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Epidemiological Characteristics and Surgical Outcomes of Unruptured Intracranial Aneurysms: A Real-world Study

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Abstract

BACKGROUND: This study was aimed at epidemiological analysis of unruptured intracranial aneurysms (IAs) regarding their location, size, multiplicity, type of intervention provided, and associated complications in the Kazakhstani population.

METHODS: We performed a retrospective analysis of a cohort of 400 patients diagnosed with IA admitted to the Central Clinical Hospital of Almaty, Republic of Kazakhstan, a referral hospital for the treatment of cerebrovascular disease. Patients admitted between January 1, 2019 and December 31, 2019 with radiologically confirmed diagnosis of unruptured IA were included in the study.

RESULTS: Overall, there were 400 patients with a 2.8 female/male ratio. The bulk of aneurisms – 96.0% – were of size <25 mm in diameter and single. Median age of patients was 55 years and the youngest patient was 22-years-old, while the oldest patient aged 83 years. The left internal carotid artery (ICA) was the most common site if IA localization followed by the right ICA. The left and right middle cerebral arteries were the second most common localization sites. More than a half of patients presented with aneurysm-related complications before the intervention, of which subarachnoid hemorrhage was the most common type. Embolization with or without stenting was performed in more than 50% of patients and 96.5% of all surgeries were not associated with complications.

CONCLUSION: There is a need for careful consideration of clinical characteristics and surgical outcomes of patients with unruptured IA in a real-world practice as these data are needed for the development of management strategies.

Introduction

Intracranial aneurysm (IA) is an acquired vascular abnormality manifesting as bulging of the arterial wall. Over past decades, unruptured IA is being increasingly detected due to the frequent use of imaging studies in clinical practice [1]. The prevalence of IA ranges between 1% and 5% and they account for about 80–85% of spontaneous subarachnoid hemorrhages. The latter has high mortality rate ranging from 25% to 50% and up to half of the survivors develop some degree of disability. Still, the majority of IA (up to 80%) does not rupture during a lifespan [2].

Women are around 3 times more predisposed to IA as compared with men. Although IA is predominantly sporadic, there is hereditary form associated with certain congenital disorders. A positive family history is an important risk factor for IA and the risk for developing an aneurism during a lifespan constitutes 4% for individuals with one affected first-degree family member and 8–10% for individuals with two or more affected family members. Moreover, aneurysm multiplicity is more typical for individuals with positive family history [3]. Modifiable risk factors include arterial hypertension, smoking, and alcohol use. Like female gender and genetic predisposition, age is a non-modifiable risk factor and the peak of incidence is observed at the age of 50–60 years [1].

Magnetic resonance angiography and computed tomography angiography are two most common techniques used to detect unruptured IA. With improved sensitivity, they can identify aneurysms as small as 3–4 mm in diameter. However, smaller aneurisms can only be visualized through cerebral arteriography [4]. Bifurcations of the circle of Willis and internal carotid artery (ICA) are the most common sites of IA location in adults. Other sites include anterior and posterior communicating arteries, proximal middle cerebral artery, anteroinferior cerebellar artery, basilar artery, posteroinferior cerebellar artery, and superior cerebellar artery [2]. IA of large size (more than 10 mm in diameter) is associated with aneurysmal mass effect that may include cranial nerve deficits, seizures, sensory, and motor deficits. Sometimes unruptured IA is detected on imaging studies performed for headaches or other reasons [5].

There is a dearth of international studies published within the past decade on epidemiology of IA in different world nations. This study was aimed at epidemiological analysis of intracranial aneurysms regarding their location, size, multiplicity, type of intervention provided, and associated complications in the Kazakhstani population. These data are needed for planning and evaluation of existing health-care programs targeted on management of unruptured IA.

Materials and Methods

Study design and procedures

This was a retrospective study based on medical records obtained from the Central Clinical Hospital of Almaty, Republic of Kazakhstan (hereafter – Kazakhstan) for the period from 01/01/2019 to 31/12/2019. This is the referral hospital for the treatment of cerebrovascular disease in Kazakhstan. The inclusion criteria were: Medical records of patients with unruptured IA having the code I67.1 according to the International Classification of Diseases, Revision 10 [6]. The diagnosis of unruptured IA was made by a neurologist based on clinical presentation and digital subtraction angiography or computed tomography angiography reports. From the patient records, the following data were extracted: Gender, age, and place of residence; localization, multiplicity, and size of IA; length of hospital stay, type of surgical intervention provided, and pre- and post-surgical complications. The size of IA used in the analysis was based on the biggest diameter of IA.

A total of 407 patient cases were analyzed, seven of which were excluded because the information was considered as incomplete. Thus, the resulting sample size comprised 400 patients with unruptured IA. The study was approved by the Local Ethics Committee of the Kazakh Medical University of Continuing Education (extract from the protocol №31 dated September 28, 2018). When collecting personal information of patients, the principles depictured in the declaration of Helsinki were observed.

Statistical analysis

All statistical analyses and was performed using IBM SPSS Statistics 20 software. The mode of data distribution was assessed before the application of any statistical test by the Shapiro–Wilk test. Since the data distribution has proven to be non-normal, non-parametric tests were utilized. Significance level of $\alpha < 0.05$ was used. All quantitative data were reported as absolute numbers with their percentages.

Table 1: General characteristics of study sample (n=400)

Characteristics	N	%
Age, median, and 25–75 procentiles, years*	55	46–63
Gender		
Female	294	73.5
Male	106	26.5
Region		
Almaty City	126	31.5
Almaty Region	91	22.8
West Kazakhstan Region	2	0.5
Turkestan Region	24	6.0
Zhambyl Region	50	12.5
Shymkent City	12	3.0
Mangystau Region	1	0.3
Karaganda Region	7	1.8
East Kazakhstan Region	10	2.5
Kyrgyzstan	21	5.3
Pavlodar Region	1	0.3
Kyzylorda Region	19	4.8
Aktobe Region	23	5.8
Kostanay Region	4	1.0
Atyrau Region	5	1.3
Nur-Sultan City	4	1.0
Source of financing		
Government budget	376	94.7
Out-of-pocket expenses	21	5.3
Size of IA#		
<25 mm	384	96.0
>25 mm	16	4.0
Multiplicity of IA#		
Single	396	99.0
Multiple	4	1.0
Hospital stay, median, and 25–75 procentiles, days	6	4–9

#IA: Intracranial Aneurysm. *Min: 22, Max: 83.

Results

Table 1 presents the basic characteristics of patients under study. The majority of patients (54.3%) resided in Almaty city and Almaty region, followed by Zhambyl and Turkestan regions (12.5% and 6.0%, respectively). Very few patients were referred from Western provinces of Kazakhstan – Mangystau and West-Kazakhstan regions (0.3% and 0.5%, respectively). Nearly, all patients (94.7%) were operated for the government expense and the rest paid for the surgery out-of-pocket. The bulk of aneurisms – 96.0% – were of size <25 mm in diameter and single. Median age of patients in this study was 55 years; the youngest patient was 22-years-old and the oldest patient aged 83 years (Figure 1).

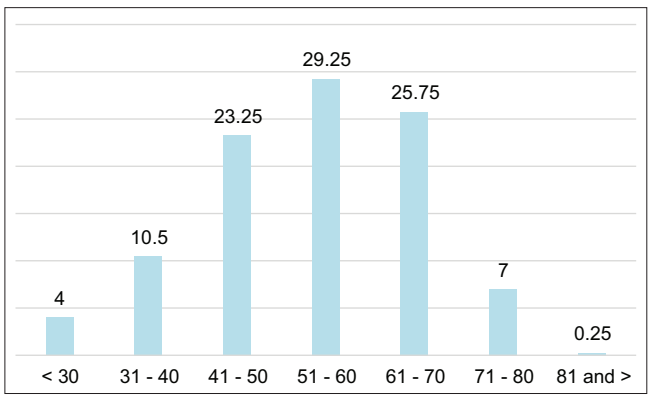

Figure 1: Distribution of patients with intracranial aneurysms by age

According to the Table 2, the left ICA was the most common site if IA localization followed by the right ICA. The left and right middle cerebral arteries were the second most common localization

Table 2: Number of aneurysms depicted by size and location

Location	Size					
	<25 mm		>25 mm		Total	
	n	%	n	%	n	%
Left ICA	147	38.3	8	50.0	155	38.8
Right ICA	70	18.2	3	18.8	73	18.3
Cavernous segment	8	2.1	0	0.0	8	2.0
Left MCA	57	14.8	1	6.3	58	14.5
Right MCA	54	14.1	4	25.0	58	14.5
Anterior cerebral – anterior communicating artery	37	9.6	0	0.0	37	9.3
Anterior cerebral artery	6	1.6	0	0.0	6	1.5
Posterior circulation	5	1.3	0	0.0	5	1.3
Total	384	100.0	16	100.0	400	100.0

ICA: Internal carotid artery, MCA: Middle cerebral artery.

sites: 14.5% each. Only aneurisms of small size (<25 mm) localized in cavernous segment, anterior cerebral artery, posterior circulation, and anterior communicating artery. Overall, aneurysms larger than 25 mm in size were observed rather seldom (4%).

Types of interventions provided and complications present before and after the intervention are presented in Table 3. Such, the majority of patients (51.8%) had complications before surgery and subarachnoid hemorrhage was the most common of these. Other complications were observed with lesser frequency and transient ischemic attack was the least common pre-surgical complication. Embolization alone or in combination with stenting were performed in more than a half of all cases (65.6%), while extracranial-intracranial bypass was performed just in 6.0% of cases. Subarachnoid hemorrhage with breakthrough into the ventricular system was the most typical complication following the surgery (seven cases – 50.0%). Liquorrea and hemorrhagic stroke were seen in one case (7.1%) each. Five patients died after the intervention and the lethality rate was 1.3%.

Table 3: Pre- and post-surgery characteristics and types of interventions

Characteristics	N	%
Complication before surgery		
No	193	48.3
Yes	207	51.8
Type of complication before surgery		
Subarachnoid hemorrhage	142	68.6
Ischemic stroke	22	10.6
Hemorrhagic stroke	32	15.5
Intraventricular hemorrhage	7	3.4
Transient ischemic attack	4	1.9
Type of intervention		
Digital subtraction angiography	114	28.5
Embolization of aneurysm	233	58.3
Embolization and stenting	29	7.3
Low-flow EC IC bypass*	24	6.0
Complication after surgery		
No	386	96.5
Yes	14	3.5
Typeof complication after surgery		
Subarachnoid hemorrhage with breakthrough into the ventricular system	7	50.0
Central retinal artery occlusion	0	0.0
Liquorrea	1	7.1
Hemiplegia	0	0.0
Hemorrhagic stroke	1	7.1
Intracerebral hematoma	0	0.0
Death	5	35.7
Surviving		
Survived	395	98.8
Died	5	1.3

EC IC bypass*: Extracranial-intracranial bypass.

Discussion

This epidemiological study was performed on a consecutive series of Kazakhstani patients with unruptured IA. Overall, there were 400 patients with a 2.8 female/male ratio. The vast majority of aneurisms was of small size, single, and located in the left or right ICA. More than a half of patients presented with aneurysm-related complications before the intervention, of which subarachnoid hemorrhage was the most common type. Embolization with or without stenting was performed in more than 50% of patients and 96.5% of all surgeries were not associated with early complications. There is lack of data on epidemiology of IA in certain areas of the world [7]. To the best of our knowledge, this is the only study involving Central Asian patients diagnosed with unruptured IA. Other studies have reported on a series of Kyrgyz patients with ruptured IA [8] and on genetics of IA in Kazakhstani patients [9].

A large proportion of patients in our study were of female gender and this finding is consistent with other published data. Such, in Finland, the proportion of patients of female gender was 54% [10], while that in China was 62% [11]. In Japan, 68% of patients with IA were females [12] as compared to 72% in the USA and Europe [13]. Probably, the highest proportion of female patients with IA (77.6%) was reported by the Brazilian investigators [14]. Thus, our findings are in line with international data, being particularly close to the proportions reported by the European and North American investigators.

The median age of patients in our study was 55 years and this was very similar to the international reports that show an average age of 50 years [15]. Of interest is the fact that female patients with unruptured IA tend to be older than male patients. Perhaps, this could be attributed to the protective role of estrogen in pre-menopausal women [16]. It might be hypothesized that vascular protective activity of estrogen manifests both through indirect effects on lipoprotein metabolism and direct effects on vascular wall [17]. However, according to the Qureshi and coauthors, hormone replacement therapy should not be recommended to post-menopausal women with unruptured IA as it is associated with an elevated risk of subarachnoid hemorrhage [18]. Thus, more studies are needed to clarify the role played by estrogen in the natural history of IA.

Aneurisms of smaller size were predominant in our study and this finding is supported by the earlier reports [14], [19]. Size is an important risk factor for IA rupture: The annual rupture rates constituted 3.3% for aneurysms sized 10–15 mm, 5.6% for aneurysms presenting with the diameter of 16–25 mm, and 8.9% for aneurysms larger than 25 mm [13]. Aneurysm size is the major factor influencing the decision on the need for surgical intervention. Such, patients with IA >7 mm in size are most commonly referred for the surgery and so do the patients with IA sized >3 mm in the presence of other risk factors for aneurysm rupture [20]. The rate of multiple

aneurisms in our study was relatively small, while globally as many as 20–30% patients harbor multiple IA [21].

In this study, aneurysms from the anterior circulation greatly predominated over those from the posterior circulation. According to the international findings [12], [14], most aneurysms localize in the middle cerebral arteries and the internal carotid arteries and our data support this evidence. Like the aneurysm size, location is also an important risk factor for aneurysm rupture. Aneurysms localizing in the anterior communicating and posterior communicating arteries are known to be most prone to rupture [22]. At present, there is no agreement on proneness to rupture of posterior circulation aneurysms. Although some investigators conclude on their greater tendency to rupture [13], other does not support this finding [12].

The decision on management of unruptured IA should be made with considering the risks of rupture if IA is left without intervention and the risks associated with a surgery by itself. Endovascular interventions are being extensively used in surgery of IA and these include coiling, stenting, and embolization by liquid embolic agents [23]. Meta-analysis conducted by Naggara *et al*. identified the 4–5% risk of unfavorable outcomes following endovascular management of unruptured IA and the 1–2% risk of death [24]. In our study, the overall rate of early surgical complications constituted 3.5% with the risk of mortality of 1.25%, which is consistent with the international findings.

Because there is a lack of published data on surgical outcomes of patients with IA in a real-world setting, the results of this research could be useful for both evaluation and planning of medical services. The resulting service improvement will lead not just to enhance outcomes but also increased patient satisfaction, which has been substantially compromised in Kazakhstani patients over past years [25].

This study has a number of strengths but also limitations, which mostly originate from its retrospective design. The main strength is that it includes a reasonable number of consecutive patients with unruptured IA operated in a large referral center. The main limitation is unavailability of data on coexisting pathologies and risk factors associated with IA development and progression. In general, epidemiological studies on unruptured IA could be very difficult to perform for a number of reasons. First, sudden deaths associated with IA rupture may happen outside the hospital setting and could stay unverified. Second, as many IA are silent and do not rupture during a lifespan, it is very difficult to assess their prevalence. Thus, it would be reasonable to conclude that perfect studies on the epidemiology of unruptured IA literally do not exist. Still, it does not mean that the search of answers on pathophysiology and management of unruptured IA should be stopped, as more data are needed to enable the higher standards of care for this vulnerable category of patients.

Conclusion

This study investigates important characteristics of a large number of Kazakhstani patients with unruptured IA regarding aneurysm location, size, multiplicity, type of intervention, and associated complications. There is a need for careful consideration of clinical characteristics and surgical outcomes of patients with unruptured IA in a real-world practice. It is of big importance to monitor how these patients are managed in reality to envisage modern treatment approaches. It might prove to be useful to introduce a national IA registry in Kazakhstan to obtain information needed to develop the targeted management strategies and to improve patient survival.

Authors Contributors

All authors have contributed to manuscript writing and review and have approved the final version.

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