



Original Article

Outcome of Cerebral Aneurysm Clipping in Nigeria: A Single-Centre Experience

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Abstract

Background: Ruptured cerebral artery aneurysms (RCAA) are devastating diseases with high morbidity and mortality rates if not promptly managed. In Nigeria, access to timely neurosurgical services remains a challenge and aneurysm coiling is still not possible in virtually all centres in Nigeria. The aim of this study is to report on our 9 years' experience with clipping of cerebral aneurysm and on the attendant clinical outcomes.

Methodology: A retrospective analysis of all consecutive operated RCAA between March 2012 and June 2021 was conducted. Patients' demographic parameters, World Federation of Neurosurgical Societies (WFNS) grade, Hunt and Hess (HH) grade, aneurysm location, timing of surgery and outcome were analysed. Outcome was measured using Glasgow Outcome Scale (GOS) score.

Results: A total 29 were included in the study. The most common age group affected was between 50-59 years. RCAA were mainly in the region of the middle cerebral artery and posterior communicating artery (PCoMA) territories. All the patients presented after 24 hours of the ictus. Two (6.9%) patients had multiple aneurysms. Early clipping (<72hours after presentation) was possible in 8 (27.6%) patients. At least one episode of a rebleed occurred in 19 (65.5%) patients prior to surgery. Mortality rate was 17.2%. None of the patients with PCoMA aneurysm died. The patients' pre-operative WFNS and HH grades were significantly associated with GOS.

Conclusion: Modifiable factors like under diagnoses, delayed referral, cultural belief and financial challenges may account for the low number of patients presenting for neurosurgical care. The possibility of a sizeable number of patients dying due to these factors is a strong possibility for the low number of patients presenting for neurosurgical care.

Keywords: Aneurysm; Anterior Communicating Artery; Clipping; Middle Cerebral Artery; Posterior Communicating Artery.

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Introduction

Cerebral artery aneurysms are out pouching of a weakened arterial wall. It has a prevalence of 2–4% in the general population.[1] They are usually silent over their lifetime, but they sometimes rupture.

A ruptured cerebral artery aneurysm (RCAA) can lead to subarachnoid, intraparenchymal, and or subdural haemorrhage. Several complications ranging from rebleeding, hyponatraemia from hypothalamic injury, cardiac arrhythmias, vasospasm, obstructive hydrocephalus and death have been associated with RCAA. This clinical condition is a neurosurgical emergency with case fatality rate that has declined from 35.4% in 2000 to 27.2% in 2015.[2] Though the high mortality rate of RCAA has decreased over the decades, it still remains a devastating neurologic problem. Approximately 10-15% of patients dying before reaching the hospital has been reported;[3] with 30% of survivors suffering moderate-to-severe neurological disability following RCAA. [4,5]

The demography, relative frequency and site of RCAA vary among different populations. In the western countries they are relatively common with an estimated incidence of 6.9 per 100,000 people in North America.[3] The demography, incidence and outcome of RCAA are probably related to socio-economic and health system of various communities. The true incidences of these aneurysms are not known in Nigeria and most African countries. Tokpa and his colleagues in Côte d'Ivoire noted 128 surgical cases of RCAA over a 7-year period while Nabaweesi-Batuka et al in Kenya noted 121 cases over a 4-year study period.[6,7] A study conducted by El Khamlichi et al. in Morocco called into question the notion that intracranial aneurysms are rare in the Middle Eastern and African populations.[8] Ohaegbulam suggested that the apparent low hospital incidence may be due to poor medical awareness, limited neurosurgical facilities and resources in the developing countries.[9]

Most cerebral aneurysms occur within the Circle of Willis with 85% of the aneurysms been located within the anterior circulation and occurring at junctions or bifurcations.[10] A significant difference between genders also exists concerning the aneurysm location.[11] In women, who tend to have multiple aneurysms, about 54% of RCAA are within the internal carotid artery territory while close to 15% are found in the region of the anterior communicating artery (ACoM). [11] In contrast, men have 29% of all aneurysms in the ACoM territory.[11]

The definitive treatment of a RCAA has evolved over the last four decades. The definitive treatment options ranging from craniotomy (clipping with or without wrapping, bypass), endovascular approach (coiling, balloon-assisted coiling, stent-assisted coiling, liquid embolic material, flow-diverting stent) or a combination of both. Endovascular approach is virtually absent in most neurosurgical centres in Africa, including Nigeria. The definitive management of RCAA is by and large craniotomy and clipping in Nigeria.

Data on the status of RCAA in the African population are not common while reports of RCAA studies from Nigerian population are rare. This study aims to determine the demographic profiles, aneurysm sac location and surgical outcome of patients with RCAA in our environment. Hopefully, the findings from this study will guide future studies regarding RCAA amongst Nigerians.

Methodology

Study Design and Participants

We conducted a single-centre retrospective analysis of a consecutive series of patients with RCAA, who underwent surgery between March 2012 and June 2021. The study was conducted at the Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria. Institutional ethical committee permission was taken before the study. Confidentiality was ensured and existing de-identified data was used. Data stores were encrypted to prevent unauthorized access.

All included patients were consecutive cases with clinical and radiological diagnosis of RCAA aneurysm who were operated at our centre. The study exclusion criteria included patients who refused surgical treatment, those who had previous surgical management at another centre or patients that expired before surgical intervention.

Patients' biodata, time of first ictus to hospital presentation, type of aneurysm, anatomic location of the aneurysmal sac, side of aneurysm, pre-operative Hunt and Hess (HH) grade (Table 1), World Federation of Neurosurgical Societies (WFNS) grade (Table 1), timing of surgery (Early: within 72 hours of presentation; Late: after 72 hours of presentation) and Glasgow Outcome Scale (GOS) grade (Table 2) at 6 weeks post-surgery were documented and recorded electronically. Ruptured cerebral aneurysm was confirmed either by computerized tomographic angiography or by Magnetic resonance angiography. Surgery for RCAA was classified as early (0–3 days post ictus) and late (>3 days post ictus). The primary surgical outcome was to assess the mortality rate, while secondary outcome was morbidity using Glasgow outcome scale. The minimum follow-up period was 8 weeks. All information was recorded in Microsoft Excel spreadsheet prior to analysis. The poor outcome was determined as mortality within 6 weeks of surgical intervention.

Clinical management of RCAA

Headaches are controlled with analgesics; seizure prophylaxis is commenced and anxiolytics given to restless patients. We also manage the patient in a quiet room while undergoing bed rest, with administration of stool softeners and non-pharmacologic venous thromboembolism prevention techniques. Patients who were on anticoagulants before presentation had it stopped and reversed to avoid rebleeding. Short-term (less than 72 h) use of tranexamic acid is allowable to reduce the risk of rebleeding if a delay in the definitive treatment of the aneurysm is unavoidable. Hypertension is promptly controlled with the systolic blood pressure maintained at less than 160 mmHg while avoiding hypotension. Nimodipine 60 mg every 4 hours is administered and continued for 21 days. The dose is reduced or discontinued if there is hypotension, especially in patients with higher grades of subarachnoid haemorrhage.

The policy of our unit is to treat every RCAA within 72 hours of presentations. This is to prevent a second rupture thus reducing the daily risk of rebleeding of the aneurysm which is well known to be associated with a worse clinical outcome. Early surgery also allows immediate removal of vasospasmogenic agents such as blood clots from contact with cerebral arteries, consequently reducing the risk of vasospasm. It also helps to ensure a more aggressive medical treatment of vasospasm by allowing induction of arterial hypertension and hypervolemia with no risk of aneurysm bleeding. All aneurysms were treated by craniotomy and clipping with alpha type Sugita aneurysm clips. Clipping is done without the aid of any adjuncts such as micro-doppler ultrasonography, indocyanine green videoangiography or intra-operative digital subtraction angiography due to non-availability locally. Post-operatively, patients are managed at the intensive care unit for at least a day prior to transfer to the ward. Symptomatic hydrocephalus is managed by external ventricular drainage in the acute phase and ventriculoperitoneal shunt in the chronic phase.

Statistical analysis

The HH, WFNS and GOS grade were dichotomized (HH- Good: 1-3, Poor: 4-5; WFNS- Good: 1-3, Poor: 4-5; GOS- Good: 4-5, Poor: 1-3). Differences in categorical and continuous variables between groups were compared using Chi-square test (χ^2) analysis (or Fisher's exact test). Statistical significance was set at a p value < 0.05. All statistical analysis was performed with IBM Statistical Product and Service Solutions (SPSS) version 23.

Results

Twenty-nine patients met the inclusion criteria. The male-female ratio was 1:2.6. Patient characteristics are as depicted in Table 3. The median age was 50 years (26-68 years). Male patients had a median age of 50 years (27-63 years) just like the females (26-68 years). Age group 50-59 years (Figure 1) was the most common age group, irrespective of gender.

All the patients presented after 24 hours of the ictus. At presentation only one patient had a smoking history. Most patients (17, 58.6%) had pre-operative HH grade of 3 while 14 (48.3%) patients had WFNS grade 3.

RCAAs were most commonly detected regardless of gender at the middle cerebral artery (MCA) and posterior communicating artery (PCoMA) territory (Figure 2). The most common site for aneurysm was PCoMA (38.1%) in females and MCA (37.5%) in males. However, there was no significant statistical association between gender and aneurysm location ($p=0.396$), age distribution ($p=0.946$), HH grade ($p=0.135$) and WFNS grade ($p=0.281$). Two (6.9%) patients had multiple aneurysms. The male and female patient with multiple aneurysms had it in the region of the MCA.

All patients were treated by aneurysm clipping (Figure 3). Despite our policy of treating patients with RCAA as soon as possible, twenty-one patients (72.4%) had delayed surgical clipping (after 72 hours at presentation) due to patient challenges (inadequate funds for investigations and surgery). Nineteen patients (65.5%) had at least a rebleed after the initial rupture prior to definitive surgery.

Five (17.2%) patients died. All the patients that did not have a rebleed prior to surgery survived.

Two of the deaths which were confirmed at autopsy were due to ischaemic brain disease from vasospasm. The other three were due to pneumonia, disseminated intravascular coagulopathy and iatrogenic central venous vein injury. None of the patients with PCoMA aneurysm died. Mortality was not statistically associated with location of the aneurysm ($p=0.064$), WFNS grade ($p=0.140$), HH grade ($p=0.174$), patients gender ($p=0.677$) or age distribution (0.566); likewise, aneurysm rupture location was not significantly associated with GOS (Table 4). The pre-op HH and WFNS grades were significantly associated with GOS (Table 4).

Table 1: Preoperative clinical grading scales- World Federation of Neurosurgical Societies and Hunt and Hess grade

Grade	WFNS	HH
0		Unruptured aneurysm
1	GCS score of 15 without focal deficit	Asymptomatic or mild headache;
2	GCS score of 13 or 14 without focal deficit	Cranial nerve palsy, moderate to severe headache/nuchal rigidity
3	GCS score of 13 or 14 with focal deficit	Mild focal deficit, lethargy, or confusion
4	GCS score of 7-12	Stupor and/or hemiparesis
5	GCS score of 3-6	Deep coma, decerebrate posturing, moribund

*HH- Hunt and Hess; WFNS- World Federation of Neurosurgical Societies

Table 2: Post-operative clinical grading scale Glasgow Outcome Scale

Grade	
1	Death
2	Vegetative state
3	Severe disability requiring daily care
4	Moderate disability with some independence
5	Good recovery

Table 3: Patients' characteristics and outcome

Nos	Gender	Age	WFNS	H&H	Aneurysm site	Aneurysm side	Type of aneurysm	GOS
1.	Female	57	3	3	MCA	Right	Saccular	5
2.	Female	40	4	4	MCA	Right	Saccular	5
3.	Male	49	3	3	ACoMA	ACoMA	Saccular	5
4.	Male	63	3	3	PCoMARight		Saccular	5
5.	Female	38	3	3	ACoMA	ACoMA	Saccular	5
6.	Female	53	4	4	MCA	Right	Saccular	1
7.	Male	53	3	3	MCA	Right	Saccular/blister 5	
8.	Male	44	2	3	ACoMA	ACoMA	Saccular	5
9.	Male	27	3	3	MCA	Right	Saccular	5
10.	Female	50	3	3	PCoMALeft		Saccular/Giant	5
11.	Female	40	2	3	PCoMA	Right	Saccular	5
12.	Female	53	2	3	ACoMA	ACoMA	Saccular	5
13.	Female	26	3	3	PCoMARight		Saccular	5
14.	Female	36	3	3	MCA	Right	Saccular	1
15.	Female	59	4	4	ACoMA	ACoMA	Saccular	1
16.	Female	30	2	3	PCoMALeft		Saccular	5
17.	Male	38	3	3	PCoMALeft		Saccular	5
18.	Male	54	3	3	DACA	Left	Saccular	1
19.	Female	40	3	2	PCoMARight		Saccular	5
20.	Female	57	2	3	PCoMALeft		Saccular	5
21.	Female	58	2	2	ACoMA	ACoMA	Saccular	5
22.	Female	42	3	3	ACoMA	ACoMA	Saccular	1
23.	Female	36	4	4	MCA	Right	Saccular	3
24.	Female	51	1	2	PCoMALeft		Saccular	5
25.	Female	63	3	2	ACoMA	ACoMA	Saccular	1
26.	Male	57	2	2	MCA	Left	Saccular	5
27.	Female	68	2	2	MCA	Left	Saccular	5
28.	Female	52	2	2	PCoMARight		Saccular	5
29.	Female	42	2	2	MCA	Right	Saccular	5

*ACoMA- Anterior communicating artery, DACA- Distal anterior cerebral artery, GOS- Glasgow Outcome Scale grade, HH- Hunt and Hess grade, MCA- Middle cerebral artery, PCoMA- Posterior communicating artery, WFNS- World Federation of Neurosurgical Societies grade

Table 4: Relationship (p-value) of gender, age distribution, aneurysm location, preoperative Hunt and Hess/World Federation of Neurosurgical Societies grading system and outcome

Characteristic	GOS	GOS Dichotomized	Mortality
Gender	0.734	0.457	0.575
Age	0.642	0.237	0.501
Age distribution	0.428	0.418	0.566
Rebleed	0.756	0.623	0.680
Aneurysm location	0.153	0.070	0.064
HH grade	0.028	0.015	0.174
HH grade Dichotomized	0.004	0.020	0.127
WFNS grade	0.045	0.018	0.140
WFNS grade Dichotomized	0.004	0.020	0.127

*GOS- Glasgow outcome scale grade, HH- Hunt and Hess grade, WFNS- World Federation of Neurosurgical Societies grade

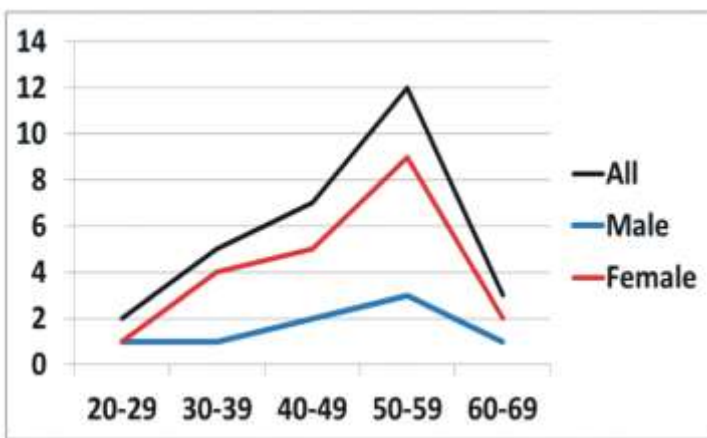


Figure 1: Age distribution (in years) of male and female patients with ruptured aneurysm

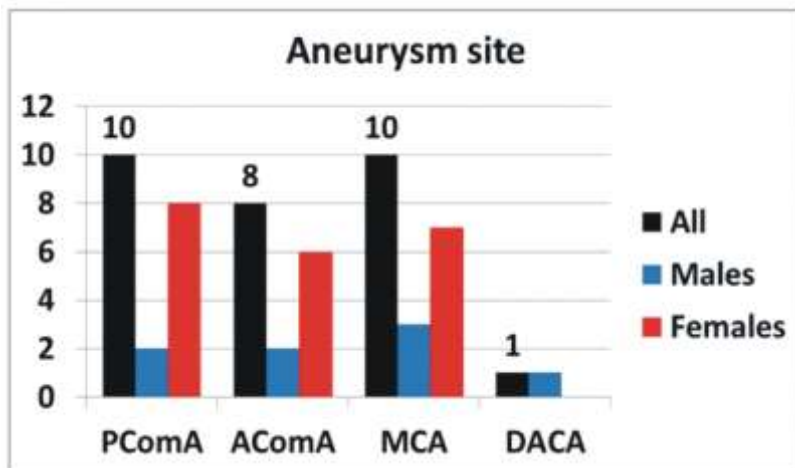


Figure 2: Aneurysm location (ACoMA- Anterior communicating artery, DACA- Distal anterior cerebral artery, MCA- Middle cerebral artery, PComA- Posterior communicating artery) based on gender

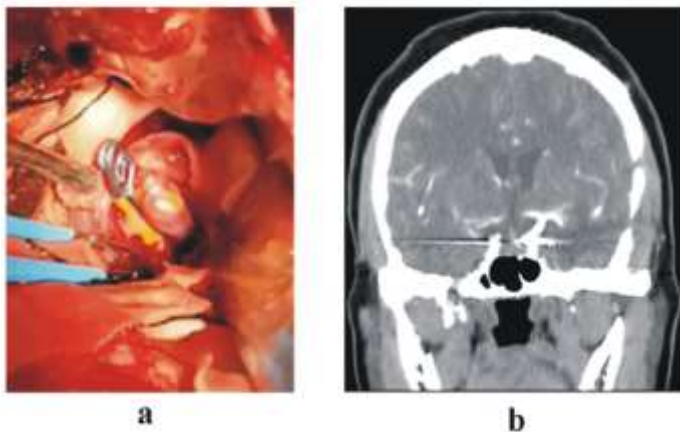


Figure 3a, b: Intra operative (a) and post-operative (b) images of clipped middle cerebral artery aneurysm

Discussion

Some of the known risks factors for the development and growth of intracranial aneurysms include age older than 50 years (3.8% per year compared with 0.9% per year, $P < .01$), female sex (3.2% per year versus 1.3% per year, $P < .01$), prior smoking history (5.5% per year versus 3.5% per year, $P < .01$), hypertension, high cholesterol intake, excessive alcohol consumption, family history of aneurysms (especially first-degree relatives), sickle cell disease, bacteraemia, trauma, radiotherapy, connective tissue disorders, metastatic lesions to the brain, location of aneurysm and aneurysm morphology and nonsaccular shape.[12-16] While factors associated with rupture includes age, hypertension, heart disease, diabetes mellitus, cerebral atherosclerosis, cigarette smoking, alcohol consumption, hypertension aneurysms located at the internal carotid artery and neck width and aspect ratio correlated negatively with rupture risk.[17] All these risk factors for aneurysm formation, growth and rupture are fairly present in our population. Autopsy and histological studies conducted in Nigeria on recently deceased patients found that the anatomic variations of distribution, incidence of abnormalities of the circle of Willis and vascular histology were similar to what has been described in the literature for Caucasians. [18,19] Despite this, intracranial aneurysms seem relatively uncommon in Nigeria. We operated only 29 cases in our centre over a 9-year period, despite aneurysmal surgery being possible in few centres in Nigeria. This low surgical case of RCAA aneurysm we opined can be accounted for by prevailing adverse cultural and social beliefs, challenged access to prompt, adequate and appropriate orthodox medicine facilities, financial constraint and paucity of neurologists and neurosurgeons.[20]

The male to female ratio in our study is 1:2.6. In this study, females presented with a higher prevalence than males from aged 30-39 years. This was most pronounced at 50-59-year age group. The mean age of RCAA is 50 years with male to female ratio of 1:1.[21] This is similar to our study. After the age of 50, a female predominance of 2:1 is seen.[21] Globally, women are known to have a higher incidence of intracranial aneurysms than men.[22,23] Epidemiological studies show that the female preponderance of intracranial aneurysms becomes significant only during the peri- and post-menopausal periods (fourth or fifth decades of life).[24,25] Before the fourth or fifth decades, there is no difference between men and women in the incidence of intracranial aneurysms and RCAA.[24,25] These observations suggest the potential roles of sex steroids, particularly oestrogen, in the pathophysiology of cerebral aneurysms. Earlier studies have demonstrated the protective effects of oestrogen against various types of vascular injury, particularly atherosclerosis.[26] This effect is by modulating inflammation, nitric oxide production, cytokine and growth factor expression and the reduction of oxidative stress.[27] In post-menopausal women, a relative deficiency in oestrogen may increase the risks for aneurysmal formation and growth.[28]

The point prevalence of multiple aneurysms in our series is 6.9%. The two patients (1 male and 1 female) who had multiple aneurysms in our series had the aneurysm in the region of the MCA territory. This prevalence over a 9 year period is significantly lower than in most populations (15-30%).[29-32]

The ACoMA has been described as the most common site for RCAA aneurysm. It accounts for 25-39% of all aneurysm locations and there is evidence that these aneurysms may have a higher tendency to rupture.[33] However, in our study, regardless of gender, the PComA (34.5%) and MCA (34.5%) territories were the predominant location for RCAA aneurysm in our study. In females most of the aneurysms were in the PComA territory compared to MCA areas in males. ACoMA aneurysm was found in 27.6% of patients. The middle cerebral artery is a common location for cerebral aneurysms and is associated with a lower risk of rupture than aneurysms located in the anterior or posterior communicating arteries.[34]

In environments with better health system and access to it, approximately 12 percent of patients with intracranial aneurysms die before receiving medical attention.[3] The risk of sudden death is statistically higher with RCAA in the vertebrobasilar regions (44.7%; 95% CI, 7.4–86%) than with anterior circulation RCAA (12.1%; 95% CI, 5.8–20%); with a relative risk of 3.85 (95% CI, 2.5–6.0).[35] In communities with inadequate health systems and barriers to neurosurgical care under-diagnosis and delay in treatment of a lethal condition like RCAA will be common. This we hypothesize may explain the lack of any single case of RCAA within the posterior circulation.

The timing of surgery for aneurysmal subarachnoid haemorrhage influences the outcome. This is to prevent a rerupture and rebleed. Timing of surgical treatment of ruptured intracranial aneurysms has undergone a drastic change in the last few decades with preference for early surgery. This approach prevents a rerupture with its attendant bleeding and complications of the intraparenchymal haematoma, intraventricular haemorrhage, hydrocephalus and raised intracranial hypertension; in addition it ensures early evacuation of blood which is a vasospasmogenic agent.[36] Many studies have showed that early surgery is superior to late surgery in reducing a poor outcome and mortality rate when patients present with good WFNS or HH grades; they noted that early surgery decreases the incidence of poor outcome when patients were in poor condition on admission.[37-39]. Early surgery was superior to late surgery in reducing a poor outcome and death rate when patients were in good condition on admission, and decreased the incidence of poor outcome when patients were in poor condition on admission. Compared with late surgery, early surgery significantly decreased the incidence of poor outcome, regardless of whether patients were in good condition (RR, 0.65 [95%CI, 0.50 0.84]; $p = 0.001$) or in poor condition on admission (RR, 0.71 [95%CI, 0.61 0.83]; $p < 0.0001$).[40] Moreover, when patients were in good condition on admission, early surgery also effectively reduced the death rate (RR, 0.61 [95%CI, 0.46 0.82]; $p = 0.001$).[40] Additionally, early surgery reduced the death rate compared with late surgery in patients older than 50 years (RR, 0.49 [95%CI, 0.27 0.89]; $p < 0.002$).[40] The critical time frame for ruptured aneurysm repair is set at <72 hours after ictus, unless the patient is in a moribund condition.[41,42] Immediate management and delayed management after poor-grade subarachnoid bleed are associated with similar morbidity and mortality at 12 months. Therefore, delaying intervention in poor-grade patients may be a reasonable approach, especially if time is needed to plan the procedure or stabilise the patient adequately.[43]

If a patient survives the initial aneurysmal rupture, the major early complication is a rebleed from the RCA aneurysm. The reported incidences of rebleed are 8% to 23% in the first 72 hours after an ictus.[44] The consequence of a rebleed is enormous with reported mortality rates close to 60%.[44] Ellamushi et al noted that a rebleed was associated with increased mortality, with a tendency towards poor outcome (Mortality rate of 36 vs. 20 %, $p=0.02$) (Poor outcome of 47 vs. 33 %, $p=0.06$).[45] Nineteen of all the patients rebleed before surgery. The mortality rate of those that rebleed prior to surgery was 26.3%. All the patients that did not have a rebleed prior to surgery survived. This further underscores the importance of surgery before rebleeding occurs. Fewer than 30% of our patients had surgical intervention within 72 hours of an initial rupture. This was mainly due to prevailing local challenges of delay in confirmation of diagnosis (delayed referral, patients sourcing for funds for investigations, etc.) and access to theatre. Hence, patients with delay in access to appropriate medical care may die from fatal early rebleed or other complications prior to presentation, referral or surgical intervention. All these may account for the significantly low number of cases we have operated over a 9-year period.

Limitations

Shortage of Neurosurgical personnel, facilities and barriers to health care accessibility still persist in Nigeria and are quite different in many states in the country. This may influence the frequency of cases, resulting in a sample size over a 9-year period. Though this study is limited to one of the 2 tertiary public neurosurgical centres in the most populated state in Nigeria, with personnel and facilities for management of RCAA, the data may not be generalizable to other parts of the state and country.

Conclusion

This study showed that RCAA are essentially in the anterior circulation amongst our population, with a peak at the 5th decade of life and a female preponderance. Multiple aneurysms are rare and association of smoking with aneurysms are not common in our patient population. The prevalence of surgically treated RCAA is low when compared to western populations. Delays in surgical clipping encountered in this study were mainly patient related. The patients' gender, age and aneurysm location are not significantly associated with mortality or GOS grade. However, patients' admission WFNS and HH grade are good predictors of outcome using the GOS grade. Prevailing local factors like adverse cultural and social beliefs, under diagnoses, late referral, challenged access to prompt, adequate and appropriate neuroradiological facilities, delay in patient investigations, financial constraint and paucity of skilled specialists (neurologists and neurosurgeons) may account for the low capture and surgical rate of RCAA in Nigeria. Multifaceted efforts should be directed at these adverse factors so as improve early diagnosis and management of patients with RCAA.

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Conflict of interest: There are no conflicts of interest.

Abbreviations: GOS: Glasgow Outcome Scale; HH: Hunt and Hess; PComA: posterior communicating artery, RCAA: Ruptured cerebral artery aneurysms, WFNS: World Federation of Neurosurgical Societies

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