6)	32
Richardson and Hyland [66]	1941				13 (25)			13 (25)	16 (30)			11 (21)		53
Dinning and Falconer [19]	1953[a]				90 (33)			5 (2)	127 (46)			52 (19)		274
Wilson et al. [83]	1954		53 (29)	7 (4)	60 (33)	55 (30)	6 (3)	61 (34)	39 (21)			22 (12)		182
Chason and Hindman [10]	1958				61 (31)	18 (9)	45 (23)	63 (32)	53 (27)			19 (10)		196
Housepian and Pool [29]	1958		26 (23)	5 (4)	31 (27)	44 (38)	14 (12)	58 (50)	17 (15)			9 (8)		115
Stehbens [71]	1963		76 (23)	11 (3)	87 (27)			79 (24)	124 (38)			37 (11)		327
McCormick and Nofzinger [60]	1965		52 (25)	8 (4)	60 (29)	33 (16)	35 (17)	68 (33)	66 (32)			12 (6)		206
Berry et al. [3]	1966				31 (21)			60 (40)	36 (24)			24 (16)		151
Sugai and Shoji [74]	1968[c]	F	18 (23)	4 (5)	22 (28)			15 (19)	23 (29)			18 (23)		78
		M	26 (37)	2 (3)	28 (40)			7 (10)	22 (31)			13 (19)		70

Table 3 (continued)

CA/author	Year	Gender	Site, *n* (%)										
			ACA			ICA			MCA	VBA			
			Total	ACoA	Others	Total	IC-PCoA	Others	Total		VA	BA	Total	Unknown	Total
McCormick [58]	1973		44 (30)	6 (4)	50 (34)				22 (15)	45 (30)			31 (21)		148
			62 (24)	6 (2)	68 (26)				62 (24)	106 (41)			23 (9)		259
Char and Persaud [9]	1984				26 (31)	6 (7)		14 (17)	20 (24)	31 (37)			7 (8)		84
Inagawa and Hirano [45, 46]	1990				77 (29)				94 (35)	73 (28)			21 (8)		265
Iwamoto et al. [51]	1999		22 (30)	11 (15)	33 (45)	8 (11)			8 (11)	23 (32)	7 (10)	2 (3)	9 (12)		73

[a]Forensic autopsies

[b]Immediate death patients

[c]Studies of patients with major aneurysms measuring ≥ 2 mm

ACA anterior cerebral artery, *ACoA* anterior communicating artery, *BA* basilar artery, *CA* cerebral aneurysm, *F* female, *ICA* internal carotid artery, *IC-PCoA* internal carotid-posterior communicating artery, *M* male, *MCA* middle cerebral artery, *RCA* ruptured cerebral aneurysm, *SAH* subarachnoid hemorrhage, *UCA* unruptured cerebral aneurysm, *VA* vertebral artery, *VBA* vertebrobasilar artery

RCAs, the largest aneurysm had ruptured in 79 (88%), and that when the combination of ICA and MCA aneurysms was on the same side, proximal aneurysms ruptured more often.

In 1964, Wood [85] performed an angiographic study of multiple aneurysms and concluded that the largest aneurysm was the one most prone to rupture.

In the Izumo Study [40], the average annual incidence rates of SAH in patients with multiple aneurysms and in those with single aneurysms were higher in women than in men, and the age-specific incidence rates of SAH in both groups tended to increase with age. In the Izumo Study for multiple aneurysms, the RCAs were mostly larger than UCAs, and the largest were most likely to rupture [40]. Multivariate analyses demonstrated that only the size of RCAs was a significant positive predictor of multiplicity [40, 43]. There is a possibility that the greater the aneurysm size at rupture, the longer the interval from development. Furthermore, the longer the interval from development to rupture, the higher the possibility that further new aneurysms will develop, resulting in an increase in both the number and/or size of the aneurysms [40]. Aneurysm multiplicity is related mainly to aneurysm size at rupture; in other words, whether newly developed aneurysms rupture easily when they are small [40]. In CBSs, the frequency of multiple aneurysms has ranged from 18 to 34% [40, 52, 62, 68], depending mainly on the completeness of the diagnostic procedures. Inagawa [40] roughly estimated that the frequency of multiple aneurysms based on CBSs and autopsy studies was approximately 30%.

Minute cerebral aneurysms

In autopsy studies, aneurysms of microscopic size and some larger ones constitute a definite group that is seldom discovered without the aid of special measures. In 1941, Richardson and Hyland [66] reported two patients with minute unruptured berry aneurysms; one was at the MCA bifurcation and the other was at the angle between the posterior cerebral and posterior communicating arteries. Each was a minute outpouching about 2 mm in diameter, which they thought could be a very early stage of aneurysm formation. In 1958, Brolin and Hassler [5] examined 35 randomly selected brains, and although macroscopic examination did not reveal any aneurysms, four small aneurysms were discovered by microscopic examination. Hassler [27] divided CAs into two groups according to their maximum diameters in fixed preparations: minute aneurysms with a maximum diameter of less than 2 mm and major aneurysms with a maximum diameter of at least 2 mm. Sugai and Shoji [74] adopted Hassler's definition of minute and major aneurysms.

In clinical studies, UCAs a few millimeters in diameter, which were not found by preoperative angiography, were

Table 4 Size distribution of cerebral aneurysms in autopsy series

CA/author	Year	Gender		Size (mm)															
				–4	–5	2–5	5–7	8–	5–9	6–10	10–14	11–	11–15	15–19	16–19	16–20	20–	21–	Total
UCA																			
McCormick [58]	1973		CA, *n* (%)			133 (71)				46 (24)			4 (2)			2 (1)		3 (2)	188
Inagawa and Hirano [45]	1990	F	CA, *n* (%)	30 (49)					25 (41)		4 (7)			2 (3)					61
		M	CA, *n* (%)	20 (63)					8 (25)		1 (3)			3 (9)					32
		Total	CA, *n* (%)	50 (54)					33 (35)		5 (5)			5 (5)					93
RCA																			
Freytag [21]	1966[a]		CA, *n* (%)		30 (13)					155 (66)		50 (21)							235
McCormick [58]	1973		CA, *n* (%)			5 (7)				28 (39)			18 (25)			8 (11)		12 (17)	71
Inagawa and Hirano [46]	1990		CA, *n* (%)	18 (17)					50 (46)		23 (21)			9 (8)			9 (8)		109
Gonsoulin et al. [25]	2002[a]		CA, *n* (%)		92 (49)					42 (23)			33 (18)		3 (2)		16 (9)		186
UCA and RCA																			
Sugai and Shoji [74]	1968[b]		CA, *n* (%)	53 (37)			47 (33)	43 (30)											143
McCormick [58]	1973		CA, *n* (%)			138 (53)				74 (29)			22 (8)			10 (4)		15 (6)	259
Inagawa and Hirano [45, 46]	1990		CA, *n* (%)	68 (34)					83 (41)		28 (14)			14 (7)			9 (4)		202

CA cerebral aneurysm, *F* female, *M* male, *RCA* ruptured cerebral aneurysm, *UCA* unruptured cerebral aneurysm

[a]Forensic autopsies

[b]Studies of patients with major aneurysms measuring ≥ 2 mm

Table 5 Sites and sizes of cerebral aneurysms in autopsy series

CA/author	Year	Site	Size (mm)							Total
			–4	5–7	8–	5–9	10–14	15–19	20–	
UCA										
Inagawa and Hirano [45]	1990	ACoA, *n* (%)	20 (74)			6 (22)	1 (4)	0 (0)	0 (0)	27
		ICA, *n* (%)	10 (40)			10 (40)	2 (8)	3 (12)	0 (0)	25
		MCA, *n* (%)	19 (54)			12 (34)	2 (6)	2 (6)	0 (0)	35
		VBA, *n* (%)	1 (17)			5 (83)	0 (0)	0 (0)	0 (0)	6
		Total, *n* (%)	50 (54)			33 (35)	5 (5)	5 (5)	0 (0)	93
UCA and RCA										
Sugai and Shoji [74]	1968[a]	ACoA, *n* (%)	22 (50)	18 (41)	4 (9)					44
		ICA, *n* (%)	3 (14)	8 (36)	11 (50)					22
		MCA, *n* (%)	12 (27)	12 (27)	21 (47)					45
		VBA, *n* (%)	9 (39)	9 (39)	5 (22)					23
		Others, *n* (%)	7 (78)	0 (0)	2 (22)					9
		Total, *n* (%)	53(37)	47 (33)	43 (30)					143

[a]Studies of patients with major aneurysms measuring ≥ 2 mm

ACoA anterior communicating artery, *CA* cerebral aneurysm, *ICA* internal carotid artery, *MCA* middle cerebral artery, *RCA* ruptured cerebral aneurysm, *UCA* unruptured cerebral aneurysm, *VBA* vertebrobasilar artery

occasionally encountered during surgery for known aneurysms [6, 33]. However, even in the large UCAS Japan survey [77], all 6697 registered UCAs were ≥ 3 mm in size, and none were < 3 mm.

Table 7 shows the age distribution of patients with minute UCAs. In 1961, Hassler [27] autopsied a normal series of 250 individuals whose clinical signs suggested that there had been no direct cause of death in the brain and found 32 minute UCAs in 27 (11%). All of these minute UCAs were observed in 27 (19%) of 144 individuals aged ≥ 31 years, and 18 (67%) of them were ≥ 61 years of age. However, no minute aneurysms were found among 106 individuals aged ≤ 30 years. Minute UCAs were observed more frequently in women (15 of 123, 12%) than in men (12 of 127, 9%). Multiple minute aneurysms were found in 5 (19%) of 27 individuals. In addition, 8 minute UCAs were encountered in 5 of 10 patients with major RCAs. In another two patients, SAH was suspected to have been caused by rupture of minute aneurysms; one was a 46-year-old woman and the other a 46-year-old man. Sugai and Shoji [74] reported that the occurrence of minute UCAs was very frequent in SAH patients as compared with the remaining disease groups. In these two studies, minute UCAs were found in about half of patients with SAH. Minute aneurysms were observed at the junction of the cerebral arteries, as was the case for major aneurysms, and in patients with multiple aneurysms, minute aneurysms were located mostly distal to the major aneurysms, especially in the MCA [27, 74]. About 60% of minute aneurysms were located at the MCA (Table 8) [27, 74].

With increasing patient age, these minute aneurysms increased in size accompanied by arteriosclerotic changes and developed into saccular aneurysms [74]. A few of the minute aneurysms became atherosclerotic without any increase in size. Due to the fact that both minute and major aneurysms were dome-shaped and had similar histological structures, minute aneurysms were considered to be in the very early stages of formation, and major aneurysms probably originated from them [5, 27, 66, 74]. If major aneurysms develop from minute aneurysms, then the abundance of the latter would suggest that only a few minute aneurysms undergo this change [27]. The chances of a minute aneurysm growing into a major aneurysm presumably depend to a great extent upon the size of the media defect [27]. These autopsy studies suggest that CAs occur more frequently than indicated in the literature, and that many minute aneurysms are overlooked. As for the age distribution, most minute aneurysms appear from the fourth decade [27].

Discussion

To discuss the prevalence of CAs, it is more understandable to divide aneurysms into two groups according to maximum diameter: minute aneurysms measuring < 2 mm, and major aneurysms measuring ≥ 2 mm [27]. In autopsy studies involving total brain examinations across all age groups, the prevalence of CAs was 0.3–4.0% for UCAs alone [3, 10, 17, 45, 58] and 1.3–7.6% for CAs including UCAs and RCAs [3, 10, 17, 29, 45, 46, 51, 58, 71]. In patients with

Table 6 Multiple cerebral aneurysms found at autopsy

Multiple CAs/author	Year	Patients with multiple CAs, *n* (%)			Patients with CAs, *n*		
		Gender			Gender		
		F	M	Total	F	M	Total
Multiple CAs without SAH							
Inagawa and Hirano [45]	1990	13 (25)	3 (10)	16 (19)	53	31	84
Mostafazadeh et al. [63]	2008	1 (17)	1 (13)	2 (14)	6	8	14
Multiple CAs with SAH							
Dinning and Falconer [19]	1953[a]			15 (6)			250
Wilson et al. [83]	1954			27 (19)			143
McCaughey [57]	1956	10 (15)	0 (0)	10 (10)	65	37	102
Crawford [13]	1959			20 (12)			163
Crompton [15]	1966			90 (31)			289
Freytag [21]	1966[a]			30 (12)			250
Sugai and Shoji [74]	1968[b]			28 (28)			100
Char and Persaud [9]	1984	5 (14)	1 (3)	6 (9)	37	29	66
Inagawa and Hirano [46]	1990	18 (20)	6 (15)	24 (18)	92	41	133
Gonsoulin et al. [25]	2002[a]			22 (10)			219
Multiple CAs with and without SAH							
Richardson and Hyland [66]	1941			10 (33)			40
Cohen [12]	1955			8 (36)			22
Chason and Hindman [10]	1958			43 (31)			137
Housepian and Pool [29]	1958			14 (12)			113
Stehbens [71]	1963			52 (21)			252
McCormick and Nofzinger [60]	1965			38 (25)			153
Berry et al. [3]	1966			22 (19)			118
McCormick [58]	1973			48 (26)			185
Inagawa and Hirano [45, 46]	1990	31 (21)	9 (13)	40 (18)	145	72	217
Iwamoto et al. [51]	1999			12 (21)			57

CA cerebral aneurysm, *F* female, *M* male, *SAH* subarachnoid hemorrhage

[a]Forensic autopsies

[b]Studies of patients with major aneurysms measuring ≥ 2 mm

UCAs [45], RCAs [17, 25, 46], and CAs including UCAs and RCAs [10, 45, 46, 51], the prevalence of CAs was higher in women. Patients with UCAs were generally older than those with RCAs [10, 17, 45, 46, 51, 58]. UCAs tended to be smaller than RCAs, whereas the latter tended to be larger [21, 45, 46, 58]. MCA aneurysms usually predominated in autopsy material in comparison with clinical studies [45]. In autopsy studies, ACoA aneurysms were more frequent in men, but ICA aneurysms were more common in women [63, 74], and ACoA aneurysms were smaller than ICA and MCA aneurysms [45, 74]. Similar findings have also been suggested in CBSs [42, 43, 55]. In autopsy studies of SAH patients with multiple aneurysms, the proportion of ACA aneurysms was higher in RCA series than in UCA series [3, 9, 46, 83]. That is, ACoA aneurysms were prone to rupture [61]. However, most of these data were derived from patients with major aneurysms.

Minute aneurysms were found by microscopic examination at autopsy [5, 27, 66, 74] or encountered occasionally during surgery for known aneurysms [6, 33], but it is difficult to detect them using conventional imaging techniques, such as MRA, CTA, and DSA. In recent studies, 3-T MRA has improved the ability to diagnose small aneurysms 2–3 mm in diameter, but a clear diagnosis is still difficult for aneurysms smaller than 2 mm [30, 31, 56]. Autopsy studies, especially microscopic examinations, are more sensitive for detection of CAs than imaging techniques [5]. However, even autopsy can miss minute aneurysms due to post-mortem shrinkage because of blood flow arrest and formalin fixation [45, 59]. Minute aneurysms are thought to be in the very early stages of formation because of the similarity of their histological structure to major aneurysms [5, 27, 66, 74]. In terms of age distribution, minute aneurysms appear from the fourth decade and are not detected in neonates or younger age groups

Table 7 Age distribution of patients with minute unruptured cerebral aneurysms measuring < 2 mm in autopsy series

Author	Year	Group	Gender	Patients	Age (years)														
					0–10	11–20	–29	21–30	30–39	31–40	40–49	41–50	50–59	51–60	60–69	61–70	70–	71–80	81–90	Total
Hassler [27]	1961	Normal series[a]	F	Minute UCAs, *n*	0	0		0		3		4		1		7		4	0	19
				Brains with minute UCAs, *n* (%)	0 (0)	0 (0)		0 (0)		2 (33)		3 (30)		1 (10)		5 (28)		4 (20)	0 (0)	15 (12)
				Brain examinations, *n*	37	8		6		6		10		10		18		20	8	123
			M	Minute UCAs, *n*	0	0		0		0		0		3		5		5	0	13
				Brains with minute UCAs, *n* (%)	0 (0)	0 (0)		0 (0)		0 (0)		0 (0)		3 (25)		5 (26)		4 (25)	0 (0)	12 (9)
				Brain examinations, *n*	42	7		6		9		13		12		19		16	3	127
			Total	Minute UCAs, *n*	0	0		0		3		4		4		12		9	0	32
				Brains with minute UCAs, *n* (%)	0 (0)	0 (0)		0 (0)		2 (13)		3 (13)		4 (18)		10 (27)		8 (22)	0 (0)	27 (11)
				Brain examinations, *n*	79	15		12		15		23		22		37		36	11	250
Sugai and Shoji [74]	1968	SAH		Minute UCAs, *n*			0		2		16		23		4		5			50
				Brain examinations, *n*			5		6		25		37		16		11			100
		ICH		Minute UCAs, *n*					0		0		4		0		2			6
				Brain examinations, *n*					2		3		10		6		7			28
		Others		Minute UCAs, *n*			1		0		0		1		0		1			3
				Brain examinations, *n*			6		7		13		9		10		9			54
		Total		Minute UCAs, *n*			1		2		16		28		4		8			59
				Brain examinations, *n*			11		15		41		56		32		27			182

F female, *ICH* intracerebral hemorrhage, *M* male, *SAH* subarachnoid hemorrhage, *UCA* unruptured cerebral aneurysm

[a]Clinical signs suggest that there is no direct cause of death in the brain

Table 8 Sites of minute unruptured cerebral aneurysms measuring < 2 mm in autopsy series

			Site of minute UCAs, *n* (%)								
			ACA				ICA		MCA	VBA	
Author	Year	Gender	ACoA	Others	Total	IC-PCoA	Others	Total			Total
Hassler [27]	1961		6 (19)	1 (3)	7 (22)	4 (13)	1 (3)	5 (16)	20 (63)	0 (0)	32 (100)
Sugai and Shoji [74]	1968	F	2 (8)	2 (8)	4 (17)			1 (4)	18 (75)	1 (4)	24 (100)
		M	4 (15)	5 (19)	9 (35)			4 (15)	12 (46)	1 (4)	26 (100)
		Total	6 (12)	7 (14)	13 (26)			5 (10)	30 (60)	2 (4)	50 (100)

ACA anterior cerebral artery, *ACoA* anterior communicating artery, *F* female, *ICA* internal carotid artery, *IC-PCoA* internal carotid-posterior communicating artery, *M* male, *MCA* middle cerebral artery, *UCA* unruptured cerebral aneurysm, *VBA* vertebrobasilar artery

[27], suggesting that aneurysms are acquired lesions. The high prevalence of UCAs and RCAs in the elderly and in women can be attributed to the more frequent development of minute aneurysms in these populations. With regard to the sites of minute aneurysms and major aneurysms, MCA aneurysms accounted for a much higher proportion of the former [27, 74]. In patients with ipsilateral ICA and MCA aneurysms, proximal aneurysms tended to rupture more easily [15]. Therefore, hemodynamic stress on dilation from minute aneurysms to major aneurysms may be weaker in MCA aneurysms than at other aneurysm sites, resulting in a high frequency of minute MCA aneurysms [45]. If so, hemodynamic stress may not contribute much to aneurysm formation, as the frequency of minute MCA aneurysms is high. Recent clinical studies have discussed risk factors for the development and rupture of CAs based on the prevalence of major aneurysms [38, 41]. However, risk factors for the development of CAs that have been discussed previously appear to be risk factors for the enlargement of minute aneurysms to major aneurysms rather than the formation of minute aneurysms. The true risk factors for the development of CAs should be studied in relation to minute aneurysms. After minute aneurysms develop, most of them are stable, but some become unstable as they enlarge to major aneurysms. Some major UCAs remain unruptured, and the size of UCAs increases with age. In this situation, new minute aneurysms may develop, resulting in multiple aneurysms. However, some UCAs will eventually rupture as UCAs grow to a critical size that varies with age and aneurysm site [13, 15, 59, 71, 75].

As the prevalence of minute aneurysms is much higher than that of major aneurysms, only a small number of the former develop to the latter [27, 74]. To date, most autopsy and clinical studies have discussed major aneurysms, and the exact prevalence of minute aneurysms is unknown. In the present study, due to the poor autopsy data for minute aneurysms, their prevalence was tentatively estimated by taking into account the prevalence of minute and major UCAs at autopsy. As a result, it can be hypothesized from this review analysis that, in the very early stages, minute aneurysms will develop in approximately 10–20% of the general population mostly after middle age [27, 74]. Minute aneurysms are difficult to detect by conventional imaging techniques, but some enlarge to major aneurysms that can be diagnosed in this way. In clinical studies, the reported prevalence of UCAs, mostly diagnosed by conventional imaging techniques, is estimated to be 1–2% among the general population, mainly in middle-aged and older individuals, with higher detection rates in women [1, 78, 84]. In CBSs, CAs will rupture in 0.1–0.2% of the general population within 10 years [18, 36, 47]. The prevalence of RCAs increases with age and is higher in women [34, 36]. As a rough estimate, the following assumptions are possible. In a general population of 10,000, minute UCAs will develop in 1000–2000 individuals (10–20%), minute UCAs will enlarge to major UCAs in 100–200 (1–2%), and major UCAs will eventually rupture in 10–20 (0.1–0.2%) within 10 years. In other words, minute UCAs will develop in 10–20% of the general population, 10% of minute UCAs will enlarge to major UCAs, and 10% of major UCAs will eventually rupture within 10 years. At present, risk factors for the development and enlargement of minute aneurysms are unknown and difficult to investigate. In the future, advances in imaging technology such as MRA, CTA, and DSA may enable more accurate diagnosis of minute aneurysms. If so, risk factors for the development and enlargement of minute aneurysms may become clearer.

Conclusions

Despite dramatic improvements in imaging techniques, such as MRA, CTA, and DSA, the diagnosis of small CAs is still limited. In autopsy studies, UCAs tended to be smaller than RCAs, and patients with UCAs were generally older than those with RCAs. Microscopic examination at autopsy revealed the existence of minute CAs (< 2 mm), which are considered to be in a very early stage of aneurysm formation. Minute UCAs were occasionally seen during surgery

on known aneurysms, but it is difficult to detect them using conventional imaging techniques. Most of the minute CAs were located at the MCA. Based on autopsy and clinical studies, it can be hypothesized that minute UCAs develop in 10–20% of the general population, that 10% of minute UCAs enlarge to major UCAs (≥ 2 mm) detectable by conventional imaging techniques, and that 10% of major UCAs will eventually rupture within 10 years. The high prevalence of UCAs and RCAs in the elderly and in women can be attributed to the more frequent development of minute aneurysms in these populations. However, a potential limitation of this study was that data on minute CAs has been scant to date, and it is not expected that more such autopsy data will be available in the future. Further advances in diagnostic technology may lead to the detection of minute CAs, and if so, the natural course of CA prevalence may be clarified more accurately.

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Declarations

Ethics approval and consent to participate Not applicable.

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References

1. Agarwal N, Gala NB, Choudhry OJ, Assina R, Prestigiacomo CJ, Duffis EJ, Gandhi CD (2014) Prevalence of asymptomatic incidental aneurysms: a review of 2,685 computed tomographic angiograms. World Neurosurg 82:1086–1090. https://doi.org/10.1016/j.wneu.2013.01.082
2. Anim JT (1985) Cerebral macroaneurysms in a Ghanaian adult population. An autopsy study. Atherosclerosis 54:37–42. https://doi.org/10.1016/0021-9150(85)90151-0
3. Berry RG, Alpers BJ, White JC (1966) The site, structure and frequency of intracranial aneurysms, angiomas and arteriovenous abnormalities. Res Publ Assoc Res Nerv Ment Dis 41:40–72
4. Bowen DA (1984) Ruptured berry aneurysms: a clinical, pathological and forensic review. Forensic Sci Int 26:227–234. https://doi.org/10.1016/0379-0738(84)90027-6
5. Brolin SE, Hassler O (1958) Minute aneurysms, detected by microdissection of basal cerebral arteries. Acta Pathol Microbiol Scand 44:59–63. https://doi.org/10.1111/j.1699-0463.1958.tb01053.x
6. Burkhardt JK, Chua MH, Winkler EA, Rutledge WC, Lawton MT (2019) Incidence, classification, and treatment of angiographically occult intracranial aneurysms found during microsurgical aneurysm clipping of known aneurysms. J Neurosurg 132:434–441. https://doi.org/10.3171/2018.11.JNS182416
7. Carmichael R (1950) The pathogenesis of noninflammatory cerebral aneurysms. J Pathol Bacteriol 62:1–19. https://doi.org/10.1002/path.1700620102
8. Carter BS, Sheth S, Chang E, Sethl M, Ogilvy CS (2006) Epidemiology of the size distribution of intracranial bifurcation aneurysms: smaller size of distal aneurysms and increasing size of unruptured aneurysms with age. Neurosurgery 58:217–223. https://doi.org/10.1227/01.NEU.0000194639.37803.F8
9. Char G, Persaud V (1984) Berry aneurysms of the circle of Willis. Results of an autopsy study at the University Hospital of the West Indies. West Indian Med J 33:151–157
10. Chason JL, Hindman WM (1958) Berry aneurysms of the circle of Willis; results of a planned autopsy study. Neurology 8:41–44. https://doi.org/10.1212/WNL.8.1.41
11. Chyatte D, Bruno G, Desai S, Todor DR (1999) Inflammation and intracranial aneurysms. Neurosurgery 45:1137–1146. https://doi.org/10.1097/00006123-199911000-00024 (discussion 1146-1147)
12. Cohen MM (1955) Cerebrovascular accidents; a study of two hundred one cases. AMA Arch Pathol 60:296–307
13. Crawford T (1959) Some observations on the pathogenesis and natural history of intracranial aneurysms. J Neurol Neurosurg Psychiatry 22:259–266. https://doi.org/10.1136/jnnp.22.4.259
14. Crompton MR (1962) Intracerebral haematoma complicating ruptured cerebral berry aneurysm. J Neurol Neurosurg Psychiatry 25:378–386. https://doi.org/10.1136/jnnp.25.4.378
15. Crompton MR (1966) Mechanism of growth and rupture in cerebral berry aneurysms. Br Med J 1(5496):1138–1142. https://doi.org/10.1136/bmj.1.5496.1138
16. Crompton MR (1966) The pathogenesis of cerebral aneurysms. Brain 89:797–814. https://doi.org/10.1093/brain/89.4.797
17. de la Monte SM, Moore GW, Monk MA, Hutchins GM (1985) Risk factors for the development and rupture of intracranial berry aneurysms. Am J Med 78(6 Pt 1):957–964. https://doi.org/10.1016/0002-9343(85)90218-9
18. de Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ (2007) Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry 78:1365–1372. https://doi.org/10.1136/jnnp.2007.117655
19. Dinning TAR, Falconer MA (1953) Sudden or unexpected natural death due to ruptured intracranial aneurysm; survey of 250 forensic cases. Lancet 265(6790):799–801. https://doi.org/10.1016/S0140-6736(53)90467-X
20. Forbus WD (1930) On the origin of miliary aneurysms of superficial cerebral arteries. Bull Johns Hopkins Hosp 47:239–284
21. Freytag E (1966) Fatal rupture of intracranial aneurysms. Survey of 250 medicolegal cases. Arch Pathol 81:418–424
22. Frösen J, Tulamo R, Paetau A, Laaksamo E, Korja M, Laakso A, Niemelä M, Hernesniemi J (2012) Saccular intracranial aneurysm: pathology and mechanisms. Acta Neuropathol 123:773–786. https://doi.org/10.1007/s00401-011-0939-3
23. Garland HG (1932) The pathology of aneurysm: a review of 167 autopsies. J Pathol Bacteriol 35:333–350
24. Glynn LE (1940) Medial defects in the circle of Willis and their relation to aneurysm formation. J Pathol Bact 51:213–222
25. Gonsoulin M, Barnard JJ, Prahlow JA (2002) Death resulting from ruptured cerebral artery aneurysm: 219 cases. Am J Forensic Med Pathol 23:5–14. https://doi.org/10.1097/00000433-200203000-00002
26. Gull WM (1859) Cases of aneurism of the cerebral vessels. Guys Hosp Rep 5:281–304
27. Hassler O (1961) Morphological studies on the large cerebral arteries, with reference to the aetiology of subarachnoid haemorrhage. Acta Psychiatr Scand Suppl 154:1–145
28. Hassler O (1963) Media defects in human arteries. Angiology 14:368–371
29. Housepian EM, Pool JL (1958) A systematic analysis of intracranial aneurysms from the autopsy file of the Presbyterian Hospital,

1914 to 1956. J Neuropathol Exp Neurol 17:409–423. https://doi.org/10.1097/00005072-195807000-00001
30. Igase K, Matsubara I, Igase M, Miyazaki H, Sadamoto K (2012) Initial experience in evaluating the prevalence of unruptured intracranial aneurysms detected on 3-tesla MRI. Cerebrovasc Dis 33:348–353. https://doi.org/10.1159/000336015
31. Imaizumi Y, Mizutani T, Shimizu K, Sato Y, Taguchi J (2018) Detection rates and sites of unruptured intracranial aneurysms according to sex and age: an analysis of MR angiography-based brain examinations of 4070 healthy Japanese adults. J Neurosurg 130:573–578. https://doi.org/10.3171/2017.9.JNS171191
32. Inagawa T (1990) Multiple intracranial aneurysms in elderly patients. Acta Neurochir (Wien) 106:119–126. https://doi.org/10.1007/BF01809453
33. Inagawa T (1991) Surgical treatment of multiple intracranial aneurysms. Acta Neurochir (Wien) 108:22–29. https://doi.org/10.1007/BF01407662
34. Inagawa T (1997) What are the actual incidence and mortality rates of subarachnoid hemorrhage? Surg Neurol 47:47–52. https://doi.org/10.1016/S0090-3019(96)00370-9 (discussion 52-53)
35. Inagawa T (1999) Dissection from fundus to neck for ruptured anterior and middle cerebral artery aneurysms at the acute surgery. Acta Neurochir (Wien) 141:563–570. https://doi.org/10.1007/s007010050344
36. Inagawa T (2001) Trends in incidence and case fatality rates of aneurysmal subarachnoid hemorrhage in Izumo City, Japan, between 1980–1989 and 1990–1998. Stroke 32:1499–1507. https://doi.org/10.1161/01.STR.32.7.1499
37. Inagawa T (2002) Seasonal variation in the incidence of aneurysmal subarachnoid hemorrhage in hospital- and community-based studies. J Neurosurg 96:497–509. https://doi.org/10.3171/jns.2002.96.3.0497
38. Inagawa T (2005) Risk factors for aneurysmal subarachnoid hemorrhage in patients in Izumo City, Japan. J Neurosurg 102:60–67. https://doi.org/10.3171/jns.2005.102.1.0060
39. Inagawa T (2005) Trends in surgical and management outcomes in patients with aneurysmal subarachnoid hemorrhage in Izumo city, Japan, between 1980–1989 and 1990–1998. Cerebrovasc Dis 19:39–48. https://doi.org/10.1159/000081910
40. Inagawa T (2009) Incidence and risk factors for multiple intracranial saccular aneurysms in patients with subarachnoid hemorrhage in Izumo City, Japan. Acta Neurochir (Wien) 151:1623–1630. https://doi.org/10.1007/s00701-009-0479-y
41. Inagawa T (2010) Risk factors for the formation and rupture of intracranial saccular aneurysms in Shimane, Japan. World Neurosurg 73:155–164. https://doi.org/10.1016/j.surneu.2009.03.007 (discussion e23)
42. Inagawa T (2010) Site of ruptured intracranial saccular aneurysms in patients in Izumo City, Japan. Cerebrovasc Dis 30:72–84. https://doi.org/10.1159/000314623
43. Inagawa T (2010) Size of ruptured intracranial saccular aneurysms in patients in Izumo City, Japan. World Neurosurg 73:84–92. https://doi.org/10.1016/j.surneu.2009.07.001 (discussion e11)
44. Inagawa T, Hada H, Katoh Y (1992) Unruptured intracranial aneurysms in elderly patients. Surg Neurol 38:364–370. https://doi.org/10.1016/0090-3019(92)90023-G
45. Inagawa T, Hirano A (1990) Autopsy study of unruptured incidental intracranial aneurysms. Surg Neurol 34:361–365. https://doi.org/10.1016/0090-3019(90)90237-J
46. Inagawa T, Hirano A (1990) Ruptured intracranial aneurysms: an autopsy study of 133 patients. Surg Neurol 33:117–123. https://doi.org/10.1016/0090-3019(90)90020-P
47. Inagawa T, Ishikawa S, Aoki H, Takahashi M, Yoshimoto H (1988) Aneurysmal subarachnoid hemorrhage in Izumo City and Shimane Prefecture of Japan. Incidence. Stroke 19:170–175. https://doi.org/10.1161/01.STR.19.2.170
48. Inagawa T, Takahashi M, Aoki H, Ishikawa S, Yoshimoto H (1988) Aneurysmal subarachnoid hemorrhage in Izumo City and Shimane Prefecture of Japan. Outcome Stroke 19:176–180. https://doi.org/10.1161/01.STR.19.2.176
49. Inagawa T, Tokuda Y, Ohbayashi N, Takaya M, Moritake K (1995) Study of aneurysmal subarachnoid hemorrhage in Izumo City, Japan. Stroke 26:761–766. https://doi.org/10.1161/01.STR.26.5.761
50. Inagawa T, Yamamoto M, Kamiya K, Ogasawara H (1988) Management of elderly patients with aneurysmal subarachnoid hemorrhage. J Neurosurg 69:332–339. https://doi.org/10.3171/jns.1988.69.3.0332
51. Iwamoto H, Kiyohara Y, Fujishima M, Kato I, Nakayama K, Sueishi K, Tsuneyoshi M (1999) Prevalence of intracranial saccular aneurysms in a Japanese community based on a consecutive autopsy series during a 30-year observation period. The Hisayama study. Stroke 30:1390–1395. https://doi.org/10.1161/01.STR.30.7.1390
52. Kaminogo M, Yonekura M, Shibata S (2003) Incidence and outcome of multiple intracranial aneurysms in a defined population. Stroke 34:16–21. https://doi.org/10.1161/01.STR.0000046763
53. Kiyohara Y, Ueda K, Hasuo Y, Wada J, Kawano H, Kato I, Sinkawa A, Ohmura T, Iwamoto H, Omae T, Fujishima M (1989) Incidence and prognosis of subarachnoid hemorrhage in a Japanese rural community. Stroke 20:1150–1155. https://doi.org/10.1161/01.STR.20.9.1150
54. Kosierkiewicz TA, Factor SM, Dickson DW (1994) Immunocytochemical studies of atherosclerotic lesions of cerebral berry aneurysms. J Neuropathol Exp Neurol 53:399–406. https://doi.org/10.1097/00005072-199407000-00012
55. Kozák N, Hayashi M (2007) Trends in the incidence of subarachnoid hemorrhage in Akita Prefecture, Japan. J Neurosurg 106:234–238. https://doi.org/10.3171/jns.2007.106.2.234
56. Li MH, Li YD, Gu BX, Cheng YS, Wang W, Tan HQ, Chen YC (2014) Accurate diagnosis of small cerebral aneurysms ≤5 mm in diameter with 3.0-T MR angiography. Radiology 271:553–560. https://doi.org/10.1148/radiol.14122770
57. McCaughey WTE (1956) Ruptured intracranial aneurysms. Ulster Med J 25:111–118
58. McCormick WF (1973) Intracranial arterial aneurysm: a pathologist's view. Curr Concepts Cererbrovasc Dis Stroke 8:15–19
59. McCormick WF, Acosta-Rua GJ (1970) The size of intracranial saccular aneurysms. An autopsy study. J Neurosurg 33:422–427. https://doi.org/10.3171/jns.1970.33.4.0422
60. McCormick WF, Nofzinger JD (1965) Saccular intracranial aneurysms: an autopsy study. J Neurosurg 22:155–159. https://doi.org/10.3171/jns.1965.22.2.0155
61. McKissock W, Richardson A, Walsh L, Owen E (1964) Multiple intracranial aneurysms. Lancet 1:623–626. https://doi.org/10.1016/S0140-6736(64)91449-7
62. Menghini VV, Brown RD Jr, Sicks JD, O'Fallon WM, Wiebers DO (2001) Clinical manifestations and survival rates among patients with saccular intracranial aneurysms: population-based study in Olmsted County, Minnesota, 1965 to 1995. Neurosurgery 49:251–256. https://doi.org/10.1097/00006123-200108000-00003 (discussion 256-258)
63. Mostafazadeh B, Farzaneh Sheikh E, Afsharian Shishvan T, Seraji FN, Salmasian H (2008) The incidence of berry aneurysm in the Iranian population: an autopsy study. Turk Neurosurg 18:228–231
64. Ohkuma H, Fujita S, Suzuki S (2002) Incidence of aneurysmal subarachnoid hemorrhage in Shimokita, Japan, from 1989 to 1998. Stroke 33:195–199. https://doi.org/10.1161/hs0102.101891
65. Qureshi AI, Sung GY, Suri MF, Straw RN, Guterman LR, Hopkins LN (2000) Factors associated with aneurysm size in patients with subarachnoid hemorrhage: effect of smoking and aneurysm location. Neurosurgery 46:44–50. https://doi.org/10.1093/neurosurgery/46.1.44

66. Richardson JC, Hyland HH (1941) Intracranial aneurysms: a clinical and pathological study of subarachnoid and intracerebral haemorrhage caused by berry aneurysms. Medicine 20:1–83
67. Rinkel GJ, Djibuti M, Algra A, van Gijn J (1998) Prevalence and risk of rupture of intracranial aneurysms: a systematic review. Stroke 29:251–256. https://doi.org/10.1161/01.STR.29.1.251
68. Rinne J, Hernesniemi J, Puranen M, Saari T (1994) Multiple intracranial aneurysms in a defined population: prospective angiographic and clinical study. Neurosurgery 35:803–808. https://doi.org/10.1227/00006123-199411000-00001
69. Ronkainen A, Miettinen H, Karkola K, Papinaho S, Vanninen R, Puranen M, Hernesniemi J (1998) Risk of harboring an unruptured intracranial aneurysm. Stroke 29:359–362. https://doi.org/10.1161/01.STR.29.2.359
70. Stehbens WE (1959) Medial defects of the cerebral arteries of man. J Pathol Bacteriol 78:179–185. https://doi.org/10.1002/path.1700780119
71. Stehbens WE (1963) Aneurysms and anatomical variation of cerebral arteries. Arch Pathol 75:45–64
72. Stehbens WE (1963) Histopathology of cerebral aneurysms. Arch Neurol 8:272–285. https://doi.org/10.1001/archneur.1963.00460030056005
73. Stehbens WE (1989) Etiology of intracranial berry aneurysms. J Neurosurg 70:823–831. https://doi.org/10.3171/jns.1989.70.6.0823
74. Sugai M, Shoji M (1968) Pathogenesis of so-called congenital aneurysms of the brain. Acta Pathol Jpn 18:139–160
75. Suzuki J, Ohara H (1978) Clinicopathological study of cerebral aneurysms. Origin, rupture, repair, and growth. J Neurosurg 48:505–514. https://doi.org/10.3171/jns.1978.48.4.0505
76. Turnbull HM (1918) Intracranial aneurysms. Brain 41:50–56
77. UCAS Japan Investigators, Morita A, Kirino T et al (2012) The natural course of unruptured cerebral aneurysms in a Japanese cohort. N Engl J Med 366:2474–2482. https://doi.org/10.1056/NEJMoa1113260
78. Vernooij MW, Ikram MA, Tanghe HL, Vincent AJ, Hofman A, Krestin GP, Niessen WJ, Breteler MM, van der Lugt A (2007) Incidental findings on brain MRI in the general population. N Engl J Med 357:1821–1828. https://doi.org/10.1056/NEJMoa070972
79. Vlak MH, Algra A, Brandenburg R, Rinkel GJ (2011) Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. Lancet Neurol 10:626–636. https://doi.org/10.1016/S1474-4422(11)70109-0
80. Walker AE, Allegre GW (1954) The pathology and pathogenesis of cerebral aneurysms. J Neuropathol Exp Neurol 13:248–259. https://doi.org/10.1097/00005072-195401000-00020
81. Weir B, Disney L, Karrison T (2002) Sizes of ruptured and unruptured aneurysms in relation to their sites and the ages of patients. J Neurosurg 96:64–70. https://doi.org/10.3171/jns.2002.96.1.0064
82. Whisnant JP, Sacco SE, O'Fallon WM, Fode NC, Sundt TM Jr (1993) Referral bias in aneurysmal subarachnoid hemorrhage. J Neurosurg 78:726–732. https://doi.org/10.3171/jns.1993.78.5.0726
83. Wilson G, Riggs HE, Rupp C (1954) The pathologic anatomy of ruptured cerebral aneurysms. J Neurosurg 11:128–134. https://doi.org/10.3171/jns.1954.11.2.0128
84. Winn HR, Jane JA Sr, Taylor J, Kaiser D, Britz GW (2002) Prevalence of asymptomatic incidental aneurysms: review of 4568 arteriograms. J Neurosurg 96:43–49. https://doi.org/10.3171/jns.2002.96.1.0043
85. Wood EH (1964) Angiographic identification of the ruptured lesion in patients with multiple cerebral aneurysms. J Neurosurg 21:182–198. https://doi.org/10.3171/jns.1964.21.3.0182
86. Yong-Zhong G, van Alphen HA (1990) Pathogenesis and histopathology of saccular aneurysms: review of the literature. Neurol Res 12:249–255. https://doi.org/10.1080/01616412.1990.11739952