ASSESSMENT OF THE WALL CHARACTERISTICS OF INTRACRANIAL ANEURYSMS IN MAGNETIC RESONANCE IMAGING AND ITS CORRELATION WITH CONVENTIONAL AND ANGIOGRAPHIC RUPTURE RISK FACTORS

THESIS

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Certificate

This is to certify that the work incorporated in this thesis titled **"Assessment of the wall characteristics of intracranial aneurysms in Magnetic Resonance Imaging and its correlation with conventional and angiographic rupture risk factors"** for the degree of DM (Neuroimaging and Interventional Neuroradiology) has been carried out by Dr Pooja Gupta under my supervision and guidance. The work carried out in connection with this thesis has been carried out by the candidate herself and is genuine.

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DECLARATION

I hereby declare that this thesis titled **"Assessment of the wall characteristics of intracranial aneurysms in Magnetic Resonance Imaging and its correlation with conventional and angiographic rupture risk factors"** has been prepared by me under the supervision and guidance of Dr Bejoy Thomas (Professor & Head) , Dr Santhosh K, (Additional Professor), Dr Jayadevan E.R (Professor), Dr C Kesavadas, (Professor), Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

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CONTENTS

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INTRODUCTION

Intra-cranial aneurysms (IA) are the commonest cause of non-traumatic sub-arachnoid haemorrhage (1). These are ominous entities with aneurysmal SAH being associated with significant morbidity and mortality. The prevalence of IA in literature has been reported as approximately 2% of the general population (2)

Once an Intracranial aneurysm (IA) is diagnosed, the risk of rupture should be weighed against the risk of treatment, a cause of significant stress and anxiety for patients, emphasizing the need of an individual criteria for predicting rupture in clinical decision making. Previous studies have identified a number of factors that potentially contributed to aneurysm rupture, by which several rupture prediction models were built, such as the PHASES score [3,4]. Aneurysmal rupture occurs when the stress imposed by blood flow exceeds the mechanic strength at a location of the aneurysm wall. Thus, investigating the characteristics of aneurysm wall may help in deepening our knowledge on the mechanism of aneurysm rupture. Histopathological studies indicated that inflammation may play an important role in the formation, growth, and rupture of IAs [3,8]. Inflammatory cell infiltration is commonly observed in ruptured IAs and numerous inflammation cytokines are involved in the process [8]. Therefore, the ability to image inflammation in IAs may aid in assessing IA rupture risk in individual clinical decision-making.

The advancement of Vessel Wall- Magnetic Resonance Imaging (VW-MRI) offers a potential noninvasive mean to detect in-vivo inflammation in IAs at a pathological level [6,7,9]. Recent improvements in VW- MRI makes this a viable method for investigating inflammatory processes in the aneurysmal wall [10]. Previous studies suggested that aneurysmal wall enhancement (AWE) on VW-MRI was more

frequently observed in ruptured IAs and might help to identify unruptured aneurysms with a high rupture risk [6,7]. However, the association between the presence of AWE and other wall characteristics and conventional IA rupture risk characteristics, like aneurysmal size and location, has not been well described. Investigating the relationships between these quantities might help to build an understanding of the cause of AWE and its possible role in improving IA rupture prediction. Aneurysm size is a widely accepted predictor for rupture and the primary consideration in clinical decision-making for unruptured IAs [10,11]. Studies on natural course of unruptured IAs, including the international study of unruptured intracranial aneurysms (ISUIA) and the unruptured cerebral aneurysms study, have demonstrated that the risk of rupture increased with increasing size of the aneurysm [10,11]. Not many studies have been done studying the wall characteristics of both ruptured and unruptured aneurysms [6]. Recently, some rupture prediction models have been developed by integrating several conventional rupture-related characteristics, and the PHASES score might be one of the most acceptable models and has been applied in some current studies [3,4]. The PHASES Score based on ethnicity, age, hypertension, earlier hemorrhage, aneurysm size and location, which was first introduced by Greving et a [3] by pooling the analyses of 6 prospective large-scale cohort studies. Therefore, the purpose of this work was to reveal possible relationships between wall characteristics of the aneurysms and conventional and angiographic rupture-related risk factors in patients with IAs. Apart from the PHASES score criteria, other conventional risk factors like history of smoking, presence of other associated comorbid conditions like collagen vascular disorders is assessed in these patients with intracranial aneurysms.

AIMS & OBJECTIVES

Our study is a prospective study aimed at analysing the wall characteristics of intracranial aneurysms on MRI and angiography and their correlation with conventional and angiographic rupture risk factors in patients who have had out-patient or in-patient care at out institute between June 2019 till June 2021.

The specific objectives of the study are as detailed below:

1. To investigate the correlation between wall characteristics of unruptured intracranial aneurysms on Magnetic Resonance Imaging with conventional and angiographic rupture risk factors.
2. To study the characteristic wall features of ruptured intracranial aneurysms on Magnetic Resonance Imaging and Angiography
3. The unruptured/ruptured intracranial aneurysms are subjected to Vessel wall imaging, Susceptibility weighted imaging and Magnetization transfer imaging and enhancement of the wall of the aneurysm is estimated. The size of the aneurysm, location, presence of daughter sacs and wall irregularity is assessed by Angiography (Computed Tomographic Angiography/Digital Subtraction Angiography/Magnetic Resonance Angiography). The PHASES [1] risk prediction score is calculated. Other conventional risk factors of the aneurysm like history of smoking, presence of other associated comorbid conditions like collagen vascular disorders is also assessed.
4. The relationship between wall characteristics of unruptured aneurysm and PHASES SCORE and other conventional and Angiographic rupture risk factors is estimated.

REVIEW OF LITERATURE

Intra-cranial aneurysms (IA) are a major cause of life threatening sub-arachnoid haemorrhage (SAH). Approximately 75%-85% cases of spontaneous SAH have been attributed to IA (1). There is high propensity of significant neurological disability and mortality associated with aneurysmal SAH and also there is increased risk of subsequent future rupture of the aneurysms (12,13). Aneurysms may also be associated with neurological symptoms associated with mass effect and ischemic symptoms.

Intracranial aneurysms have a propensity to occur at arterial bifurcation points and these aneurysms are very commonly associated with vascular anatomical variants like persistent carotid basilar anastomoses, agenesis of the internal carotid artery, fenestrations and asymmetry of the circle of Willis. These suggest a hemodynamic pathogenesis of IAs(14).

It is seen that people with certain genetic and connective tissue disorders like polycystic kidney disease, Ehler Danlos syndrome develop IA and hemodynamic factors alone cannot explain their occurrence in these cases (2).

Consumption of alcohol and cigarette smoking are exogenous factors which are associated with increased incidence and rupture of saccular aneurysms (15). If we consider the genetic basis of occurrence of IA a number of , a number of chromosomes like 18q11.2, 10q24.32, 8q11.23-q12.1 and 9p21.3 were commonly associated with formation of intracranial aneurysms (16). \ Only up to 5% of the familial incidence of these intracranial aneurysms can be explained by these chromosomes; so, the genetic

risk prediction tests available to us are not properly established screening methods for intracranial aneurysms (16).

Patients with multiple intracranial aneurysms have certain features which can tell us about the pathogenesis of the cerebral aneurysm formation.

For example, there is a predisposition for aneurysms to occur in the ophthalmic artery than in the anterior communicating artery in cases of multiple aneurysms; this indicates that factors which cause aneurysm formation differ by anatomical location (17).

And it has been seen that those patients who have multiple intracranial aneurysms have an important subgroup in them of 'mirror aneurysms' (i.e., two different aneurysms occurring at symmetrically opposite arteries in the two hemispheres). In all patients with IA the incidence of mirror aneurysms is 10% and mirror aneurysms are seen in one third of the patients with multiple aneurysms.

The fate of neural crest cell derivatives in quail-chicken chimeras has shown that the precursor cells of the vessel wall move out bilaterally towards the vessels of both the hemispheres (18).

Based on this it was hypothesised that there is transmission of the genes from the parent cells to the clones present on homologous segments of the circle of Willis in bilateral cerebral hemispheres. This has led to the increased frequency and non-random occurrence of mirror aneurysms (19).

These considerations imply that multiple factors interact in the formation of classical saccular aneurysms.

There are various known risk factors for the formation and rupture of intracranial aneurysms such as increasing age, female sex, alcohol consumption, presence of hypertension, history of smoking, family history of IA, presence of polycystic kidney disease and history of previous subarachnoid haemorrhage. Genetic susceptibility also has important role in IA formation (2).

Also, the perianeurysmal environment has an important effect on the morphological characteristics, growth and rupture risk of IA, which in turn will help in deciding the choice and treatment efficacy of endovascular and surgical approaches (20,21).

Unruptured intracranial aneurysms (UIA) are not congenital and are acquired during the life course of a patient and are unusual in less than 20 years of age (22). There is increase prevalence of UIA in people who have a first degree relative with intracranial aneurysm or SAH (prevalence ratio (PR) 3.4, 95% CI 1.9-5.9), or those with presence of other disorders like polycystic kidney disease (PR 6.9, 95% CI 3.5-14.0), compared with reference population (23, 24-26).

One of the risk factors which has been considered for the occurrence of intracranial aneurysms are connective tissue disorders but there are no studies to support this and various studies have disapproved this association (27-29).

The risk factors which lead to formation of sporadic IA and their true incidence is difficult to estimate. Maximum data which is available of the formation of sporadic

IA is obtained from the patients who have had an episode of subarachnoid haemorrhage from a different aneurysm (30-34). This subpopulation has been hypothesized to develop more aneurysms compared to the general population. The annual rate of de novo aneurysm formation in this population ranges from 0.2-1.8% (30-34).

There are various environmental and genetic factors which lead to formation of IA and there may be reinforcement of these factors (31). For example, those people who have a strong family history of intracranial aneurysms, in these smokers have at least a threefold increased risk of having and IA compared to non-smokers (31).

Evidence has shown that people with a history of prior subarachnoid haemorrhage or a family history of intracranial aneurysms are at increased risk of formation of IC, however there are no specific genes identified with this association. A meta- analysis was done which had data from 61 gene association studies and included 32,887 sporadic aneurysms and 83,683 controls and it identified three single nucleotide polymorphisms (SNPs) associated with IA.

These SNPs were seen residing on chromosome 9 in the CDKN2B-AS1 gene, on chromosome 8 near SOX17 transcription regulator gene and on the chromosome 4 near endothelin receptor gene (32). These loci have common polymorphisms which are responsible for increased occurrence of structural malformations and disorders of the cardiovascular system.

On additional genomic studies other loci were found on chromosome 7 near HDAC9 and in chromosome areas 1p34.3–p36.13, 19q13.3, Xp22 and 7q11.

There is a strong evidence of linkage with the chromosome 7q11. The gene in 7q11 encodes for elastin which maintains the integrity of the vessel wall. This genetic association of IA needs to be validated in larger aneurysm cohorts in the population.

There are certain structural differences in the walls of the cerebral arteries from those of the extracranial arteries. The intracranial arteries have less elastin fibres in their walls, and they have sparse tunica adventitia. Also, the cerebral arteries are surrounded by cerebrospinal fluid present as opposed to the extracranial arteries which have connective tissue around them (36,37).

These factors cause increased risk of aneurysm formation in the cerebral arteries.

In the cerebral arteries the internal elastic lamina at the arterial bifurcation maintains the elasticity and structural integrity of the vessel wall (38,39).

Any abnormality in the internal elastic lamina at the bifurcation points like degeneration or destruction is the key event leading to formation of an intracranial aneurysm. Degeneration or disruption of the internal elastic lamina at a bifurcation is a key event in the formation of an intracranial aneurysm. However, the actual cause of this degeneration occurring in certain individuals still remains unknown.

Variations in the anatomy of the circle of Willis can lead to intracranial aneurysm formation (40). When a study was done on people with familial preponderance to occurrence of intracranial aneurysms it was found that bifurcation points involving the circle of Willis with hypoplastic branching arteries or with sharp angles were risk factors leading to formation of the intracranial aneurysms. According to the

researchers this increased risk was probably because of the increased hemodynamic stress caused by the anatomical variations (41).

One of the factors which contributes towards the formation of the saccular intracranial aneurysms is flow within the aneurysm which can cause structural instability.

Whenever due to hemodynamic stress there is disruption of the internal elastic lamina with shift in tensile forces there is activation of the fibroblasts and vascular smooth muscle cells which synthesizes collagen type I and V (42). Initially whenever there is hemodynamic stress, the vascular smooth muscle cells which are present in the media migrate to the tunica intima. The smooth muscle cells undergo a change in location and phenotypic modulation into the synthetic type, which in turn leads to collagen synthesis leading to myointimal hyperplasia.

This is an ongoing process and the sustained hemodynamic stress on the vessel wall leads to dysfunction of the endothelial cells, destruction and remodulation of the extracellular matrix and phenotypic change of the smooth muscle cells into proinflammatory, dedifferentiated cells.

As this process continues, the mechanical pressure on the vessel wall and myointimal injury further leads to overwhelming of the molecular mechanisms which were trying to compensate this injury and there is activation of humoral and cellular inflammatory responses which are the main factors now leading to formation of the IA (43,44). These inflammatory responses are mediated by various cytokines such as interleukins, tumour necrosis factor and matrix metalloproteinases (MMPs) and these cause

influxes of macrophages and these is associated degeneration and degradation of the elastin and collagen fibres (45-48).

Whenever there is pressure of impinging blood flow on the wall of the vessel or high wall shear stress it causes mural cell mediated destructive wall remodelling which in turn causes formation and increase in size of aneurysms. This mechanism is supposed to be responsible for the formation of small, thin-walled aneurysms.

On the other hand, low wall shear stress leads to inflammation mediated, destructive wall remodelling due to disturbed intra-aneurysmal blood flow leading to the formation of large, thick walled aneurysms (49).

Sometimes high and low wall shear stress occurs together in any aneurysm but how these varying flow conditions and aneurysm subtypes affect the aneurysmal rupture risk still remains unclear.

Recently a large number of studies have highlighted the role of aneurysmal wall inflammation causing growth of the aneurysm and their subsequent rupture (48,50,51).

Over the last one decade several studies have tried to find as association between wall inflammation of the aneurysm and its stability. Most of these studies have done contrast MRI sequences which if shows enhancement in the wall of the aneurysm is suggestive of ongoing inflammatory pathology. A prospective study was done with a total of 108 cases of unruptured intracranial aneurysms in 87 patients and in these circumferential enhancement in the aneurysmal wall was associated with

growth/rupture of the aneurysm (9). In another prospective study of 30 UIAs in 22 patients, ferumoxytol-enhanced MRI was used to look for macrophages in the wall of the aneurysm as inflammatory marker. This was confirmed on histopathological examination in four of these aneurysms which ruptured.

The other three aneurysms which also showed ferumoxytol uptake were followed up and ruptured within 6months of initial imaging (50). These findings suggest that uptake of ferumoxytol in UIAs indicates wall inflammation and increased rupture risk of the aneurysms.

The role of wall inflammation in the rupture of intracranial aneurysms was further supported by a control study of patients with unruptured aneurysms who were on anti-inflammatory medications. In this study the use of aspirin or acetylsalicylic acid more than three times in a week was associated with significant reduction in the risk of aneurysmal rupture (51).

Subsequently other imaging studies have also investigated the association between the wall inflammation of the aneurysms and rupture risk (52,53). There was a randomized study of 11 patients in a phase I trial (52) in which ferumoxytol-enhanced MRI was used to study the aneurysm and it was found that aspirin pretreatment reduced the aneurysmal wall inflammation. treatment with aspirin. After this trial, aspirin treatment resulted in reduced radiological and histological indicators of aneurysm wall inflammation.

At the cellular level the stability of the aneurysms depends on the balance between two processes: repair of aneurysmal wall by collagen formation, proliferation of

vascular smooth muscle cells and regeneration of the extracellular matrix and destruction of the aneurysmal wall by collagen destruction and degradation of collagen and extracellular matrix (49,54). When the destructive processes outweigh the constructive processes the structural integrity of the aneurysms is lost and it becomes prone for rupture.

The destructive process leading to the rupture of the UIA is caused by hemodynamically caused flow related destruction or apoptosis of the endothelial cells, dysfunction and degradation of the smooth muscle cells and extracellular matrix and thrombus formation (38,55). These destructive processes cause various inflammatory mediators like IL-1ß, TNF, monocyte chemoattractant protein -1, MMPs to come into play in the aneurysmal wall (44,48,56-60).

Also it has been seen on various gene expression studies that various destructive immune responses and lysosomal degradation occurs in the wall of the aneurysm which further leads to the rupture of the aneurysms (60).

The exact mechanisms and mediators that cause rupture of aneurysms is still uncertain. Those aneurysms which were defined as having high rupture risk on radiological studies when subjected to histological assessment were seen to have infiltration of inflammatory mediators such as neutrophils, mast cells and T cells in their walls. There were other factors described such as an imbalance between the proinflammatory M1 macrophages and anti-inflammatory M2 macrophages and loss of extracellular matrix and mural cells (50). Cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) are enzymes which cause prostaglandin synthesis from

arachidonic acid and these are also important in the pathogenesis of rupture of IA. This hypothesis is based on the findings that there is increased levels of COX-2 in the walls of ruptured aneurysms and inhibition of COX-2 with administration of aspirin reduces histological and radiological aneurysm wall inflammation and rupture risk (52,53,61,62). The exact mechanism that causes the beneficial effects of aspirin on the wall inflammation of aneurysms is interesting the exact mechanisms that underlie these effects remain to be further elucidated before clinical conclusions can be drawn.

There were major trials conducted to study the course and natural history of unruptured intracranial aneurysms.

One of these was the International Study for Unruptured Intracranial Aneurysms (ISUIA) which was a prospective Trial published in 2008 (63). The aim was to assess the natural history of unruptured intracranial aneurysms and to know the risk of repair. Patients in USA, Canada and Europe were enrolled for the assessment of unruptured aneurysms. The natural history of aneurysm in patients who did not undergo surgery was evaluated and the morbidity and mortality associated with repair of unruptured aneurysms was assessed. 4060 patients with intracranial aneurysms were included in the study, 90% were located in the anterior circulation. In the patient cohorts 1692 patients with 2686 aneurysms did not undergo any intervention, 1917 underwent open surgery and in 451 patients endovascular management was done. 3% of untreated aneurysms ruptured (51 pts) with a mortality of 65%. Increased size of the aneurysms were associated with increased risk of rupture. Those located in ACA/MCA territory and in posterior circulation and involving PCom had higher incidence of rupture than in the cavernous ICA. There was better outcome in endovascular group vs the open

surgical group. Aneurysms located in the posterior circulation and with size>12mm are predictors of bad outcome in both the endovascular and surgical groups.

Another study done in Japan which was the Unruptured Cerebral Aneurysms in Japanese Cohort (UCAS) in 2012 describes natural history of UIAs in Japanese population (64). Between January 2001 and April 2004, 5720 patients with newly identified, unruptured intracranial that were 3mm or more in size were enrolled in the Japanese population. Out of the 6697 aneurysms 111 patients had rupture of the aneurysms with the rate of rupture of the aneurysms annually of 0.95%. There was increased risk of rupture with the increasing size of the aneurysms. It was seen that aneurysms located in the anterior and posterior communicating arteries had incidence of rupture compared to those in the middle cerebral arteries. Aneurysms having a daughter sac also were more likely to rupture.

In the study by Juvela et al (65) 142 patients with 181 unruptured intracranial aneurysms which were diagnosed between 1956 and 1978 and not treated were followed till death or till the occurrence of subarachnoid haemorrhage or till the year 2011/12. There were 34 cases of aneurysm rupture indicative of an annual incidence of 1.1%. There were eighteen deaths because of rupture of the aneurysms. History of cigarette smoking, aneurysms in the anterior communicating artery, younger patient age and diameter of aneurysm >7mm were associated with aneurysmal rupture.

Murayama et al (66) in a prospective 10 year cohort study underwent risk analysis of unruptured intracranial aneurysms from January 2003 to December 2012. 2897 aneurysms in 2252 patients were analysed and 1960 aneurysms were conservatively

managed. During follow up 56 aneurysms ruptured resulting in rupture rate of 0.76% per year. Increased risk of rupture was seen in aneurysms which were ≥ 5mm**.** The mortality rate after rupture of large and giant aneurysms was 69% and for aneurysms ≥ 5mm, the mortality rate was 18%.

Sonobe et al (67) conducted a prospective study to determine the natural history and management of incidentally detected small unruptured aneurysms. 448 unruptured aneurysms <5mm in size were followed up for an average of 41 months. The annual rupture risk of these small aneurysms were 0.54%, being 0.34% for single aneurysms and 0.95% for multiple aneurysms. The predictors for aneurysm rupture are <50yrs of age, diameter of ≥ 4mm, presence of hypertension and multiple aneurysms.

Zheng et al (68) in his study identified various morphological parameters and locations associated with rupture of intracranial aneurysms. They assessed 150 patients with 82 unruptured and 68 ruptured aneurysms on three-dimensional digital subtraction angiography. They evaluated these aneurysms based on nine morphological parameters and aneurysm location. There results showed that compared with unruptured aneurysms ruptured aneurysms had higher size ratio, aspects ratio, height-width ratio, flow angle, aneurysm inclination angle and vessel angle. Size and parent artery angle was not different between the ruptured and unruptured aneurysms.

Earlier Weir et al (69) in his study had found that 88% of unruptured aneurysms had an aspects ratio of > 1.6 while 56% of ruptured aneurysms had an aspects ratio of 1.6.

Dhar et al (70) had suggested that the size ratio is a very important parameter associated with the rupture risk of intracranial aneurysms ($p<0.001$). He had found thar 77% of all ruptured aneurysms had a size ratio of >2.05, however more than 83% of all unruptured aneurysms had a size ratio of <2.05.

Inflow angle has been stated as an independent parameter associated with risk of aneurysmal rupture. Increased inflow angle results in increased transmission of the energy of the flowing blood into the dome of the aneurysmal sac and thus is associated with increased risk of aneurysmal rupture (71).

Baharoglu et al (72) studied morphological characteristics of side wall aneurysms in 102 patients with 116 aneurysms. They found the maximum height, height-width ratio, dome-neck ratio was greater in ruptured aneurysms compared to unruptured aneurysms on univariate analysis. The inflow angle was also significantly more in the ruptured aneurysms. They postulated that increased inflow angle resulted in greater velocity of the inflowing blood on the wall of the aneurysm leading to greater wall shear stress.

In the study done by Ramachandran et al (73) 178 patients with 198 unruptured IA were followed up with imaging surveillance for 4 years. Only 20 aneurysms (10.1%) grew in size. Stable and unstable aneurysms could not be differentiated based on size of the aneurysm, non sphericity index, peak wall tension, low shear stress area and these indices could not predict the growth of the aneurysms.

A case-control design was used to assess the morphological characteristics of aneurysms in the International Study of Unruptured Intracranial Aneurysms database

associated with their rupture (74). 57 patients with ruptured aneurysms were compared based on 12 morphological indices with 198 patients with unruptured intracranial aneurysms during follow-up. It was seen that perpendicular height and size ratio were predictors of rupture of aneurysms on the univariate analysis. Other indices like the aspect ratio, presence of daughter sacs, aneurysm angle, neck diameter, parent artery diameter, and aneurysm volume were not statistically significant predictors of rupture. While on multivariate analysis, perpendicular height was the only index which was a significant predictor of rupture (Chi-square 7.1, P-value .008).

A systematic review and meta-analysis was done by Brinjikji et al (75) which included twenty-one studies consisting of 3954 patients with 4990 aneurysms with 13,294 aneurysm-years of follow-up.

The proportion of aneurysms which were growing was 3.0% per aneurysm-year (95% CI, 2.0%-4.0%). The various patient risk factors associated with growth included >50 years of age, (3.8% per year versus 0.9% per year, $P < .01$), female sex (3.2% per year versus 1.3% per year, $P < .01$), and history of smoking (5.5% per year versus 3.5% per year, $P < .01$). Other factors associated with increased growth rate included Location in the cavernous ICA (14.4% per year), nonsaccular shape (14.7% per year versus 5.2% per year for saccular, $P < .01$) and size of the aneurysm ($P < .01$). Growth of the aneurysms was associated with rupture rate of 3.1% per year while it was 0.1% per year for aneurysms which were stable ($P < .01$).

Factors involved in aneurysm rupture

Risk factors for aneurysm rupture

The risk of rupture of UIA have been investigated in various prospective studies and in different time periods (10,11, 76-80). It should be noted that most of these cohort studies deal with asymptomatic UIA as unruptured but symptomatic aneurysms are known to have a high risk of rupture and thus are often treated (10,81). However these cohort studies dealing with the risk of asymptomatic UIA rupture have focussed on specific selected populations and this is their major limitation. This is the reason that they are known as aneurysm rupture risk studies rather than being studies on natural history of these aneurysms.

There was a metanalysis done on rupture risk of UIA which comprised of six cohort studies and included 8,382 patients and a total of 10,272 UIAs. Based on this meta-analysis there were six independent risk factors for aneurysm rupture which were identified: patient age ≥70 years, a prior history of hypertension, previous history of SAH from another aneurysm, the site and size of the aneurysm, and the patient's geographical region (3). Based on these risk factors the PHASES score for predicting the rupture risk of the aneurysms was identified and it gave estimates for the 5-year rupture risk of aneurysms which ranges from 0.3% to ≥15%.

A consensus on assessment of UIAs was developed among a group of specialists from different fields involved in treatment of UIAs to counsel patients about the various treatment options for unruptured intracranial aneurysms (UIA) (82).

This panel proposed 60 features which they thought were important for deciding on the treatment of an UIA. These features were classified as patient, aneurysm, or treatment related factors. The various patient related factors which were considered relevant for aneurysm treatment were (1) patient age <30 years (2) familial intracranial aneurysms (3) previous SAH from a different aneurysm and (4) current nicotine consumption. Age <30 years though was highly relevant, the interrater agreement for this was moderate.

Additionally, the only factors which were highly relevant with high or very high IRA favouring treatment were familial intracranial aneurysms and current nicotine consumption.

Very relevant patient-related factors that independently supported conservative management of a UIA were (1) chronic diseases associated with a life expectancy <5 or 5 to 10 years and (2) neurocognitive disorders. For both these factors the interrater agreement on relevance was very high.

The aneurysm related factors considered important in support of treatment were (1) UIA size >13 mm, (2) UIA lobulation, (3) UIA location (anterior or posterior communicating artery or basilar artery bifurcation), (4) UIA growth, and (5) symptoms from the UIA. IRA for these factors were consistently high.

Among the treatment related factors, the most important factor which was considered to increase risk of treatment was aneurysm diameter >20 mm. A factors considered relevant to favour conservative management were patient age >80 years or life expectancy <5 years and the IRA among the members for these was very high.

MATERIALS & METHODS

The study is a prospective study conducted from July 2019 till June 2021.

Patients who have ruptured/unruptured intracranial aneurysms were included in the study (between June 2019 after obtaining IEC approval till June 2021). Consecutive 34 patients who had intracranial aneurysms, both ruptured and unruptured fulfilling the inclusion criteria attending the Neurointerventional Radiology/ Neurosurgery/ Neurology OPD/Ward of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) were screened for eligibility and willingness to participate in the study and were included in the study. Informed written consent was obtained from all the patients included in this study.

ELIGIBILITY:

The following inclusion/exclusion criteria were considered for the study:

Inclusion criteria:

- ruptured/unruptured intracranial aneurysms
- with complete medical records and
- patients giving consent

Exclusion criteria:

- patients not giving consent
- contraindications for undergoing MRI, DSA or CT Angiography
- IAs other than saccular—that is fusiform, traumatic, dissecting, and infectious

These patients underwent MRI of the brain. All MR images were acquired by using a 3.0 Tesla MR scanner (GE Discovery 750, ADW4.6, GE Healthcare, Wisconsin, US). The routine sequences which were acquired to assess the aneurysm characteristics were Precontrast: 3D TOF, Sag Cube T1 fs, Axial SWI, Axial T1 without Magnetization factor, Axial T1 with Magnetization factor, Axial T2W1 Propeller. Postcontrast: Sag CUBE T1 fs with an 24-channel head coil. Post contrast scan was done after administration of 0.1 mmol/kg IV of gadobutrol (Gadavist; Bayer Healthcare Pharma) followed by Sag Cube T1 fs acquisitions. All SWI sequences were performed prior to gadolinium administration.

The images were acquired using the following protocol- Ax SWAN: response time (TR), 35.4 msec; echo time (TE), 21.1 msec; flip, 15; pixel bandwidth, 31.25 Hz/pixel; FOV, 22 × 19.8 cm; matrix size, 384 × 384 ; voxel size, 0.5 × 0.5 × 0.6, slice thickness, 1.4 mm; frequency, 384; phase, 384; number of averages, 3.

Sag Cube T1 fs (precontrast & postcontrast): response time (TR), 602 msec; echo time (TE), 11.6 msec; flip, 15; pixel bandwidth, 62.5 Hz/pixel; FOV, 16 × 16 cm; matrix size, 192 × 192 ; voxel size, 0.8 × 0.8 × 0.6, slice thickness, 1.4 mm; frequency, 192; phase, 192; number of averages, 2.

Following this the patients underwent Digital Subtraction Angiography (DSA). In case of rupture aneurysms DSA was performed first followed by MRI once the patient was stable. The mean time interval between MRI and DSA in case of unruptured aneurysms was 2 days and in the case of ruptured aneurysms it was 7 days. DSA was done on General Electric Innova biplane 3131 Machine.

The rupture risk of each unruptured aneurysm was calculated by the PHASES score which is based on population (P, score 0-5), hypertension (H, score 0-1), age (A, score 0-1), size (S, score 0-10), early history of SAH (E, score 0-1), and location (S, score 0-4). Other conventional risk factors like history of smoking, presence of other associated comorbid conditions like collagen vascular disorders were assessed in these patients with intracranial aneurysms.

For the purpose of the study magnetic resonance imaging and Angiography images were obtained from picture archiving and communication system (PACS), anonymized and stored separately in numbered folders. The anonymized images in the separate folders were analyzed by two neuroradiologists independently.

On MRI the following factors were assessed:

The SWI images were evaluated for presence of any hypointensities suggestive of microbleeds along the wall of the aneurysm.

The post contrast vessel wall images were compared with the precontrast images for presence of any enhancement along the wall of the aneurysm. Enhancement was categorised as concentric or eccentric and extent of enhancement was graded as absent, faint (<enhancement of infundibular stalk), strong (comparable to enhancement of infundibular stalk).

The magnetic transfer factor ratio (MTFR) was calculated along the wall of the aneurysms. For this pre and post MT images were acquired. Three mirror ROIs were

placed along the wall of the aneurysm on post pre and post MT images and the average MT values were calculated. The MTFR was calculated by the following method:

$$MTFR = \frac{M_0 - M_{TR}}{M_0}$$

(M_0 = MT value on pre MT image, M_{TR} = MT value on post MT image)

On DSA other wall characteristics like irregularity of aneurysm wall and presence of daughter sacs were assessed.

Various ratios were calculated on DSA which are as follows:

1.Aspects ratio: The aspects ratio was calculated from the maximum perpendicular height of the aneurysm divided by the average neck diameter of the aneurysm.

2. Size ratio: The size ratio was calculated from the dome height of the aneurysm divided by the parent vessel average diameter

3. Flow angle: The flow angle was calculated from the angle between the inlet vessel central line and the dome maximum height.

4. Aneurysmal inclination angle: The aneurysmal inclination angle was calculated from the angle between the dome maximum height and neck plane.

In our study the unruptured aneurysms were classified into three groups based on the PHASES score; PHASES score 0-3 was considered as low, 4-6 as medium and 7->10

high. There were 3 cases (12%) with high PHASES score, 10 (42%) with medium score and 11 (46%) with high score.

The relationship between PHASES score and wall characteristics of the unruptured aneurysms like wall characteristics of unruptured intracranial aneurysms on MRI was assessed. The relationship between PHASES score and characteristics of the unruptured aneurysms on DSA was also assessed. The characteristic features of ruptured intracranial aneurysms were studied on Magnetic Resonance Imaging and Angiography. Thereafter the various features of ruptured and unruptured aneurysms on MRI and DSA was compared and their differences were statistically assessed.

STATISTICAL ANALYSIS:

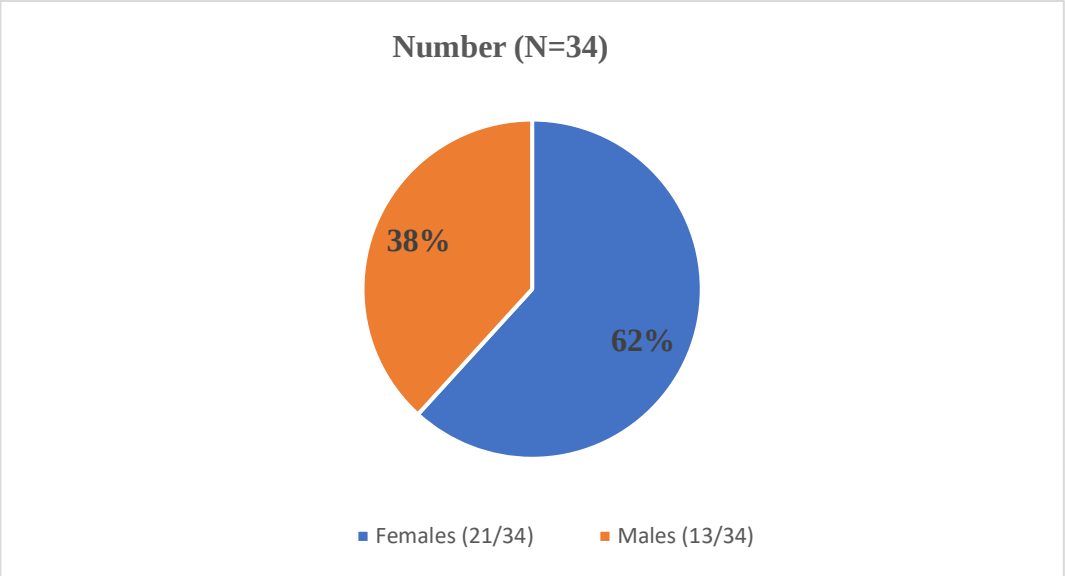
The data collected was entered into excel sheets for analysis. Mean and percentages were calculated for continuous and categorical variables respectively. Chisquare test was performed for hypothesis testing to determine heterogeneity among groups. Difference between mean values among two groups was determined using t-test. Logistic regression was carried out. The statistical analysis was carried out in R version 4.0.3. A p value of less than 0.05 was considered as statistically significant

RESULTS

Patient profile:

A total of 34 patients with intracranial saccular aneurysms were identified and evaluated in the study. There were 24 cases of unruptured aneurysms and 10 cases of ruptured aneurysms. The gender distribution of the patients is detailed in Fig 1.1. There were 21 females and 13 males with intracranial aneurysms in the present study.

Fig 1.1 Gender distribution of patients



The age wise distribution of patients is detailed in table 1.1 The mean age of the patients was 54 years within the range of 30 years to 80 years

Table 1.1: Age wise distribution of patients

Age Group (In yrs)	**0-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**
No of patients	0	0	0	2	11	14	4	3

15 of the 34 patients (44%) had hypertension (HTN) while 9 patients (26.5%) had co-existing diabetes mellitus (DM).

Comorbidities	No of ruptured aneurysms	% of ruptured aneurysms	No of unruptured aneurysms	% of unruptured aneurysms
Hypertension	6	60	9	37.5
Diabetes Mellitus	1	10	8	33

60 % of the patients with ruptured aneurysms had hypertension while only 37.5% of the patients with unruptured aneurysms had hypertension.

On the other hand only one case of ruptured aneurysm was diabetic while 33% of the patients with unruptured aneurysms had diabetes mellitus.

Aneurysm Location:

25 aneurysms (73.5 %) were located in the anterior circulation while 9 (26.5 %) were located in the posterior circulation. The artery-wise distribution of aneurysms in the anterior and posterior circulation are detailed in table 1.2. 15 cases were located in the ICA, 2 were in PCOM, 2 in MCA, 6 involving ACA/ACOM, 9 in BA.

Table 1.2 : Location of Aneurysms

	Anterior Circulation (23)				**Posterior Circulation (11)**		
Location	ICA	PCOM	MCA	ACA/ACOM	PCA	VA	BA
Number	15	2	2	6	-	-	9

Table 1.3: Location of ruptured/unruptured aneurysms

Location		**Anterior Circulation**				**Posterior Circulation**		
		ICA	PCOM	MCA	ACA/ACOM	PCA	SCA/AICA	BA
Ruptured	No	4	-	1	2	-	1	2
	Percentage	40	-	10	20	-	10	20
Unruptured	No	11	2	1	4	-	1	5
	Percentage	46	8	4	17		4	21

Fig 1.3: Clustered column depicting location of ruptured/unruptured aneurysms

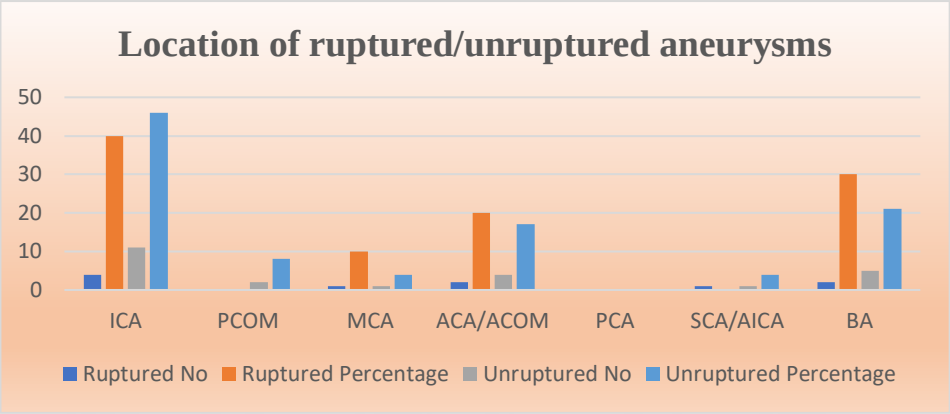


Table 1.3 and Fig 1.3 show the distribution of ruptured and unruptured aneurysms in the patient cohort by location. Out of 10 cases of ruptured aneurysms 4 (40%) were in the ICA, 2 (20%) cases were involving the basilar artery, 2 (20%) were in the ACOM, 1 case (10%) was involving the MCA and one (10%) was in the right SCA. Out of the 24 cases of unruptured aneurysms 11 (46%) were involving the ICA, 5 (21%) were located in the basilar artery, 4 (17%) were in ACA/ACOM, 2 (8%) were involving the PCOM and 1 (4%) each was located in the MCA and AICA.

Table 1.4: Distribution & Percentages of ruptured and unruptured aneurysms

Type of aneurysm	Number	Percentage
Ruptured	10	29.5%
Unruptured	24	70.5%

Table 1.4 shows the distribution of ruptured and unruptured aneurysms by numbers. Out of 34 aneurysms 10 (10.3%) were ruptured and 24 (71%) were unruptured aneurysms.

Determinants of Initial Clinical Presentation:

Table 1.5 and Fig 1.5A and Fig 1.5B shows the distribution of clinical events within the patients in the study

Table 1.5: Distribution of Clinical events

Clinical Event	Ruptured aneurysms		Unruptured aneurysms	
	No of patients	Percentage (%)	No of patients	Percentage (%)
Headache	10	100	16	67
Seizure	3	30	2	8
Vomiting	9	90	10	42
Loss of consciousness	3	30	0	0
Weakness	2	20	0	0
Sensory symptoms	1	10	3	12.5
Visual symptoms(blurring/diplopia)	1	10	5	21
Giddiness/Vertigo	4	40	4	17
Ptosis	0	0	3	12.5

Fig 1.5A: Distribution of clinical events-ruptured aneurysms

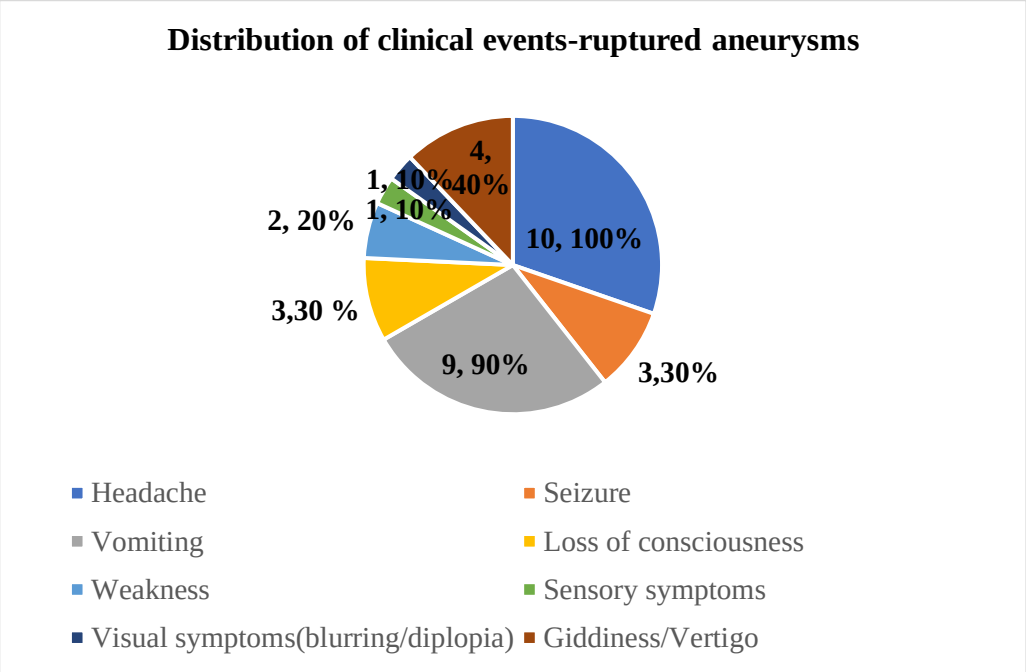
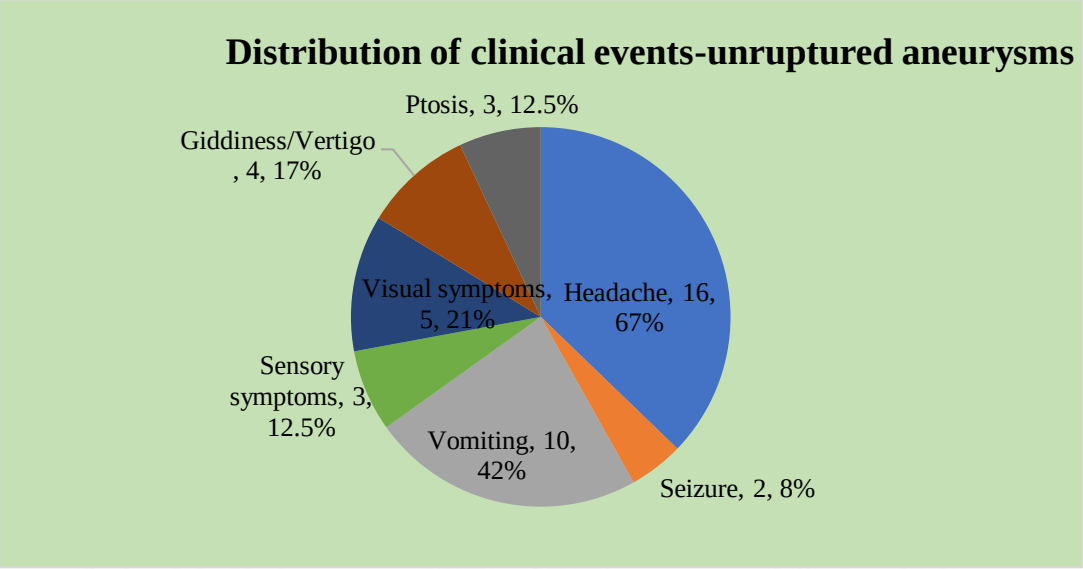


Fig 1.5B: Distribution of clinical events-unruptured aneurysms



The commonest symptoms seen in the ruptured aneurysms were presence of headache seen in all the 10 patients (100%), vomiting in 9 patients (90%), loss of consciousness

and seizures in 3 each (30%), giddiness/vertigo in 4 cases (40%) and sensory symptoms and visual symptoms were noted in 1 case each (10%).

In case of unruptured aneurysms commonest symptom was headache noted in 16 out of 24 patients (67%), history of vomiting was present in 10 (42%) cases, giddiness/vertigo was there in 4 (17%) patients, 5 patients (21%) had visual symptoms, sensory symptoms were there in 3 patients (12.5%), 2 patients (8%) had history of seizure while 3 patients (12.5%) had ptosis.

Table 1.6 Distribution of unruptured aneurysms based on PHASES score

PHASES Score	Number	Percentage
High	3	12
Medium	10	42
Low	11	46

Table 1.6 shows the distribution of the unruptured aneurysms based on the Phases score. PHASES score 0-3 was considered as low, 4-6 as medium and 7-10 high. There were 3 cases (12%) with high PHASES score, 10 (42%) with medium score and 11 (46%) with high score.

Table 1.7A: Enhancement features of wall of ruptured aneurysms on MRI

Location of aneurysm	**Enhancement Features on MRI**		
	Wall enhancement	**Faint /strong**	**Eccentric/Concentric**
R ICA communicating	Yes	S	C
R ICA communicating	Yes	F	C
Basilar artery	Yes	S	E
Basilar top	Yes	F	E
ACOM	Yes	S	E
L MCA bifurcation	Yes	S	E
R SCA	Yes	S	E
ACOM	No	-	-
L ICA comm	No	-	-
L anterior choroidal	No	-	-

R-right, L-left, ACOM-Anterior communicating artery, MCA- Middle cerebral artery, SCA-superior cerebellar artery, S-Strong, F-Faint, E-Eccentric, C-Concentric

Table 1.7B: Enhancement features of wall of unruptured aneurysms on MRI

Location of aneurysm	**Enhancement Features on MRI**		
	Wall enhancement	**Faint /strong**	**Eccentric/Concentric**
R Ophthalmic	No	-	-
ACOM	Yes	F	E
Ophthalmic segment	No	-	-
Ophthalmic segment	No	-	-
L MCA	Yes	F	E
L carotid cave	No	-	-
L Ophthalmic segment	No	-	-
L carotid cave	Yes	F	C
Basilar top	Yes	F	E
ACOM	No	-	-
Distal A2 azygous	Yes	S	C
Basilar top	Yes	S	E
R ICA communicating	No	-	-
R AICA	Yes	S	C
R ophthalmic segment	No	-	-
L PCOM	No	-	-
Basilar artery	Yes	F	E
R PCOM	Yes	S	C
R ophthalmic segment	No	-	-

Location of aneurysm	Enhancement Features on MRI		
	Wall enhancement	Faint /strong	Eccentric/Concentric
R ophthalmic segment	Yes	S	E
L carotid cave	No	-	-
Distal basilar artery	Yes	S	E
ACOM	Yes	S	E
Basilar top	Yes	F	E

R-right, L-left, ACOM-Anterior communicating artery, MCA- Middle cerebral artery, SCA-superior cerebellar artery, PCOM-posterior communicating artery, AICA-Anterior inferior cerebellar artery, S-Strong, F-Faint, E-Eccentric, C-Concentric

Table 1.7C: Enhancement of wall on MR of ruptured vs unruptured aneurysms

Type of aneurysm	Number showing enhancement	% showing enhancement	Number showing strong	% showing strong enhancement	Number showing faint	% showing faint enhancement
Ruptured aneurysm	7	70	5	71	2	29
Unruptured aneurysm	13	54	7	54	6	46

Fig 1.7: Enhancement features of wall of ruptured & unruptured aneurysms on MRI

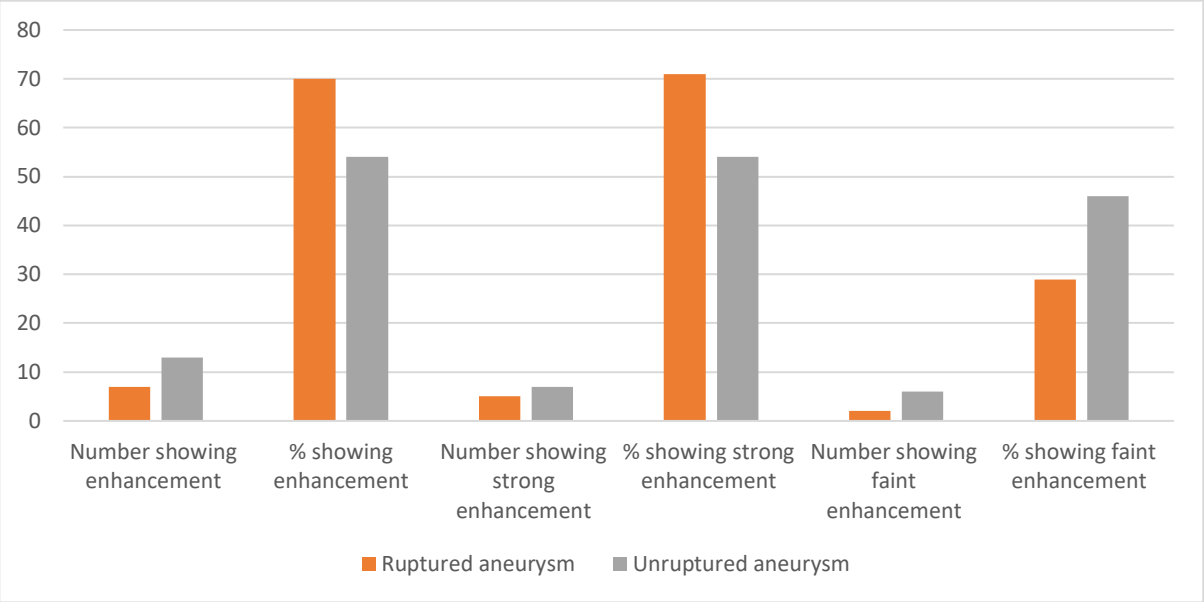


Table 1.7 A,B,C and Fig 1.7 shows wall enhancement features of ruptured and unruptured aneurysms on MRI. The post contrast vessel wall images were compared with the pre contrast images for presence of any enhancement along the wall of the aneurysm. Enhancement was categorised as concentric or eccentric and extent of enhancement was graded as absent, faint (<enhancement of infundibular stalk), strong (comparable to enhancement of infundibular stalk).

7 of the 10 cases (70%) of ruptured aneurysms showed wall enhancement out of which 5 (71%) showed strong enhancement and 2 (29%) showed faint enhancement. Among the unruptured aneurysms 13 (54%) showed enhancement of the wall out of which 7 (54%) showed strong and 6 (46%) showed faint enhancement. The percentage of

ruptured aneurysms showing wall enhancement was more than unruptured aneurysms however on Chi square test this result was not statistically significant (P value=0.6367)

Table 1.8A: Association of wall enhancement of unruptured aneurysms with PHASES score

Phases Score	No with wall enhancement +	No with wall enhancement -	% showing wall enhancement	P Value
High	3	0	100	0.03417
Medium	7	3	70	
Low	3	8	27	

Among unruptured aneurysms all 3 patients (100%) with high PHASES score showed wall enhancement of the aneurysm on MRI; among patients with medium PHASES score, 7 (70%) showed wall enhancement while among patients with low PHASES score 3 (27%) showed wall enhancement. Unruptured aneurysms with higher PHASES score were more likely to show wall enhancement and this finding was statistically significant on the Chi square test (P value=0.03417).

Table 1.8B: Association of degree of wall enhancement with PHASES score

Phases Score	Faint enhancement	Strong enhancement	% showing strong enhancement	P value
High	0	3	100	0.1809
Medium	4	3	43	
Low	2	1	33	

Among unruptured aneurysms all 3 patients (100%) with high phases score showed strong wall enhancement of the aneurysm on MRI; among patients with medium phases score, 3 (43%) showed strong wall enhancement while among patients with low phases score only 1 (33%) showed strong wall enhancement. Unruptured aneurysms with higher phases score were more likely to show strong wall enhancement however this finding was not statistically significant on the Chi square test (P value=0.1809).

Table 1.8C: Association of concentric/eccentric wall enhancement with PHASES score

Phases Score	Concentric Enhancement	Eccentric enhancement	% showing concentric enhancement	% showing eccentric enhancement	P value
High	1	2	33	66	0.983
Medium	2	5	28	71	
Low	1	2	33	66	

Among unruptured aneurysms 01 patient (33%) with high phases score showed concentric wall enhancement of the aneurysm on MRI; among patients with medium

phases score, 2 (28%) showed strong wall enhancement while among patients with low phases score only 1 (33%) showed strong wall enhancement. There was no statistically significant difference between the type of wall enhancement among aneurysms with different phases score (P value=0.983).

Table 1.9A: Blooming in aneurysmal wall on MRI

	No showing blooming	% showing blooming	
Ruptured aneurysm	8	80	0.30
Unruptured aneurysm	13	54	

Fig 1.8: Blooming in aneurysmal wall on MRI

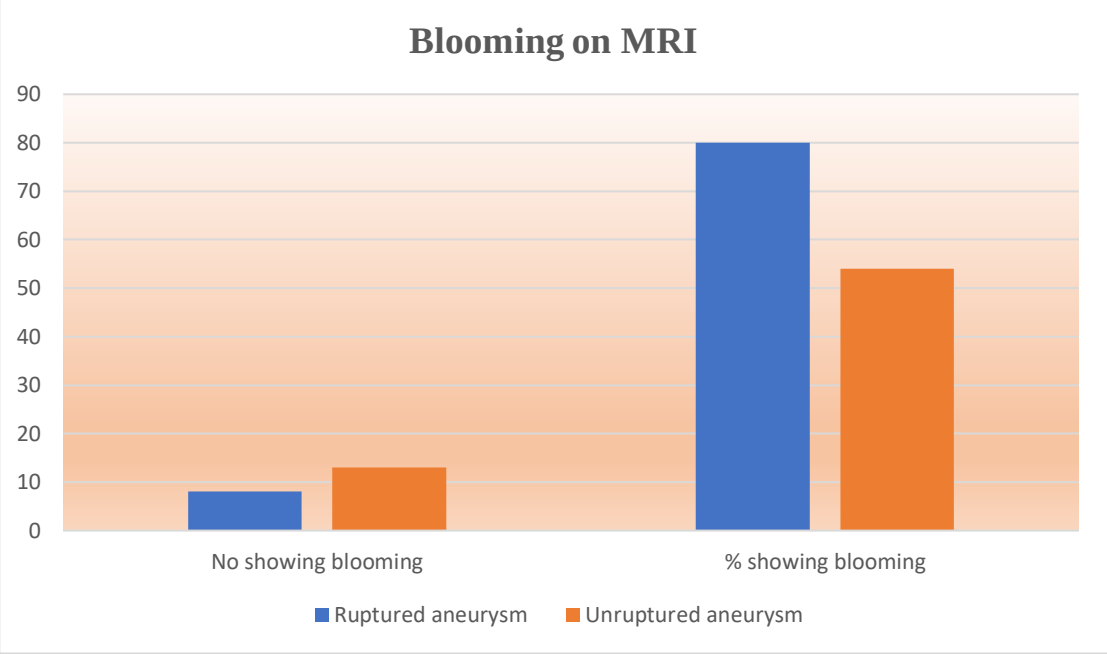


Table 1.9B: Association of blooming in wall of unruptured aneurysms with Phases score

Phases Score	Blooming +	Blooming -	% showing blooming	P value
High	3	0	100	0.03
Medium	7	3	70	
Low	3	8	27	

The SWI images were evaluated for presence of any hypointensities or blooming suggestive of microbleeds along the wall of the aneurysm. In Table 1.9A and Fig 1.8 it is seen that blooming in the wall of the aneurysms was noted in 8 (80%) ruptured aneurysms and in 13 (54%) unruptured aneurysm. However on Chi square test the result was not statistically significant (P value=0.30).

In table 1.9B among unruptured aneurysms 03 patients (100%) with high phases score showed blooming in the wall of the aneurysm on MRI; among patients with medium phases score, 7 (70%) showed blooming while among patients with low phases score only 3 (27%) showed blooming. Blooming was thus more commonly seen in unruptured aneurysms with high PHASES score and the result was statistically significant (P value=0.03).

Table 2.1A: Wall irregularity and blebs on angiogram for ruptured & unruptured aneurysms:

	No with wall irregularity	% with wall irregularity	P value	No with blebs	% with blebs	P value
Ruptured aneurysms	10	100	0.06	5	50	0.77
Unruptured aneurysms	15	62.5		9	37.5	

Fig 1.9: Wall irregularity and blebs on angiogram for ruptured & unruptured aneurysms:

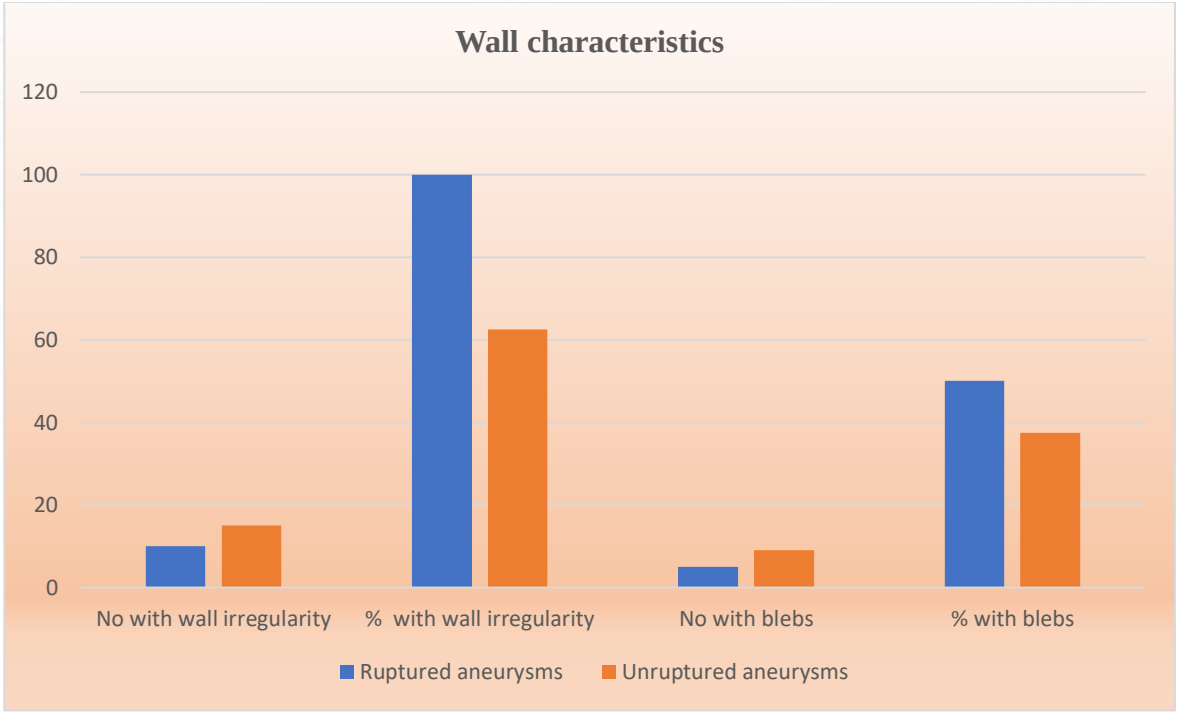


Table 2.1B: Association of wall irregularity of unruptured aneurysms with PHASES score

Phases Score	Wall irregular	Wall regular	% showing irregular wall	P value
High	2	1	67	0.0026
Medium	10	0	100	
Low	3	8	27	

Table 2.1C: Association of presence of blebs in unruptured aneurysms with PHASES score

Phases Score	Blebs present	Blebs absent	% showing blebs	P value
High	1	2	33	0.55
Medium	5	5	50	
Low	3	8	27	

In table 2.1A wall irregularity was seen in 10 (100%) cases of ruptured aneurysms and in 15 (62.5%) cases of unruptured aneurysms. However the difference was not statistically significant (P value=0.06). In table 2.1B blebs were noted in the wall of ruptured aneurysms in 5 (50%) cases while they were present in unruptured aneurysms in 9 (37.5%) cases; the difference was not statistically significant (P value = 0.77).

In table 2.1B among unruptured aneurysms 02 patients (67%) with high phases score showed wall irregularity of the aneurysm on MRI; among patients with medium phases score, 10 (100%) showed wall irregularity while among patients with low

phases score only 3 (27%) showed irregularity. Unruptured aneurysms with higher phases score were more likely to show wall irregularity and this finding was statistically significant on the Chi square test (P value=0.0026).

In table 2.1C among unruptured aneurysms 01 patients (33%) with high phases score showed presence of blebs in the wall of the aneurysm on MRI; among patients with medium phases score, 5 (50%) showed blebs while among patients with low phases score only 3 (27%) showed blebs. There was no statistically significant difference between presence of blebs among unruptured aneurysms with different phases score.

Table 2.2A: Mean MTF ratio for ruptured & unruptured aneurysms

	Ruptured aneurysms	**Unruptured aneurysms**	**P value**
Mean MTF ratio	0.19	0.17	0.76

Table 2.2B: Variation of MTF ratio among aneurysms with different PHASES score in unruptured aneurysms

Phases Subcategory	**Mean MTF ratio**	**Standard error**	**P value**
High	0.265		
Medium	0.147	-0.11793	0.0320
Low	0.177	-0.08833	0.0968

The magnetization transfer factor (MTF) ratio was calculated from the wall of the aneurysms for both ruptured and unruptured aneurysms. According to Table 2.2A the mean MTF ratio for ruptured aneurysms was 0.19 and for unruptured aneurysms was

0.17; and on T test there was no statistically significant difference between the two values (P value=0.76).

Among the unruptured aneurysms the mean MTF ratio was calculated for different PHASES categories (Table 2.2B). On Univariate logistic analysis the mean MTF ratio value for aneurysms with medium PHASES score was 0.11793 lower than of aneurysms with high phases score and the difference was statistically significant (P value=0.0320).

The mean MTF ratio value for aneurysms with low phases score was 0.08833 lower than of aneurysms with high PHASES score, however the difference was not statistically significant (P value=0.0968).

Table 2.3A: Mean Aspects ratio for ruptured & unruptured aneurysms

	Ruptured aneurysms	**Unruptured aneurysms**	**P value**
Mean Aspects ratio	1.5	1.537	0.85

Table 2.3B: Variation of Aspects ratio among aneurysms with different PHASES score in unruptured aneurysms

Phases Subcategory	**Mean Aspects ratio**	**Standard error**	**P value**
High	1.97		
Medium	1.49	-0.4767	0.226
Low	1.46	-0.5030	0.198

The aspects ratio was calculated from the maximum perpendicular height of the aneurysm divided by the average neck diameter of the aneurysm. According to Table 2.3A the mean Aspects ratio for ruptured aneurysms was 1.5 and for unruptured aneurysms was 1.537; and on T test there was no statistically significant difference between the two values (P value=0.85).

Among the unruptured aneurysms the mean Aspects was calculated for different PHASES categories (Table 2.3B). On Univariate logistic analysis the mean Aspects ratio value for aneurysms with medium PHASES score was 0.4767 lower than of aneurysms with high phases score and the difference was not statistically significant (P value=0.226).

The mean Aspects ratio value for aneurysms with low phases score was 0.5030 lower than of aneurysms with high PHASES score, however the difference was not statistically significant (P value=0.198).

Table 2.4A: Mean size ratio for ruptured & unruptured aneurysms

	Ruptured aneurysms	**Unruptured aneurysms**	**P value**
Mean Size ratio	2.011	2.010	0.9971

Table 2.4 B: Variation of Size ratio among aneurysms with different PHASES score in unruptured aneurysms

Phases Subcategory	Mean size ratio	Standard error	P value
High	3.53		
Medium	2.02	-1.5113	0.0298
Low	1.58	-1.9497	0.00625

The size ratio was calculated from the dome height of the aneurysm divided by the parent vessel average diameter. According to Table 2.4A the mean size ratio for ruptured aneurysms was 2.011 and for unruptured aneurysms was 2.010; and on T test there was no statistically significant difference between the two values (Pvalue=0.99). Among the unruptured aneurysms the mean size ratio was calculated for different PHASES categories (Table 2.4B). On Univariate logistic analysis the mean size ratio value for aneurysms with medium PHASES score was 1.5113 lower than of aneurysms with high phases score and the difference was statistically significant (P value=0.0298).

The mean size ratio value for aneurysms with low phases score was 1.9497 lower than of aneurysms with high PHASES score, and the difference was statistically significant (P value=0.198).

So the size ratio was significantly more in unruptured aneurysms with high PHASES score.

Table 2.5 A: Mean flow angle for ruptured & unruptured aneurysms

	Ruptured aneurysms	Unruptured aneurysms	P value
Mean flow angle	114	111	0.77

Table 2.5 B: Variation of mean flow angle among aneurysms with different PHASES score in unruptured aneurysms

Phases Subcategory	Mean flow angle	Standard error	P value
High	160		
Medium	108	-51.17	0.016
Low	100	-59.53	0.0056

The flow angle was calculated from the angle between the inlet vessel central line and the dome maximum height. According to Table 2.5A the mean flow angle for ruptured aneurysms was 99.26 and for unruptured aneurysms was 111.06; and on T test there was no statistically significant difference between the two values (Pvalue=0.4737). Among the unruptured aneurysms the mean flow angle was calculated for different PHASES categories (Table 2.5B). On Univariate logistic analysis the mean flow angle value for aneurysms with medium PHASES score was 51.17 lower than of aneurysms with high phases score and the difference was statistically significant (P value=0.016).

The mean flow angle value for aneurysms with low phases score was 59.53 lower than of aneurysms with high PHASES score, and the difference was statistically significant (P value=0.0056).

So the flow angle was significantly more in unruptured aneurysms with high PHASES score.

Table 2.6 A: Mean aneurysmal inclination angle for ruptured & unruptured aneurysms

	Ruptured aneurysms	**Unruptured aneurysms**	**P value**
Mean aneurysmal inclination angle	86.4	93.88	0.2039

Table 2.6 B: Variation of mean aneurysmal inclination angle among aneurysms with different PHASES score in unruptured aneurysms

Phases Subcategory	**Mean aneurysmal inclination angle**	**Standard error**	**P value**
High	97		
Medium	94	-3.2	0.763
Low	93	-4.6	0.662

The aneurysmal inclination angle was calculated from the angle between the dome maximum height and neck plane. According to Table 2.6A the mean aneurysmal inclination angle for ruptured aneurysms was 86.4 and for unruptured aneurysms was 93.8; and on T test there was no statistically significant difference between the two values (P value = 0.2039).

Among the unruptured aneurysms the mean aneurysmal inclination angle was calculated for different PHASES categories (Table 2.6B). On Univariate logistic analysis the mean aneurysmal inclination angle value for aneurysms with medium PHASES score was 3.2 lower than of aneurysms with high phases score and the difference was not statistically significant (P value=0.763).

The mean aneurysmal inclination angle value for aneurysms with low phases score was 4.6 lower than of aneurysms with high PHASES score, and the difference was not statistically significant (P value=0.662).

REPRESENTATIVE CASES

Case 1:

46 years old lady, a known case of SLE with hypertension and diabetes mellitus presented with history of headache associated with blurring of vision

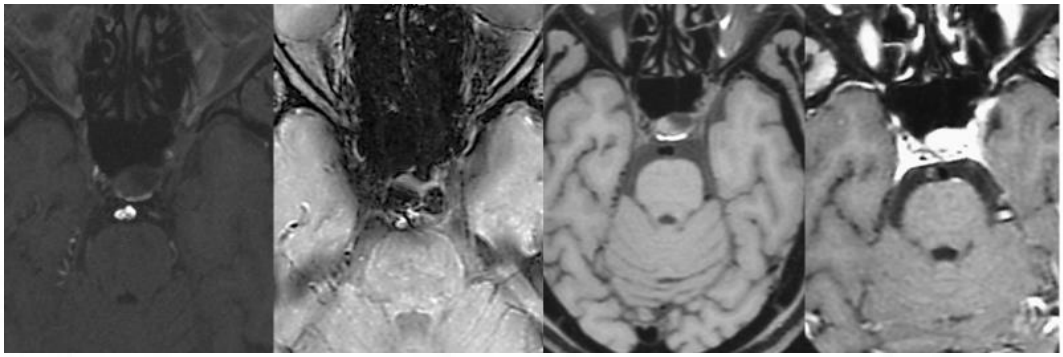


Fig 2(A) (B) (C) (D)

(A) TOF MR angiogram shows a saccular aneurysm with a dome height of 3.5mm and neck width of 1.9mm arising from the right lateral wall of the mid basilar artery

(B) On SWI images a smooth rim of susceptibility artifact suggestive of microbleed is noted eccentrically along the wall of the aneurysm

Cube T1W1 (axial) FS precontrast (C) and postcontrast (D) images shows eccentric faint enhancement along the wall of the aneurysm

Case 2:

54 years old male patient, a known hypertensive presented with headache associated with transient weakness of left upper limb, loss of consciousness and an episode of seizure

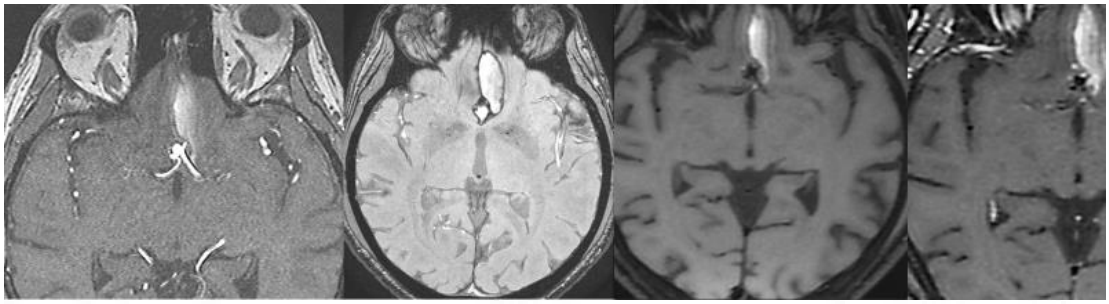


Fig 2.1 (A) (B) (C) (D)

(A) TOF MR angiogram shows a saccular aneurysm with a dome height of 4.3mm and neck width of 2.1mm arising from the ACOM

(B) On SWI images a concentric, thick and irregular rim of susceptibility artifact suggestive of microbleed is seen along the wall of the aneurysm

Cube T1W1 (axial) FS precontrast (C) and postcontrast (D) images shows eccentric strong enhancement along the wall of the aneurysm

Case 3:

54 years old lady a known hypertensive presented with sentinel headache associated with vomiting and giddiness.

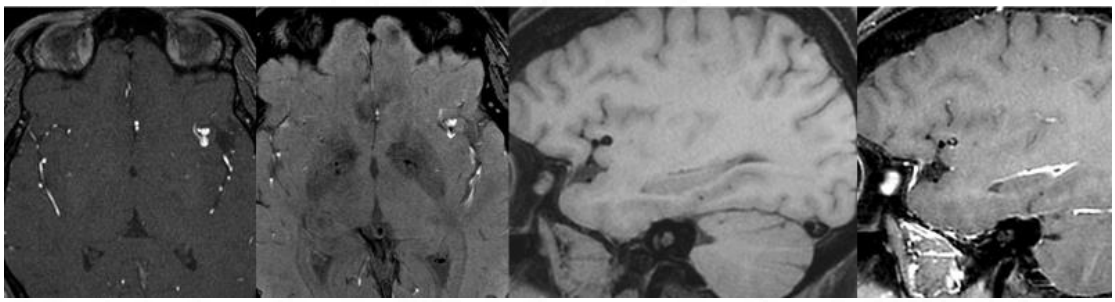


Fig 2.2(A) (B) (C) (D)

(A) TOF MR angiogram shows a saccular bilobed aneurysm aneurysm with a dome height of 5.5mm arising from the inferior division of the proximal M2 segment of the left MCA

(B) On SWI images an eccentric nodular pattern of susceptibility artifact suggestive of microbleed is seen along the wall of the aneurysm

Cube T1W1 (sagittal) FS precontrast (C) and postcontrast (D) images shows eccentric strong enhancement along the wall of the aneurysm

Case 4:

61 years old male patient, a known case of hypertension and diabetes mellitus presented with headache associated with numbness and paraesthesias in left upper limb

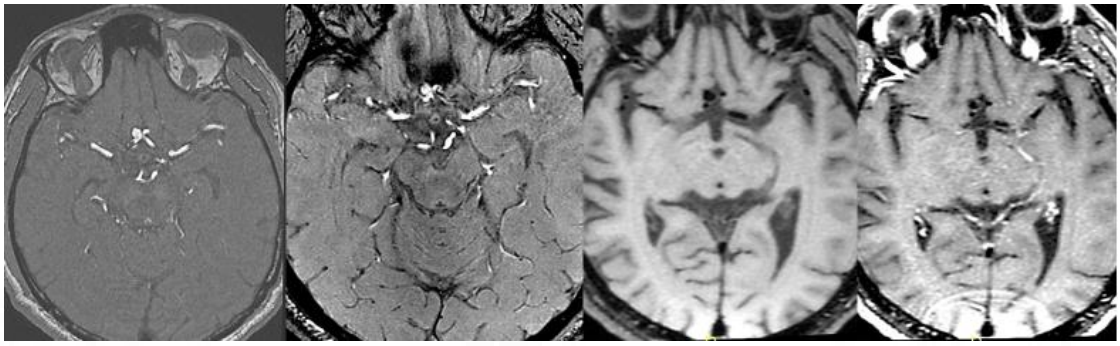


Fig 2.3(A) (B) (C) (D)

(A) TOF MR angiogram shows a saccular aneurysm with a dome height of 5.6mm and neck width of 2.3mm arising from the distal ACOM.

(B) On SWI images an eccentric, smooth rim of susceptibility artifact suggestive of microbleed is seen along the wall of the aneurysm

Cube T1W1 (axial) FS precontrast (C) and postcontrast (D) images shows eccentric faint enhancement along the wall of the aneurysm

Case 5:

58 years old male patient with no known comorbidities presented with sentinel headache associated with vomiting

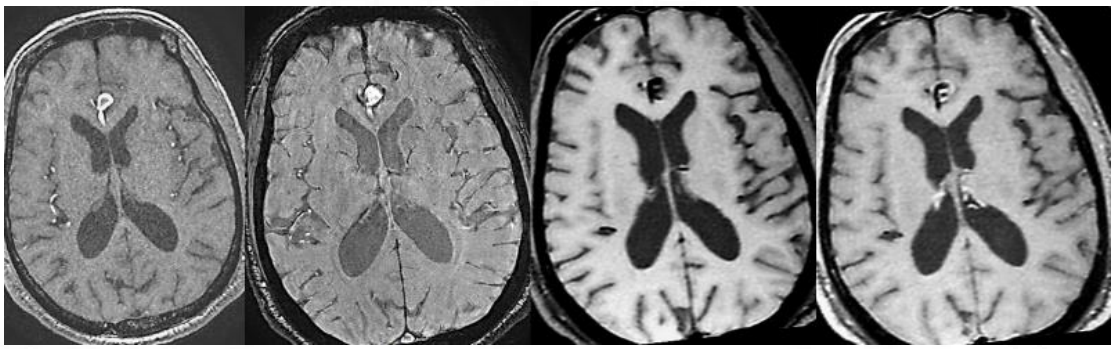
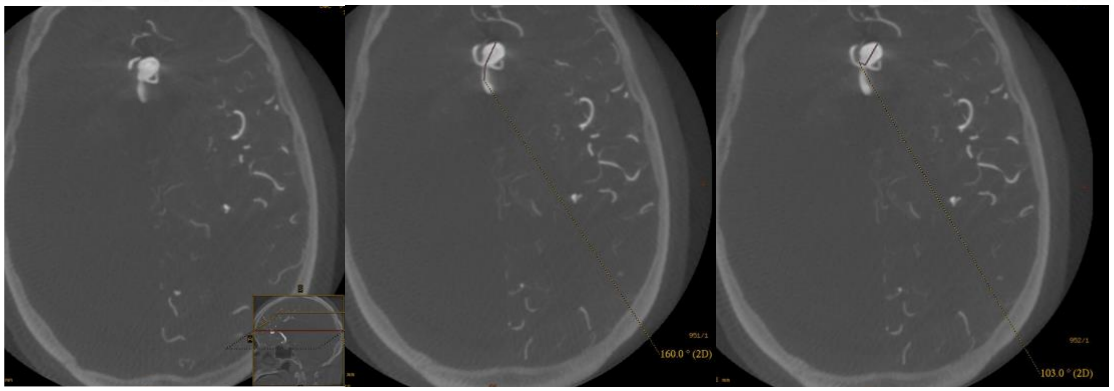


Fig 2.4(A) (B) (C) (D)

(A)TOF MR angiogram shows a saccular aneurysm with a dome height of 10mm and neck width of 4mm arising from the distal A2 segment of the azygous ACA.

(B) On SWI images an irregular, concentric rim of susceptibility artifact suggestive of microbleed is seen along the wall of the aneurysm

Cube T1W1 (axial) FS precontrast (C) and postcontrast (D) images shows eccentric strong enhancement along the wall of the aneurysm



(E) (F) (G)

(E) 3D rotational angiogram axial reformatted view shows the anteriorly directed saccular aneurysm

(F) & (G) 3D rotational angiogram axial reformatted view shows the flow angle and aneurysmal inclination angle to be 160 and 103 degrees respectively

Case 6:

A 54 years old male patient, a known case of hypertension presented with severe headache, vomiting, inability to move the right upper and lower limbs for 10 minutes and loss of consciousness. NCCT head showed presence of subarachnoid haemorrhage.

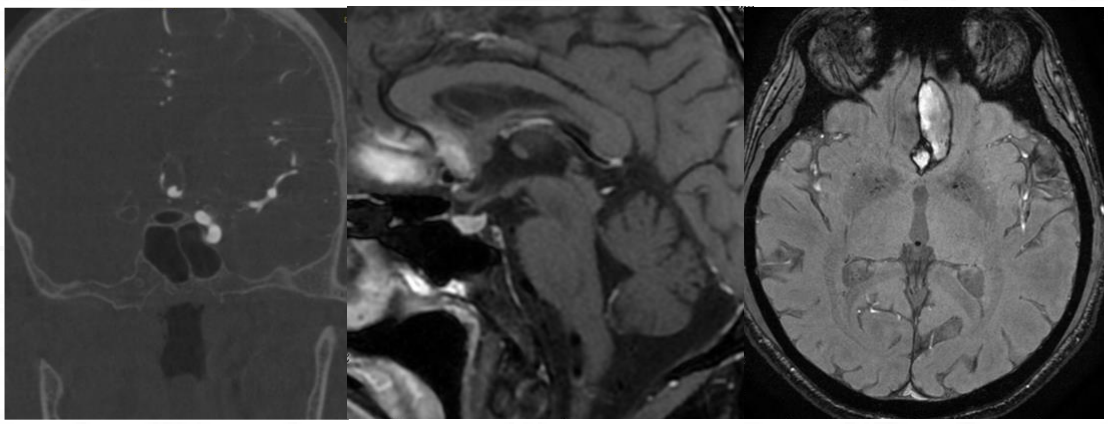
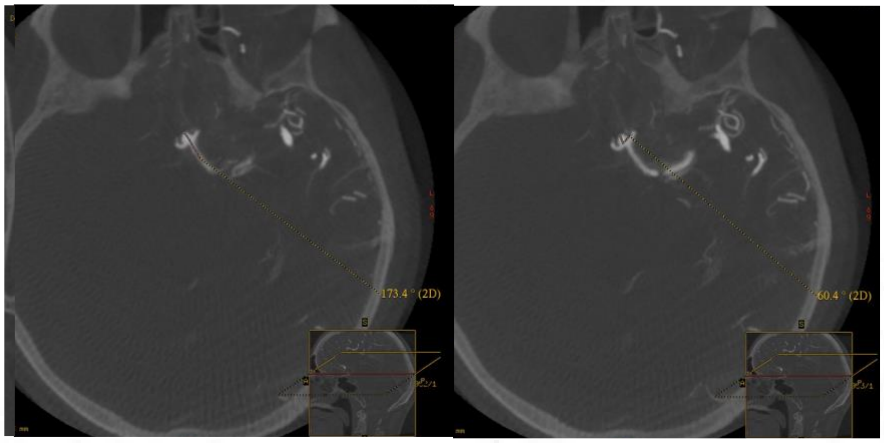


Fig 2.5(A) (B) (C)

(A) 3D rotational angiogram coronal reformatted view shows a saccular aneurysm with a dome height of 3.3mm and neck width of 3.2mm arising from the ACOM

(B) Cube T1W1 (sagittal) FS postcontrast image shows eccentric strong enhancement along the anterior wall of the aneurysm

(C) On SWI images an irregular, concentric rim of susceptibility artifact suggestive of microbleed is seen along the wall of the aneurysm. The adjacent parenchyma also shows a localized hematoma



(D) (E)

(D) & (E) 3D rotational angiogram axial reformatted view shows the flow angle and aneurysmal inclination angle to be 173 and 60 degrees respectively

Case 7:

A 74 years old female patient, a known case of hypertension and diabetes mellitus presented with severe headache, vomiting, giddiness and vertigo and loss of consciousness. NCCT head showed presence of subarachnoid haemorrhage

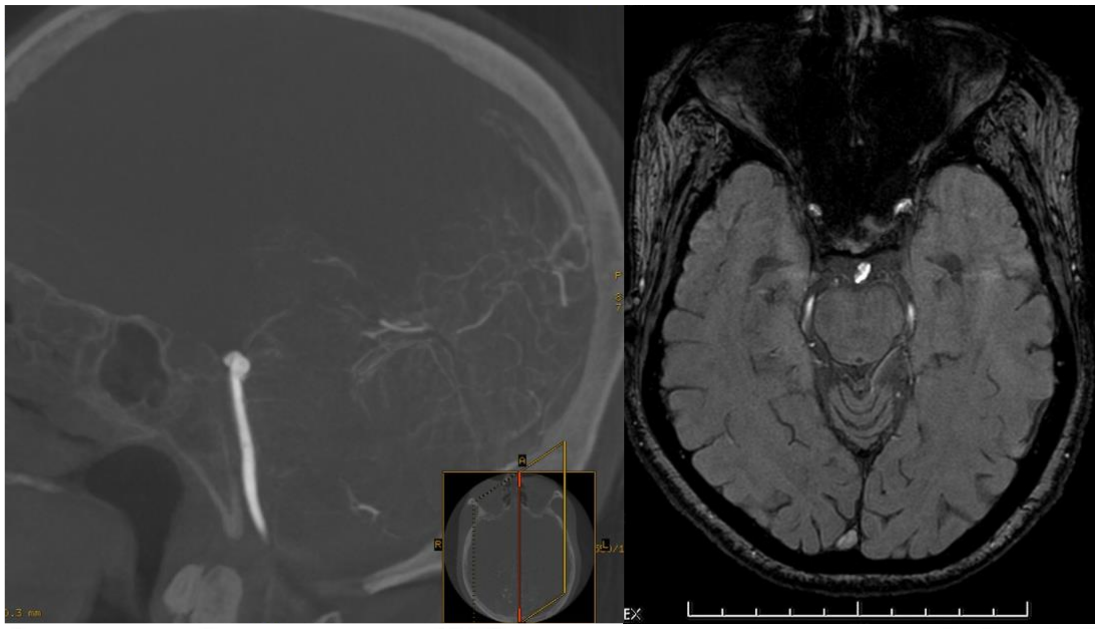
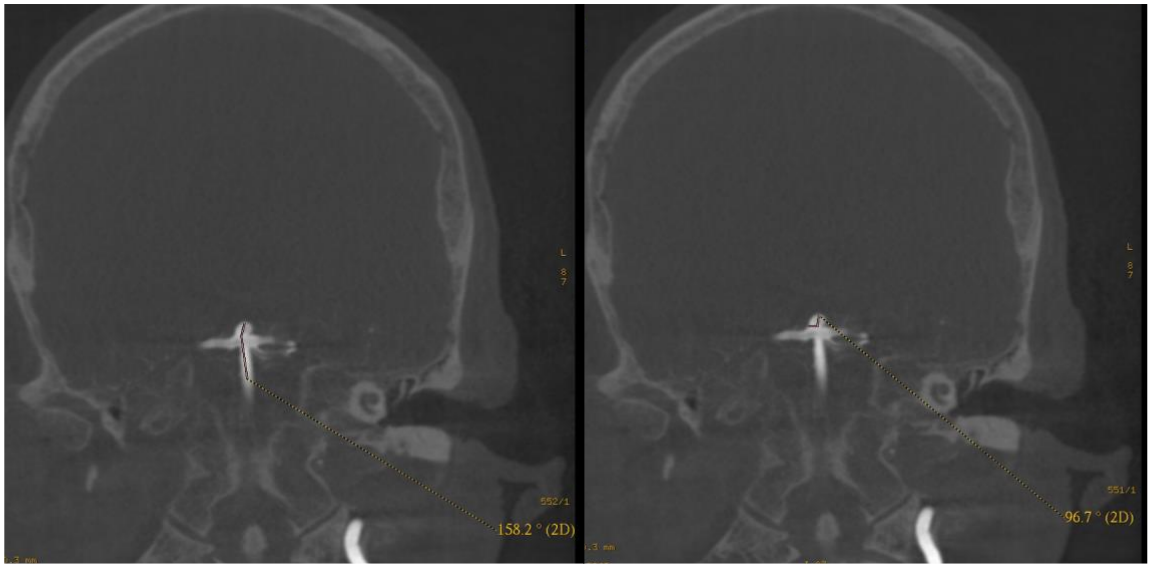


Fig 2.6 (A) (B)

(A) 3D rotational angiogram sagittal reformatted view shows the irregular shaped saccular aneurysm with dome height of 3.6mm and neck width of 3.8mm arising from the basilar top

(B) On SWI images no susceptibility artifact suggestive of microbleed is seen along the wall of the aneurysm.



(C) (D)

(C) & (D) 3D rotational angiogram coronal reformatted view shows the flow angle and aneurysmal inclination angle to be 158 and 96.7 degrees respectively

DISCUSSION

This is a prospective study of consecutive 34 patients with ruptured/unruptured intracranial aneurysms, out of which, 24 patients had unruptured intracranial aneurysms and 10 were cases of ruptured aneurysms.

I. This study dealt with and explored three different aspects of intracranial aneurysms:

1. the relationship between PHASES score and wall characteristics of the unruptured aneurysms on MRI and DSA were assessed, and it was evaluated which MR and angiographic factors were associated with high PHASES score, thus suggesting a high risk of rupture of the aneurysms.
2. The characteristic features of ruptured intracranial aneurysms were studied on Magnetic Resonance Imaging and Angiography
3. Thereafter the various features of ruptured and unruptured aneurysms on MRI and DSA was compared, and their differences were statistically assessed.

There are various studies in literature which have probed these aspects of intracranial aneurysms.

Previous research which have explored the wall characteristics of unruptured aneurysms on MRI/DSA and found its association with PHASES score are as follows:

1. Jiang et al (83) investigated the relationship between aneurysm wall enhancement on vessel wall MRI with and clinical rupture risks based on PHASES score. They found that aneurysms which had increased rupture risk on the basis of PHASES score had increased wall enhancement, intensity of wall enhancement and increased neck width on MRI. Thus presence of

increased wall enhancement index in case of unruptured aneurysms was a predictor of increased risk of rupture of the aneurysm.

2. Zhang et al (84) investigated the relationship between qualitative and quantitative wall enhancement indices, traditional risk factors for aneurysms, and ELAPSS/PHASES scores in a large cohort of intracranial unruptured saccular aneurysms. They found that a larger size of the aneurysm, non-internal carotid artery/middle cerebral artery location, and an irregular shape were factors which were independently associated with aneurysmal wall enhancement. A higher wall enhancement index had an increased risk of aneurysm growth and rupture.
3. Larsen et al (85) investigated the association of focal wall enhancement of unruptured intracranial aneurysms on vessel wall MRI with hemodynamic risk factors (calculated on flow simulations) and morphological risk factors, PHASES score and histologic markers of wall inflammation (by detection of CD34, vasa vasorum and presence of myeloperoxidase staining a subgroup of patients). Areas showing enhancement were associated with lower wall shear stress (WSS), lower oscillatory shear index and increased low shear area. Higher PHASES score and histological features of wall inflammation was associated with focal wall enhancement.

So focal wall enhancement was associated with higher PHASES score, and histological markers of wall inflammation. hemodynamic, morphological factors related to higher rupture risk. So focal wall enhancement could serve as a marker of instability of unruptured intracranial aneurysms.

II. The mean age of the patients was 54 years within the range of 30 years to 80 years. This was quite similar to other studies; in the study by Bhogal et al (86) the mean age of patients was 51.7 years, in the study by Larsen et al (85) the mean age was 60 years.

III. In our study out of 10 ruptured aneurysms 30% were located in posterior circulation, while 25% of the unruptured aneurysms were located in the posterior circulation. In the study by Backes et al (87) 7% of the ruptured aneurysms were in posterior circulation and 10% of unruptured aneurysms were in posterior circulation. . In the study by Bhogal et al (86) the majority of the aneurysms were in the anterior circulation; 16.1% of the ruptured aneurysms were in posterior circulation and 10.2% of unruptured aneurysms were in posterior circulation;. The most coomon location for both unruptured and ruptured aneurysms was the MCA, and the ICA was the second most frequent location of unruptured aneurysms and the Acom was the second most frequent location for ruptured aneurysms. In our study the commonest location for both ruptured and unruptured aneurysms was in the ICA followed by the ACA/Acom.

IV. If we consider the clinical presentation of the patients with aneurysms the commonest symptoms seen in both ruptured and unruptured aneurysms were presence of headache and vomiting. While headache was present in 100 % of the patients with ruptured aneurysms and vomiting in 90 % cases, in case of patients with unruptured aneurysms headache was seen in 67 % cases and vomiting was present in 42 % patients.

In unruptured aneurysms visual symptoms were seen 21% patients, sensory symptoms were seen in 12.5%, and ptosis was present in 12.5% patients. In ruptured aneurysms visual symptoms and sensory symptoms were noted in one patient each and none of the patients had ptosis.

Similarly previous studies (88) have also reported that the commonest symptom in patients with ruptured IA is presence of severe headache and vomiting with focal neurological deficits and seizures less commonly seen. Patients with unruptured aneurysms on the other hand apart from having history of headache and giddiness also have cranial nerve deficits and ischemic cerebrovascular disease.

V. Aneurysmal wall enhancement on vessel wall MRI is indicative of an ongoing inflammatory process in the wall of the aneurysm which makes the aneurysm susceptible to rupture. (6,7,9, 89,90,91). It has been shown in previous studies that wall enhancement is more frequently seen in ruptured aneurysms (6,7,90). They have defined wall enhancement as absent, faint and strong and have concluded that strong enhancement is associated with ruptured IA (6).

In this study, there were 3 cases (12%) with high PHASES score, 10 (42%) with medium score and 11 (46%) with high score.

7 of the 10 cases (70%) of ruptured aneurysms showed wall enhancement out of which 5 showed strong enhancement and 2 showed faint enhancement. Among the unruptured aneurysms 13 (54%) showed enhancement of the wall out of which 7 showed strong and 6 showed faint enhancement. The percentage of ruptured

aneurysms showing wall enhancement was more than unruptured aneurysms however on Chi square test this result was not statistically significant (P value=0.6367).

Wang et al (92) found that all cases of ruptured aneurysms showed wall enhancement (entire wall in 53% and partial wall in 47%) while 73% of the unruptured aneurysm showed enhancement of the wall (entire in 65% and partial in 8%). They measured the signal intensity of the wall on pre and postcontrast images and found that enhancement ratio was 0.63 in case of unruptured aneurysms and 0.90 in case of ruptured aneurysms and the difference was statistically significant (P value <0.001).

In our study unruptured aneurysms with higher PHASES score were more likely to show wall enhancement and this finding was statistically significant on the Chi square test (P value=0.03417). Unruptured aneurysms with higher phases score were also more likely to show strong wall enhancement however this finding was not statistically significant on the Chi square test (P value=0.1809). There was no statistically significant difference between the type of wall enhancement (concentric/eccentric) among aneurysms with different phases score (P value=0.983).

In the study by Nan et al (93) out of 140 cases of unruptured IA, wall enhancements was present in 82 (58%) cases which was quite similar to our findings. With increasing PHASES score the proportion of aneurysms with wall enhancement increased progressively. IA with PHASES score <5 showed wall enhancement in 33.9% cases, those with PHASES score ≥ showed enhancement in 78.2% cases while enhancement was noted in 92.3% cases in IA with PHASES score ≥ 10.

This was quite similar to our study in which 100% of the patients of unruptured aneurysms with high PHASES score showed wall enhancement of the aneurysm on MRI; among patients with medium PHASES score, 70% showed wall enhancement while among patients with low PHASES score 27% showed wall enhancement.

In the study by Zhang et al (84) aneurysms with wall enhancement had a more than three times higher estimated 5-year rupture risk than did aneurysms without AWE (3.9 ± 5.2% vs. 1.2 ± 1.6%, $P < 0.001$). Larger areas of enhancement and increased wall enhancement index were positively correlated with the 3- and 5-year growth risk and 5-year rupture risk ($r = 0.49$ and 0.40, $r = 0.49$ and 0.40, and $r = 0.36$ and 0.24, respectively; all $P < 0.001$).

VI. The SWI images were evaluated for presence of any hypo intensities or blooming suggestive of microbleeds along the wall of the aneurysm. In our study blooming suggestive of microbleeds in the wall of the aneurysms was noted in 8 (80%) ruptured aneurysms and in 13 (54%) unruptured aneurysm. However on Chi square test the result was not statistically significant (P value=0.30).

Among unruptured aneurysms blooming in the wall of the aneurysms on SWI images was more commonly seen in unruptured aneurysms with high PHASES score and the result was statistically significant (P value=0.03).

It has been seen in previous studies that blooming s/o microbleeds or iron deposition in aneurysmal wall is associated with unstable nature of the aneurysm and increased risk of rupture.

Nakagawa et al analysed 20 IA in 16 patients with history of headache. Four of these patients had history of sentinel headache. Al patients underwent MRI of the brain with quantitative susceptibility mapping sequence. The four patients with history of sentinel headache had positive QSM s/o microbleeds in the wall , other 16 aneurysms showed no microbleeds in the wall. It was further seen that the 4 aneurysms with positive QSM findings had greater undulation indices s/o unstable aneurysms.

Hasan et al (50) studied thirty unruptured aneurysms in 22 patients who underwent MRI after infusion of ferumoxytol. In 7 of these aneurysms there was pronounced early uptake of ferumoxytol within 24 hours. 4 of these aneurysms were clipped and the remaining 3 ruptured within 6 months. In 16 aneurysms there was increased uptake of ferumoxytol at 72 hours. 8 of these aneurysms were conservatively managed and none of them increased in size or ruptured at 6 months. Further dome tissue of the aneurysm was collected from these aneurysms it was stained for presence of cyclooxygenase-1, cyclooxygenase-2, microsomal prostaglandin E2 synthase-1, and macrophages. These inflammatory molecules were significantly seen in aneurysms with early uptake of ferumoxytol than late uptake. Thus, uptake of ferumoxytol in aneurysm walls within the first 24 hours is highly suggestive of instability of aneurysm and probability of rupture within 6 months.

VII. In this study wall irregularity and blebs were more commonly seen in ruptured aneurysms than unruptured aneurysms, however the difference was not statistically significant.

Among unruptured aneurysms those with higher phases score were more likely to show wall irregularity and this finding was statistically significant on the Chi square test (P value=0.0026). However there was no significant difference in the presence of blebs between unruptured aneurysms with different PHASES score.

In the study by Bhogal et al (86) most of the of the unruptured aneurysms had a smooth wall and a regular morphology (*n* = 113, 76.4%) while only 15.9% of ruptured aneurysms had a smooth morphology. In the multivariate analysis, a complex morphology of aneurysm with blebs was the strongest risk factor for rupture (OR, 29.27; 95% CI, 14.33–59.78; $P < 0.001$) Although aneurysms with a lobulated appearance showed an increased risk of rupture, this did not reach statistical significance.

In the study by Wang et al (92) 84% of ruptured aneurysms had an irregular shape, while only 40% of unruptured aneurysms had an irregular morphology and the difference was statistically significant.

Other studies have also reported that IAs with an irregular shape are associated with a higher rupture risk (95,96). The cause for the irregular shape leading to increased risk of rupture of the aneurysms is attributed to the fact that irregularity of the wall leads to alteration of blood flow vectors within the aneurysm causing increased stress and strain on the walls. This leads to inflammation of the aneurysmal wall with thinning of the intima which further leads to increased wall permeability and leakage of contrast media (6,9,97)

VIII. In this study the mean aspects ratio for ruptured aneurysms was 1.5 and for unruptured aneurysms was 1.537; and on T test there was no statistically significant difference between the two values (P value =0.85). Among the unruptured aneurysms the mean Aspects for aneurysms with higher PHASES score was more than for aneurysms with lower PHASES score, however the difference was not statistically significant (P value=0.226).

In the study by Backes et al (87) who compared features of the ruptured and unruptured aneurysms in patients with multiple IA and with subarachnoid haemorrhage it was noted that the aspect ratio ≥1.3 was significantly associated with aneurysm rupture; 69% of the ruptured aneurysms and only 33% of the unruptured aneurysms had an Aspects ratio of ≥1.3.

Hiroshi et al (98) measured the aspect ratios and the sizes of aneurysms, on angiograms of 129 patients with ruptured aneurysms and 72 patients with 78 unruptured aneurysms. There was statistically significant difference between the aspect ratio between ruptured aneurysms and unruptured aneurysms, and 80% of the ruptured aneurysms had an aspect ratio of more than 1.6, whereas 90% of the unruptured aneurysms showed an aspect ratio of less than 1.6.

In the study by Dhar S et al (70) the Aspects ratio (AR) has been found to correlate with IA rupture. They studied 45 cases of terminal or sidewall aneurysms (25 unruptured and 20 ruptured) and found that the mean Aspects ratio for ruptured aneurysms was 1.5 +/- 0.45 and for unruptured aneurysms it was 1.2 +/- 0.55 and the difference was statistically significant (P value = 0.044). Similar were the findings of

Raghavan et al (99) studied 27 patients with ruptured or unruptured aneurysms and found that the mean Aspects ratio for ruptured aneurysms was 1.85 +/- 0.79 and for unruptured aneurysms it was 1.27 +/- 0.40 and the difference was statistically significant (P value = 0.016).

Nader et al (100) studied angiograms of 75 cases with history of subarachnoid haemorrhage and multiple IA. 75 ruptured and 107 unruptured aneurysms were present. The mean AR was 2.70 for ruptured aneurysms, and 1.8 for unruptured aneurysms and the difference was statistically significant (P < 0.001).

As opposed to this finding, Beck et al. (101) reported the AR of unruptured IAs to be higher than the AR of ruptured IAs (mean, 2.3 versus 1.8).

The variable results of the Aspects ratio in different studies can be explained by the fact that some of the aneurysms have irregular shapes in which the long axis of the aneurysm is oblique and some have a lobulated appearance with a mushroom shape.

IX. In our series the mean size ratio for ruptured aneurysms was 2.011 and for unruptured aneurysms was 2.010; and on T test there was no statistically significant difference between the two values (P value = 0.99).

Among the unruptured aneurysms the size ratio was significantly more in unruptured aneurysms with high PHASES score.

In the study by Dhar et al (70) size ratio was an important parameter for the rupture risk of intracranial aneurysms. In their study 77% of all the ruptured aneurysms had size ratio > 2.05 while 83% of all the unruptured aneurysms had a size ratio < 2.05

and on multiple logistic regression size ratio remained significant. Size ratio considers not only the aneurysm size but also the calibre of the adjacent vessel. Thus, it indirectly takes into account the effect of IA location on rupture.

X. In this study the mean flow angle for ruptured aneurysms was 114 and for unruptured aneurysms was 111; and on T test there was no statistically significant difference between the two values (P value = 0.77). Similarly in the study by Backes et al (87) the mean flow angle for ruptured aneurysms was 141 while for unruptured aneurysms it was 133 with no statistically significant difference between them.

Baharoglu M et al (72) however had contradictory findings with univariate analysis showing mean flow angle being more obtuse in case of ruptured aneurysms (124.9 degrees+/-26.5 degrees in ruptured versus 105.8 degrees+/-18.5 degrees in unruptured, P=0.0001).

They argued that increased inflow angle leads to deeper migration of the flowing blood into the aneurysm with greater peak flow velocities with greater transmission of kinetic energy into the dome thus contributing to its instability and rupture.

However in our study we found that the mean flow angle for unruptured aneurysms for higher PHASES score for more than those for lower PHASES score and this difference was statistically significant.

XI. We found that the mean aneurysmal inclination angle for ruptured aneurysms was 86.4 and for unruptured aneurysms was 93.8, however the difference was not statistically significant. The mean aneurysmal inclination angle for unruptured

aneurysms with higher PHASES score for more than those for lower PHASES score but this difference was not statistically significant

Dhar et al had seen that 80% of all ruptured sidewall IAs had aneurysm angles greater than 112 degrees, whereas 81.8% of all unruptured sidewall IAs had aneurysm angles less than 112 degrees.

However their finding may be due to the technique of measuring the angle. They found that the larger aneurysm angles in ruptured aneurysms was because of presence of blebs along the main aneurysmal dome axis, which was included in the measurement of the angle.

XII. The magnetization transfer factor (MTF) ratio was calculated from the wall of the aneurysms for both ruptured and unruptured aneurysms. There was no significant difference in the MTF ratio between ruptured and unruptured aneurysms. However it was seen that the mean MTF ratio was more for unruptured aneurysms with higher PHASES score and the difference between mean MTF ratio between aneurysms with higher and medium PHASES score was statistically significant.

MT imaging is a sensitive sequence which detects subtle reductions of tissue integrity and relies on continuous interchange of magnetization between free protons and protons bound to macromolecules and thus it helps in indirect measurement of tissue integrity. It has been used to provide quantitative measurements of central nervous system damage in multiple sclerosis and other diseases (102). Low MT ratio (MTR) indicates a reduced capacity of the macromolecules in brain tissue to exchange magnetisation with the surrounding water molecules, reflecting damage to myelin or

to the axonal membrane. Recent studies have shown that low MTR correlates with histopathological findings of myelin and axonal loss (103,104).

In our study there was no significant difference between the MTF ratio in the wall of ruptured/unruptured aneurysms. However, among unruptured aneurysms those with higher PHASES score i.e. with higher risk of rupture had increased MTF ratio compared to those with lower PHASES score and the difference was statistically significant. This may reflect increased inflammatory changes or wall damage in the wall of aneurysms with high PHASES score contributing to the increased MTF ratio and larger studies are needed to validate this finding.

LIMITATIONS OF THIS STUDY:

1. The sample size is very small specially in case of ruptured aneurysms. The small number of the patients included for analysis related to ruptured aneurysms was small which can result in low statistical power of the results obtained.
2. The researchers performing the measurements were not completely blinded to the fact that the aneurysms were ruptured or unruptured and this may have resulted in bias. Though careful observations were carried out, observation bias cannot be ruled out.
3. SWI sequence was used in MRI to detect microhaemorrhages in the wall of the aneurysm. Adding a sequence like QSM could have provided a quantitative estimation of microhaemorrhage along the aneurysm wall

CONCLUSION

The study is a prospective study of consecutive 34 patients with ruptured/unruptured intracranial aneurysms, out of which, 24 patients had unruptured intracranial aneurysms and 10 were cases of ruptured aneurysms.

Our study is unique as it dealt with and studied three different aspects of intracranial aneurysms:

1. the relationship between PHASES score and wall characteristics of the unruptured aneurysms on MRI and DSA were assessed and it was evaluated which MR and angiographic factors were associated with high PHASES score, thus suggesting a high risk of rupture of the aneurysms.
2. The characteristic features of ruptured intracranial aneurysms were studied on Magnetic Resonance Imaging and Angiography
3. Thereafter the various features of ruptured and unruptured aneurysms on MRI and DSA was compared and their differences were statistically assessed.

This series helped us in reaching following inferences:

4. In our study the commonest location for both ruptured and unruptured aneurysms was in the ICA followed by the ACA/ACOM
5. Unruptured aneurysms with higher PHASES score were more likely to show wall enhancement on vessel wall MRI, blooming along the wall on SWI images and these findings were statistically significant

6. Among unruptured aneurysms those with higher PHASES score were more likely to show wall irregularity and this finding was statistically significant. High MTF ratio in the wall was also seen significantly in aneurysms with higher PHASES score.
7. In the unruptured aneurysms the size ratio and mean flow angle on angiogram were significantly more in aneurysms with high PHASES score
8. It was seen that the aneurysmal wall enhancement, blooming in the wall, wall irregularity and blebs was more commonly seen in ruptured aneurysms as compared to unruptured aneurysms however there was no statistically significant difference between the two.

Unruptured aneurysms with high PHASES score were more likely to have enhancement of the wall of the aneurysm which indirectly indicates an active inflammatory process in the wall of the aneurysm leading to increased risk of rupture. Presence of blooming in aneurysmal wall is suggestive of microbleeds in the wall which are indicative of future risk of rebleed or rupture. Other findings like presence of wall irregularity, increased MTF ratio in the wall, increased size ratio and mean flow angle are also seen more commonly in aneurysms with high PHASES score putting these aneurysms at increased risk of rupture in the future. So these findings seen in unruptured aneurysms with higher PHASES score are predictive of an ongoing pathological changes occurring in the aneurysmal wall which places these aneurysms at increased risk of rupture and thus can helps us to plan an early intervention in these cases

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ANNEXURES

Sree Chitra Tirunal Institute for Medical Sciences & Technology

Proforma

Study Title: Assessment of the wall characteristics of intracranial aneurysms in Magnetic Resonance Imaging and its correlation with conventional and angiographic rupture risk factors

Intracranial Aneurysm reporting Format for PRE & POSTCONTRAST MRI, CT ANGIOGRAM and DSA

(a) Reallocated Anonymized Image identification number: ……..

(b) Study / Sequence evaluated: MRI – (PRE & POSTCONTRAST) /MRA/CT ANGIOGRAM/DSA……...

(c) Investigator analyzing study:……

(d) Date of Image analysis:……

CLINICAL:
Age:
Sex:
Chief complaints/duration of symptoms:
History of presenting complaints: History of SAH
Past history/treatment history:
Examination :
General examination:
System examination: CVS Respiratory GIT/GUT CNS
Other /Local examination:

Imaging Findings:

1.MRI parameters:

- Lesion side : Right / Left
- Aneurysm location: ……
- Aneurysm size (mm).....(CC x TR x AP)
- Width of neck of aneurysm:…….
- Presence of wall enhancement: Type: Eccentric/concentric

Pattern: Strong/Mild/Absent

- Presence of SAH……
- Presence of blooming in wall on SWI
- MTF ratio

2. Angiogram(MR Angiogram/CT Angiogram/DSA parameters):

- Lesion side : Right / Left
- Aneurysm size (mm).....(AP x TR x CC)
- Width of neck of aneurysm:…….
- Aspect Ratio ……..
- Size ratio
- Aneurysm Shape

Regular (spherical / ellipse)

Irregular (Blebs, Protrusions, X^{le} Lobes)

Daughter Sac

- Flow Angle
- Aneurysm Inclination Angle
- Aneurysm location

Categorization of various parameters are followed based on the definitions provided in Appendix 1

Appendix 1

Pattern of Wall enhancement of the aneurysm is graded as

Strong enhancement = definite enhancement equal to choroid plexus or venous plexus

Faint enhancement = increased wall signal intensity than precontrast

No enhancement

Aspect Ratio = Perpendicular Ht. / Neck Dia.

Size Ratio = Dome Ht. / Parent A. Avg. Dia. {(D1 + D2)/2

Flow Angle (θ_F) = b/w inlet vessel centreline & Dome Max. Ht.

Aneurysm Inclination Angle (θ_A) = b/w Dome Max. Ht. & Neck Plane

Plagiarism Checker X - Report

Originality Assessment

Overall Similarity: **11%**

Date: Jul 27, 2021

Statistics: 859 words Plagiarized / 7789 Total words

Remarks: Low similarity detected, check your supervisor if changes are required.

Intra-cranial aneurysms (IA) are the commonest cause of non-traumatic sub-arachnoid haemorrhage (1). These are ominous entities with aneurysmal SAH being associated with significant morbidity and mortality. The prevalence of IA in literature has been reported as approximately 2% of the general population (2) Once an Intracranial aneurysm (IA) is diagnosed, the risk of rupture should be weighed against the risk of treatment, a cause of significant stress and anxiety for patients, emphasizing the need of an individual criteria for predicting rupture in clinical decision making. Previous studies have identified a number of factors that potentially contributed to aneurysm rupture, by which several rupture prediction models were built, such as the PHASES score [3,4]. Aneurysmal rupture occurs when the stress imposed by blood flow exceeds the mechanic strength at a location of the aneurysm wall. Thus, investigating the characteristics of aneurysm wall may help in deepening our knowledge on the mechanism of aneurysm rupture. Histopathological studies indicated that inflammation may play an important role in the formation, growth, and rupture of IAs [3,8]. Inflammatory cell infiltration is commonly observed in ruptured IAs and numerous inflammation cytokines are involved in the process [8]. Therefore, the ability to image inflammation in IAs may aid in assessing IA rupture risk in individual clinical decision-making. The advancement of Vessel Wall- Magnetic Resonance Imaging (VWMRI) offers a potential noninvasive mean to detect in-vivo inflammation in IAs at a pathological level [6,7,9]. Recent improvements in VW-MRI makes this a viable method for investigating inflammatory processes in the

aneurysmal wall [10]. Previous studies suggested that aneurysmal wall enhancement (AWE) on VW-MRI was more frequently observed in ruptured IAs and might help to identify unruptured aneurysms with the presence of AWE and a high rupture risk [6,7]. However, the association betweenother wall

CONSENT FORM

TITLE OF THE STUDY: Assessment of the wall characteristics of intracranial aneurysms in Magnetic Resonance Imaging and its correlation with conventional and angiographic rupture risk factors

Study number:……..

Participant's name: ……Date of Birth / Age (in years): ……..

I…….. , Son/daughter of (Please tick boxes)

Declare that I have read the above information provide to me regarding the study: "Assessment of the wall characteristics of intracranial aneurysms in Magnetic Resonance Imaging and Angiography(CT/DSA/MR) and its relationship with conventional rupture risk factors" and have clarified any doubts that I had. [ ]

I also understand that my participation in this study is entirely voluntary and that I am free to
withdraw permission to continue to participate at any time without affecting my usu al treatment or my legal rights. [ ]

I also understand that study investigators will be using some of the data like history and other
clinical details, Imaging details (CT/MRI/ CTA /MRA), Angiograms (DSA), Coilin g technique, outcome of the procedure (Immediate angiographic and clinical)
, delayed follow up clinical and radiological regarding the disease and treatment which I undergo in hospital. [ ]

I also understand that no additional cost will be incurred /no additional drugs will be used and there are no additional risks as a part of the research. [ ]

I understand that the study staff and institutional ethics committee members will not need my
permission to look at my health records even if I withdraw from the trial. I agree to t his access. [ ]

I understand that my identity will not be revealed in any information released to thir d parties or published. [ ]

I voluntarily agree to take part in this study. [ ]

I received a copy of this signed consent form. [ ]

Name:
Signature
Date
Name of witness
Relation to participant