INTRODUCTION

Intracranial aneurysms are common entities whose natural history and definitive management remain controversial. The overall prevalence of un ruptured intracranial aneurysms (IAs) in the general population is estimated as 3.2% ***(Vlak et al., 2011)***.

Early aneurysm treatment following subarachnoid hemorrhage (SAH) aims to improve outcomes by preventing rebleeding from the ruptured aneurysm. The risk of rebleeding is highest within the first 24 hours post-SAH, with a frequency of 4–14% ***(Connolly et al., 2012; Steiner et al., 2013)***.

Flow diverters have been introduced into the armamentarium for aneurysm treatment recently ***(Pierot and Wakhloo, 2013)***. These devices are tubular stent-like implants with low porosity. Two working mechanisms of FDs were identified as flow redirection and tissue overgrowth ***(Pierot and Wakhloo, 2013)***. In the beginning two FDs were clinically available: PED (ev3 Neurovascular, Irvine, CA, USA) and Silk (Balt, Montmorency, France). Other devices including Surpass (Stryker, Fremont, CA, USA), FRED (Microvention, Tustin, CA, USA) ***(Pierot and Wakhloo, 2013)*** and p64 Flow Modulation Device (Phenox, Bochum, Germany) have recently been introduced ***(Pierot and Wakhloo, 2013)***.

Preliminary results of FDs that were applied in large and wide-necked or fusiform aneurysms were promising ***(Monteith et al., 2014)***. In addition, evidence regarding the indications of FDs for small aneurysms, which are not amenable to standard coiling techniques, including blister-like aneurysms and the aneurysms with high procedural rupture risk, has started to accumulate ***(Lin et al., 2013)***. The current literature on the use of flow diversion for the treatment of these challenging aneurysms is limited to small case series ***(Monteith et al., 2014)***.

AIM OF THE WORK

The present work aimed to discuss the technical and management outcome of our first Flow Diverter embolizations case series.

Chapter 1

VASCULAR ANATOMY OF THE BRAIN

The blood supply of the brain consists of two circulations; anterior circulation and vertebrobasilar system which are both connected by circle of willis; Circle of willis is the anastomotic ring that connects both halves of the "anterior" circulation with each other and with the vertebrobasilar system, it lies above the sella turcica within the interpeduncular and suprasellar cisterns. A complete circle of Willis is an arterial polygon consists of two internal carotid arteries (ICAs), two anterior cerebral arteries (ACAs), the anterior communicating artery (AComA), two posterior communicating arteries (PComAs), the basilar artery (BA) and two posterior cerebral arteries (PCAs). Moreover, the middle cerebral arteries (MCA) are a continuum of the ICA distal to branching point of the ACAs. The different variations and incompleteness of circle of Willis are common. Most of the "berry" or saccular aneurysms arise from the branching points of these vessels ***(Shojima et al., 2004)*** Figure 1 shows the complete circle of Willis.

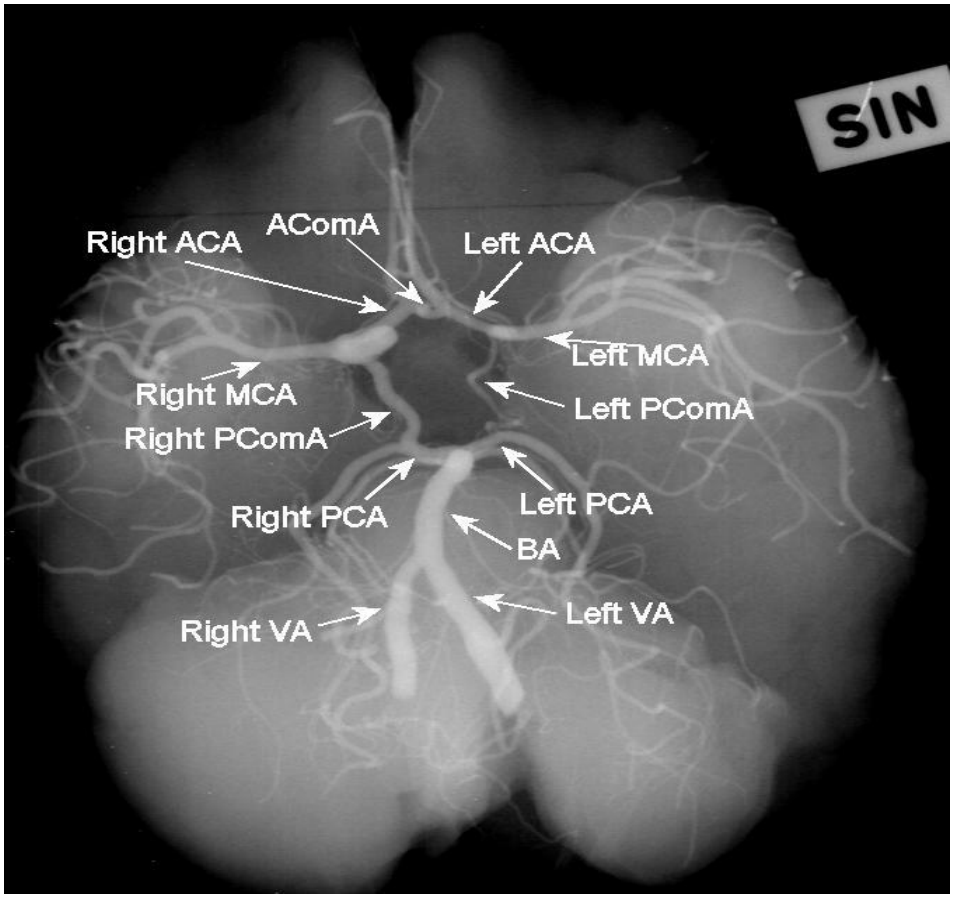

Figure (1): A diagam showing the circle of willis.

In addition to the circle of willis, there are the cortical branches of the supra tentorial cerebral artries; The distal segment of the ACA, the pericallosal arteries, gives rise to the cortical and callosal branches. The callosal branches supply the rostrum, genu and the body of the corpus callosum. These branches are joined posteriorly by the splenial branches of the PCA. In the most frequent disposition, the cortical area of supply of the ACA is the medial surface of the hemisphere extending to the superior frontal sulcus and the parieto-occipital

sulcus. On the orbitofrontal surface, the arterial territory includes the medial orbital gyri. At the most, the cortical ACA territory reaches the inferior frontal sulcus, and at the least, it includes only the anterior part of the frontal lobe ***(Shojima et al., 2004).***

The MCA is divided anatomically into four segments: horizontal segments (M1), insular segments (M2), opercular segments (M3) and cortical branches (M4). The MCA begins its division into cortical branches at the base of the Sylvian fissure, extends over the surface of the hemisphere and forms M4 segments. The most frequent area of supply of the MCA extends from the lateral surface of the hemisphere to the superior frontal sulcus, the intraparietal sulcus, and the inferior temporal gyrus. On the orbitofrontal surface, the arterial territory includes the lateral orbital gyri.

As the PCA approaches the dorsal surface of the midbrain, it gives rise to cortical branches. The branches include the hippocampal arteries and the splenial artery that anastomose with the distal part of the pericallosal artery to supply the splenium of the corpus callosum. The most frequent cortical distribution of the PCA includes the inferomedial surfaces of the temporal and occipital lobes extended to the parietooccipital fissure. In general, the parietooccipital and calcarine arteries supply the posterior one third of the brain, along with the interhemispheric fissure including the primary visual cortex ***(Shojima et al., 2004).***

There are some important perforating branches that arise from every part of the circle of willis; From anterior cerebral arteries arise the medial lenticostriatae arteries and quite often the recurrent artery of Heubner, which can supply the caudate nucleus head, anterior limb of the internal capsule and part of the basal ganglia. From anterior communicating artery arise perforating brances to supply the superior surface of the optic chiasm and anterior hypothalamus. These branches may have a significant vascular territory that includes part of the corpus callosum, columns of the fornix, parolfactory areas, lamina terminalis and hypothalamus.

From posterior communicating arteries arise number of small, but important perforating branches, the anterior thalamoperforating arteries to supply part of the thalamus, the infralenticular limb of the internal capsule and optic tracts.

From distal basilar artery and proximal posterior cerebral arteries arise numerous 24 small perforating arteries. These branches, the posterior thalamoperforating arteries and the thalamogeniculate arteries supply the midbrain and thalamus.

From the middle cerebral artery arise the lateral lenticulostriatal arteries, which supply the substantia innominata, lateral aspect of the anterior commissure, most of the putamen and lateral globus pallidus, the superior half of the internal capsule and adjacent corona radiate, and the body and the head (except the anterior inferior portion) of the caudate

nucleus. Portions of the optic radiations and arcuate fasciculus are also supplied by these branches ***(Shojima et al., 2004).***

The brainstem and cerebellum are supplied by cerebellar arterial; the posterior inferior cerebellar artery (PICA) gives rise to two branches and vascularises the inferior vermis and the inferior and posterior surfaces of the cerebellar hemispheres. The anterior inferior cerebellar artery (AICA) supplies the anterior surface of the simple, superior, and inferior semilunar lobules as well as the flocculus and the middle cerebellar peduncle. The superior cerebellar artery (SCA) divides into medial and lateral branches and vascularises the superior half of the cerebellar hemispheres, vermis and the dentate nucleus. These three cerebellar arteries also take part in the vascularisation of the brainstem. The territory of the SCA often includes the upper part of the pontine tegmentum. The PICA takes part in the lateral and posterior arterial groups of the medulla. The AICA supplies the middle cerebellar peduncle and often the lower part of the pontine tegmentum. However, the vascular anatomy of the posterior fossa can be extremely variable in different individuals.

Chapter 2

INTRACRANIAL ANEURYSMS

The first description of saccular cerebral aneurysm in the medical literature was made in the eighteenth century (1761) by Morgagni ***(Höök et al., 1963)*** and Biumi ***(Biumi et al., 1778)***, who first described the dilatation of the cerebral arteries and showed that their rupture might lead to SAH. Morgagni and Biumi's observations were not further evaluated until 1859, when Sir William Gull offered recognition of the pathological nature of the lesion by his often quoted statement: "whenever young person die with apoplexy, and after death a large effusion of blood is found, especially if the effusion be over the surface of the brain, in the meshes of the pia matter, the presence of aneurysm is probable ***(Gull et al., 1859)***.

In 1927, Egas Moniz, introduced cerebral angiography to the medical community and the clinician finally developed a method to diagnose CA. In 1933, Dott ***(Dott et al., 1933)*** presented a series of 8 patients who had undergone angiography with a diagnosis of subarachnoid hemorrhage, describing the location of their aneurysms and reporting his operative results. This was followed by many reports describing different methods for the management of CA, among which was that of Dandy who described a series of 108 patients, 30 of them having had an intracranial procedure while others had carotid ligation. The technique of angiography is considered to be the

key for all research in the field of cerebral aneurysm ***(Dandy et al., 1944)***.

Intracranial (saccular or berry) aneurysms (IAs) Are acquired lesions, accounting for about 80% of all nontraumatic subarachnoid hemorrhages (SAH) ***(Brown et al., 2010)***. IAs affects 5–10% of the general population, a fraction of which will rupture and lead to devastating consequences.

Unruptured IAs are rarely noted in children (0,5–4,6% of All aneurysms) and appear to develop with increasing Age ***(Menghini et al., 1984)*****:** the prevalence of harboring an IA within The population aged over 30 years is between 3.6 And 6.5% ***(Wardlaw et al., 2000)***. Women may be more likely to have an aneurysm than men (3:1) ratio of women compared with men in unruptured. IA may occur alone (70–75%) or as multiple aneurysms (25–30%) ***(Krex et al., 2001)***. The incidence of unruptured IAs seems to be increasing with the continuous evolution of Magnetic Resonance angiography (MRA) and Computed Tomography angiography (CTA) imaging techniques ***(Krischek et al., 2006)***. SAH due to IA rupture occurs around 1.24 times more often in women than in men ***(De Rooij et al., 2007)*** and 2.1 times more often in blacks than whites ***(Broderick et al., 1992)***. The risk of rupture depends on the size and location of the aneurysms and has been reported to be 2.7% per year in a Japanese population ***(Morita et al., 2005)*** and 1.9% in a white population ***(Rinkel et al., 1998)***.

The commonest sites of intracranial aneurysms locations are AComA 31.5%, MCA 33.1%, PComA 12.4%, ICA 8.1%, distal ACA 5.7%, VBA 9.3% ***(Hassan et al., 2005)***. According to a recent study from eastern Finland with 1068 aSAH patients (59% of these were female), the most frequent sites for cerebral sporadic, ruptured intracranial aneurysms (IA)s were reported as following; ICA (ICA and PComA) 23%, ACA (A1, AComA, A2A5) 35%, MCA (M1, Mbif, M2M5) 32%, VA(VA and posterior inferior cerebellar artery (PICA)) 3%, BA (BA bifurcation) 6% and PCA 1%. However, the most frequent site for unruptures sIAs was the MCA bifurcation (39-44% of the unruptured aneurysms) ***(Hassan et al., 2005).***

An intracranial aneurysm is a vascular disorder that occurs in the weak point of an intracranial arterial wall to form a localized dilation. As neuroimaging has become more widely used, intracranial aneurysms are now being diagnosed with greater frequency before rupture (unruptured intracranial aneurysms [UIAs]) ***(Li et al., 2014).*** The prevalence of UIAs in the general population is 1.8% to 8.4% when diagnosed by magnetic resonance angiography (MRA) ***(Igase et al., 2012).*** Because UIA rupture causes subarachnoid hemorrhage, which usually results in significant neurological deficits or death, there has been interest in evaluating the risk of aneurysm formation and enhancing the detection of UIAs before rupture. Although most of these aneurysms will never rupture, the annual risk of rupture is estimated at 0.7% in patients who have

no other risk factors, with the peak age of rupture at 55-60 years old ***(Rinkel et al., 2011).***

Furthermore it is unknown whether asymptomatic aneurysms as well as those that rupture represent two spectrums of the same disease state, or characterize two different but intertwined pathologies as many aneurysms never rupture. This pathophysiological mechanism that underlies aneurysmal rupture is not yet fully understood, what has been shown is the risk of rupture is proportional to aneurysm size and dome size: neck size ratio ***(Edlow et al., 2008).***

Rupture of an aneurysm can result in rapid increases in intracranial pressure, leading to reduced and/or cessation of cerebral perfusion, thus precipitating unconsciousness and finally brain stem death. The case fatality rate within the first 3 days and first month post-SAH is approximately 20% and 36%, respectively. The major risk factors for this condition include hypertension, smoking and excess alcohol, but also family history ***(Van Gijn et al., 2007)***. As a result of the international Subarachnoid Aneurysm Trial (ISAT) study, the less invasive intravascular treatment with coiling has been found to be safer than open surgery and has thereby potentially moved the balance towards screening more relatives, although there are really no new methods to identify relatives at risk. Identification of genes or biochemical, cellular or other markers involved in the molecular pathogenesis of SAH would be of fundamental importance, not only to identify relatives at high

risk, but also with a potential for screening of individuals in the general population, who carry a heavy load of external risk factors ***(Molyneux et al., 2002).***

The major causes of subarachnoid hemorrhage by cerebral angiography reveals three categories of vascular pathologies: (A) Ruptured saccular aneurysm of a cerebral artery In ~ 80% of cases. (B) Bleeding from an arteriovenous malformation, in 5–10 % of patients. Arteriovenous malformations are usually present from birth and arise in a variety of different forms. Neural crest cells are major contributors to mesenchymal structures in the head and neck including arteries and disorders of neural crest development may be a major factor in the formation of arteriovenous malformations ***(Bhattacharya et al., 2001).*** (C) Nonaneurysmal subarachnoid hemorrhage; SAH of unknown origin, usually a perimesencephalic type of SAH (pmSAH), represents 9% to 15% of cases of SAH patients ***(Kassell et al., 1990).***

In pmSAH, the origin of the bleeding remains unclear and various pathogenetic mechanisms, such as small cerebellar or pontine venous angiomas, capillary telangiectasias, intramural hematomas of the basilar artery or specific anatomic variations of the perimesencephalic venous drainage system have been discussed as possible explanations for nonaneurysmal pmSAH. Patients with pmSAH have been shown to regain independence for activities of daily life and have a normal life expectancy, and they are not at risk for

rebleeding. However, up to 25% of these patients are left with symptoms including headache or dizziness, fatigue, forgetfulness and irritability ***(Greebe et al., 2007).***

Other causes of subarachnoid haemorrhage include rupture of a mycotic aneurysm in which the vessel wall is weakened by bacterial ***(Frazee et al., 1980)*** or fungal infection and the artery ruptures, and trauma in which a blood vessel in the subarachnoid space is injured and bursts. SAH is also associated with aortic coarctation and hypertension and with tumours, vasculitis and bleeding diatheses. Trauma is probably the most frequent cause of SAH, but the significance of this type of SAH is difficult to assess as it usually overshadowed by the effect of other simultaneous traumatic brain lesions ***(Horten et al., 1976).*** Of the above causes of SAH, the familial causes may be the most illuminating to pathogenetic pathways because they may represent the paradigm of single isolated gene lesions representing one protein product in one pathway or structure important to the maintenance of normal structure and function of the cerebral vasculature.

Intracranial aneurysms are divided according to their phenotype (gross pathologic appearance) recognized in to *(A)* Saccular aneurysms (also known as "berry" aneurysms): By definition, a saccular or “berry”aneurysm is a berry-shaped or multi-lobed outpouching on a major cerebral vessel. Saccular aneurysms consist of three main regions; the neck, the sac and the dome. The neck is that part of an aneurysm where it joins

the parent artery, while the sac represents the cavity of the aneurysm and the dome relates to the convex wall facing the neck of the aneurysm Saccular aneurysms show a restricted location with 85–90% arising on the terminal part of the internal carotid artery and on the major branches of the anterior portion of the circle of Willis (Fig.2). The internal carotid artery is the most frequent site (40%), followed by the anterior communicating artery (30%) and the proximal portion of the middle cerebral artery (20%). In adults, 5–10% of aneurysms are associated with the posterior cerebral or vertebral arteries whereas in children 40–45% of aneurysms occur in the posterior cerebral circulation. Multiple saccular aneurysms occur in 10–31% of patients, most frequently associated with the middle cerebral artery. Saccular aneurysms occur on the feeding arteries of arteriovenous malformations in 10% of cases, adding support to the hypothesis that haemodynamic stress; namely, major vessel bifurcations, plays a significant role in the pathogenesis of aneurysms. *(B)* Fusiform aneurysms; Fusiform aneurysms are elongated, spindle-shaped dilation of vessels that can be associated either with atherosclerotic vascular disease (ASVD) or nonatherosclerotic pathology such as connective tissue disorders. *(C)* The rare, recently-described "blood blister-like" aneurysms;

The wall of the rare but dangerous "blood blister-like" aneurysm is tissue paper- thin. This entity, now well-known to neurosurgeons but rarely discussed in the imaging literature, is