Chapter 7

Carotid Intern Aneurysms

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Abstract

Cerebral aneurysms (CA) are acquired lesions, affecting 5–10% of the population, being about three times more common in women than in men. The absolute majority of CA is asymptomatic. However, in symptomatic cases, cerebral aneurysms present without about 80% of cases with severe intracranial hemorrhage, with mortality up to 50% and severe morbidity of up to 80%. At this point, the carotid siphon is particularly important because it is the blood gateway to the anterior cerebral circulation, being the most sinuous portion of the internal carotid artery, and because it houses about 30% of the intracranial aneurysm. The constant interactions of blood flow with carotid siphon curvatures are apparently intrinsically related to the epidemiology of these lesions in the various locations of the intracranial circulation and their presentation form. It is well established that a greater anterior knee angle has a significant independent relation with intracranial aneurysms located after carotid siphon, larger aneurysms, and greater risk of rupture. These findings may be associated with the hemodynamic interactions of blood flow and the curvature of carotid siphon. Little is known about the anatomical changes in carotid siphon and, consequently, the repercussions of the hemodynamic changes that the neurosurgical interventions mechanisms could entail. Devices such as intracranial stents, detachable coils, and even clips of aneurysms can modify the morphology of carotid siphon, and the knowledge of these consequences could be used to obtain better therapeutic results. In the last 10 years, a new device for the treatment of intracranial aneurysms has been presenting promising results, flow diverters stents (FDS), and its use to treat aneurysms in carotid siphon appears to cause morphological changes characterized by increased anterior and posterior angles. Specifically, the anterior angle increase was associated with better angiographic results. Aneurysms of the extracranial carotid artery (ECAA) are rare and little is known about its natural history. The etiology is diverse and most ECAA are asymptomatic, but they may progress to a pulsatile mass, cranial nerve compression, or cause a stroke. ECAA treatment is still controversial and a better insight into natural history and risk of complications of the different treatments is needed in order to get the consensus.

Keywords: carotid intern aneurysms, carotid siphon, flow redirecting stents

1. Introduction

1.1. Epidemiological aspects

Cerebral aneurysms (CA) are acquired lesions, characterized as saccular or diffuse dilation of the intracranial arteries walls. It affects 5–10% of the population, being about three times more often in women than in men [1]. About 70–75% of the patients present single lesions and the remains show multiple lesions, which can affect both hemispheres in both the carotid as well as the vertebro-basilar circulation [2].

The absolute majority of CA is asymptomatic. Among the symptomatic patients, about 80% present as hemorrhagic stroke and are characterized by spontaneous subarachnoid hemorrhages. The remaining 20% may present symptoms such as mass effect, thromboembolic events, or nonspecific headaches [3].

Spontaneous subarachnoid hemorrhage (SAH) secondary to CA rupture is commonly described as a devastating disease, accounting for about 5% of all strokes, with an incidence of 10 cases per 100,000 individuals. Vlak et al. showed that the prevalence of unruptured intracranial aneurysms was significantly higher in patients aged 30 years or older compared with those who were younger than 30 years [47]. Autopsy reports have demonstrated that the incidence of SAH or unruptured intracranial aneurysms was 3–4 times higher in patients older than 70 years and that the prevalence of aneurysms increases with aging, as well as prolonged exposure to hypertension, smoking, and atherosclerotic vessel degeneration [48]. The incidence peak is between 50 and 60 years (only 20% of cases occur before 45 years) and there is considerable predominance for females: 1.6 females for 1 male. This female predominance is probably due to hormonal changes, particularly estrogen considering primiparous views or patients with later menarche that present a risk reduction [4, 5]. Epidemiological studies show that the female preponderance of intracranial aneurysms becomes significant only after the fourth or fifth decade, during the perimenopausal and postmenopausal periods. Moreover, estrogen has a protective effect against vascular injury [46] and hormone-replacement therapy has been shown to be a protective factor for subarachnoid hemorrhage [47].

1.2. Risk factors

The exact etiology of CA formation remains unclear. However, there is no doubt that CA are acquired lesions, initiated from a lesion with genetic, atherosclerotic, traumatic, or inflammatory origin in the vascular endothelium and developed by hemodynamic stress in this region [6]. Factors such as blood hypertension, use of oral contraceptives, drugs (cigarette, cocaine, and alcohol), pregnancy, and neurosurgical diagnostic procedures (lumbar puncture and cerebral angiography) are classically associated with the development of lesions or aneurysmal rupture [6–8]. In addition, environmental and geographic factors, such as season and colder territories, increase the incidence of rupture [6–8]. Some genetic syndromes are associated with a higher incidence, such as autosomal dominant polycystic kidney disease type I and II, Marfan syndrome, neurofibromatosis type I, and Ehlers-Danlos syndrome type

II and IV [8]. Patients who have already been treated for a ruptured aneurysm also have an increased risk of developing another lesion, around 2% per year, against 1% of the general population [6–9]. Genetic inheritance related to aneurysmal development has been complex and multigenic; genes such as 1p34.4-36.13, 7q11, 19q13.3, Xp22, endothelial nitric oxide synthase gene, among others, have been frequently found in familial cases of CA [9].

It is believed that these factors converge to modify the intimal layer and increase the hemodynamic stress of the arterial wall. Hemodynamic stress is basically executed by the elements of blood flow and water hammer pulse, which explains the preferential location of the saccular aneurysms in bifurcations and convexities of vascular curvatures, facing the direction that the flow would be if there were no curves [10]. Thus, we can systematize the hemodynamic interaction as the flow inertial force, perpendicular to the arterial wall, and the parallel shear force caused by the viscosity and friction of the blood elements with the arterial wall [10]. The way these forces interact in the formation, development, and rupture of aneurysmal lesions is still a matter of debate, but apparently the shear stress would be more important at the initial moments of aneurysmal formation; whereas, the flow inertial force would be more important for late development and rupture of the lesions [11].

Considering these factors, the carotid siphon deserves special importance, since it is the blood flow gateway to the anterior cerebral circulation, being characteristically the most sinuous portion of the internal carotid artery and with the anterior communicating complex, compound 80% of the CA [4, 10].

1.3. The carotid siphon

The carotid siphon corresponds to the portion of the internal carotid artery that begins at the end of its petrous (horizontal) segment (or lacerum segment) and ends at the supraclinoid internal carotid bifurcation. The first portion, the end of the petrous segment, is characterized by the path of the carotid when exiting its exclusively intraosseous path and traversing the crease of dura mater around the foramen lacerum. This portion may have branches not easily visible angiographically, among which it can be highlighted the coraco-tympanic branch and the artery of the pterygoid canal (vidian artery) [12].

The carotid artery enters the cavernous sinus after crossing the petrolingual ligament, where it presents initially a vertical ascending segment and then we observe the first important curvature, the posterior angle, of about 90° in anterior direction. It is followed by a horizontal intra-cavernous portion, which ends at a second curvature, the anterior angle, with about 160° in upward and posterior direction. In its intracavernosal path, usually arises the meningohypophyseal trunk, close to its first curvature, and then the inferolateral trunk in the extension of its horizontal segment [13].

After the second curvature, the internal carotid crosses two dural rings and emerges to a new horizontal segment, but now supraclinoid and intradural, where it launches its main branches (ophthalmic artery, posterior communicating artery, and anterior choroidal artery), ending with its bifurcation. This bifurcation gives rise to the middle cerebral artery and the anterior cerebral artery, which also marks the end of the carotid siphon [14] (**Figure 1**).

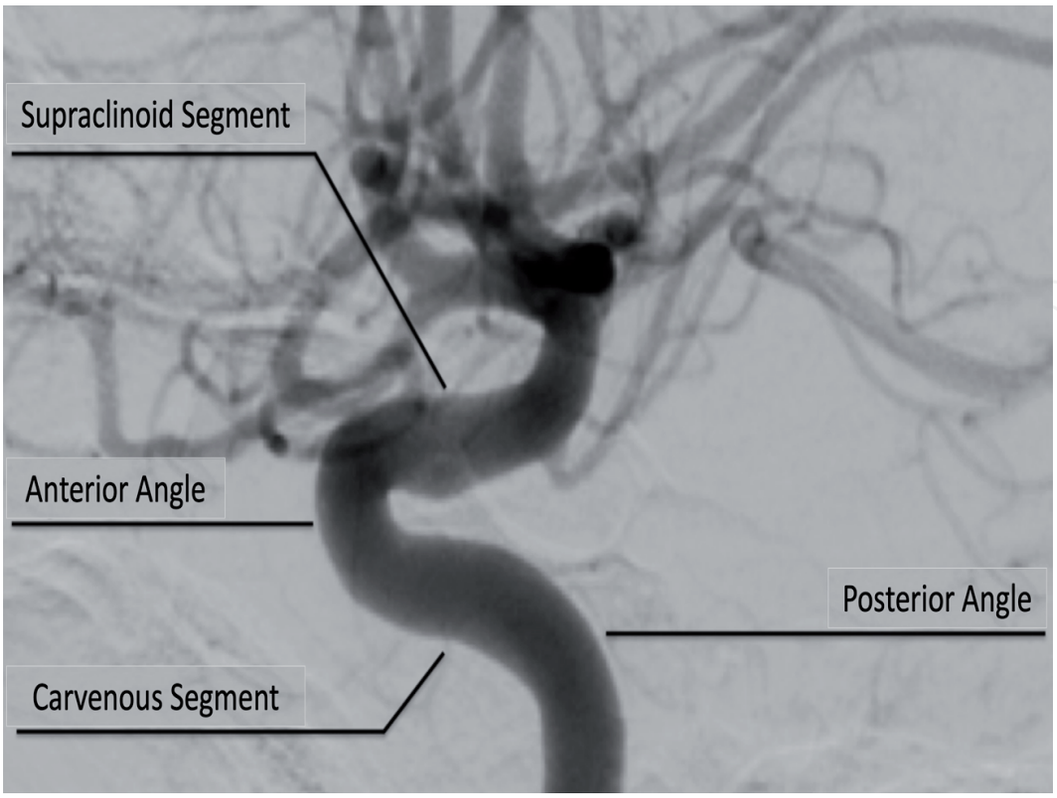

Figure 1. Carotid siphon: digital angiography with subtraction in profile incidence evidencing the segments of the carotid siphon (personal file).

Although this pattern is relativity monotonous among individuals, important anterior and posterior angles variations were identified. These variations were initially systematized by Krayenbuehl and Yasargil, who classified the carotid siphons from the purely morphological point of view into seven subtypes [15] (**Figure 2**):

- Type U, representing 40.1% in the population up to 20 years, 35% between 21 and 50 years, and 15.2% between 51 and 74 years;
- Type V, representing 14.6% in the population up to 20 years, 24.5% between 21 and 50 years, and 22.3% between 51 and 74 years;
- Type C, representing 45.2% in the population up to 20 years, 14.6% between 21 and 50 years, and 5.2% between 51 and 74 years;
- Type Omega, absent up to 20 years, representing 23.7% in the population between 21 and 50 years, and 50.7% between 51 and 74 years;
- Type Double Siphon, absent up to 20 years, representing 1.4% in the population between 21 and 50 years, and 4.1% between 51 and 74 years;
- Type Megasiphon, absent up to 20 years, representing 0.2% in the population between 21 and 50 years, and 2.3% between 51 and 74 years; and
- Type Dolicosiphon, absent up to 20 years, representing 0.4% in the population between 21 and 50 years, and 1.5% between 51 and 74 years.

Subsequently, this classification was reviewed by Zhong, simplifying and systematizing the classification in only four anatomical subtypes of the carotid siphon [16] (**Figure 3**):

- Type U (about 55% of cases): rectified supraclinoid portion with posterior angle greater than 0° and presenting a wide anterior angle of positive values;
- Type V (about 27% of cases): rectified supraclinoid portion with posterior angle greater than 0° and presenting a sharp anterior angle of positive values;
- Type C (about 16% of cases): curved supraclinoid portion, with posterior angle around 0° and presenting a wide anterior angle of negative values; and
- Type S (about 2% of cases): supraclinoid portion rectified with very acute or negative posterior angle, anterior angles of negative values and presenting a wide anterior angle.

The first attempt at geometric and mathematical systematization of the carotid siphon was performed by Lang and Reiter [17], who classified the carotid siphons into three subtypes, exclusively due to the posterior angle. Thus, the most frequent type, 49.3% of the cases, had the posterior angle around 90°. The second subtype, 36.0% of the cases, presented the inferior angle to 90° and the third subtype, 14.7%, with an angle greater than 90°.

This morphology of the siphon is not static and progressively varies with aging, development, and degenerative processes, especially by the influence from atherosclerotic and hypertensive disease [18].

It is believed that the main physiological function of these successive curvatures would be the attenuation of the vectorial force of the blood flow, with consequent reduction of hemodynamic stress to the distal cerebral circulation [18–20]. Thus, there is a constant interaction between the carotid siphon vascular walls with the shear force of the blood elements and the water hammer pulse of the arterial flow [19, 20].

1.4. Wall stressing stress

The consequences that the curvatures of the cerebral circulation generate in the hemodynamics of the carotid siphon, as well as the relation between the incidence of aneurysms and stenoses close to the regions of pronounced curvatures, have been studied in recent years [19, 20].

It is admitted that the loss of the kinetic energy of linear blood flow, when colliding with the endothelial wall of the curvatures, forcing the change of direction of blood flow and transforming the normally linear flow into turbulent flow, is related to the endothelial transformation [18, 21–23]. This phenomenon generates deceleration of the blood flow, reducing the interactions of tangential forces with the vessel wall, called wall shear stress [22].

Recent studies have evidenced the direct relation of the incidence of intracranial stenoses in follow-up with low or oscillatory wall shear stress [23–25]. The characterization of which curvatures and anatomies are more prone to the pathological scenarios has motivated several studies that seek to define the geometric risk factors [24–26]. Piccinelli et al., for example, have shown that curvatures with small radius and low angulation tend to be related to the presence of ruptured aneurysms [27]. Kim and Kang, on the other hand, have demonstrated

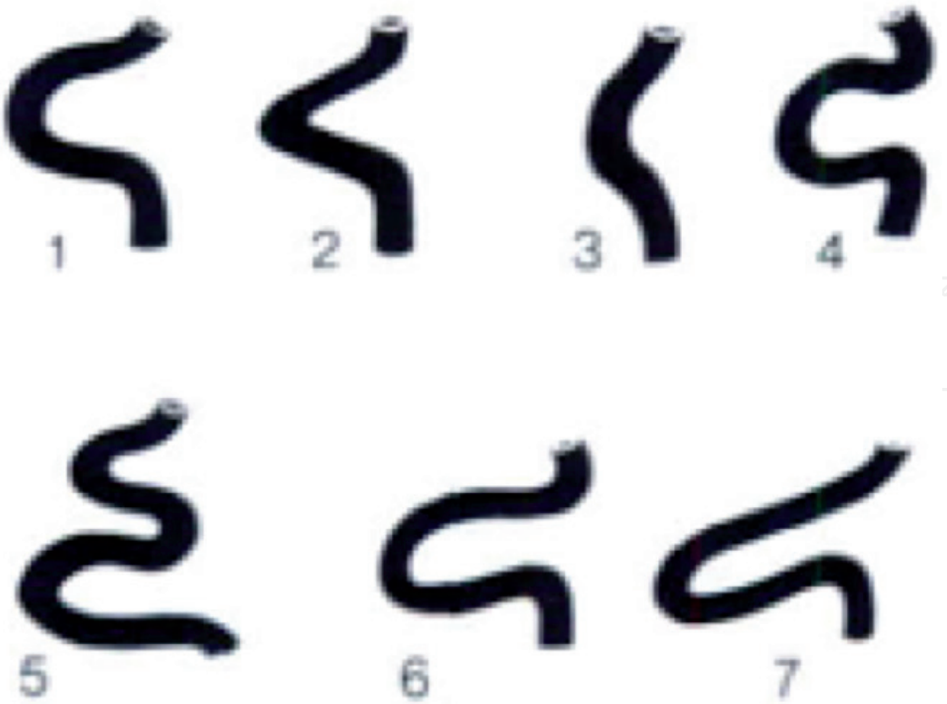

Figure 2. Types of carotid siphon described by Krayenbuehl and Yasargil. (1) Type U, (2) Type V, (3) Type C, (4) Type Omega, (5) Type Double Siphon, (6) Type Megasiphon, and (7) Type Dolicosiphon.

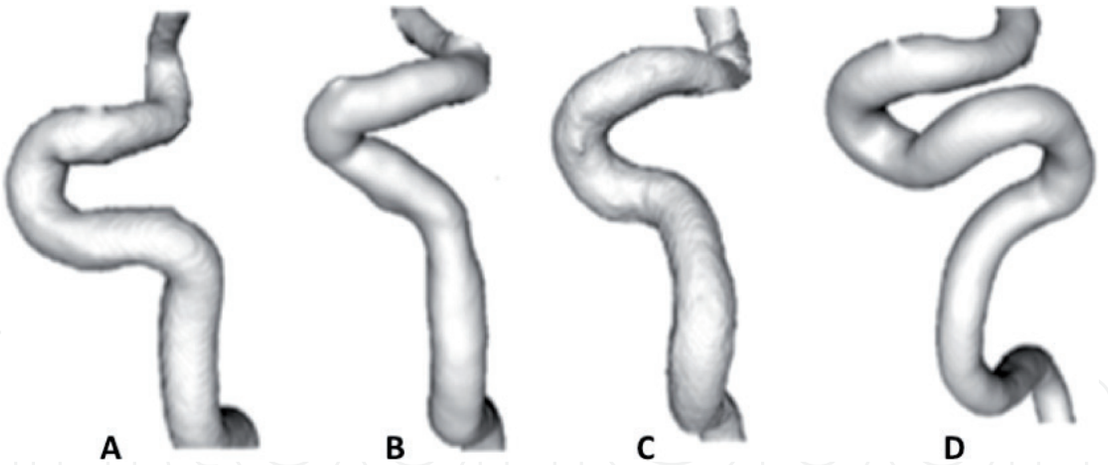

Figure 3. Types of siphons described by Zhong. (A) Type U, (B) Type V, (C) Type C, and (D) Type S [16].

that a short supraclinoid segment of the internal carotid artery is directly associated with an increased incidence of aneurysm of the posterior communicating segment [28]. Zhang et al. have showed that siphons that present more acute curvatures lead to a significant decrease and oscillation of wall shear stress right after curvatures, which are the most favorable sites for the development of stenoses [29]. Silva Neto et al., on the other hand, evidenced that more acute anterior angles are statistically related to a higher incidence of aneurysms in the posterior communicating segment [30]. Sangalli described the association between aneurysms in the most distal portions of the carotid siphon and the less acute curvatures [31]. We recently

published our study, where we saw a significant independent direct relation of greater anterior knee angle with intracranial aneurysms located after the carotid siphon, larger aneurysms, and greater risk of rupture. These findings may be associated with the hemodynamic interactions of blood flow and the curvature of the carotid siphon [49].

Anterior angles above the median of our sample (15.40°) are directly related independently to a 36% higher incidence of rupture (p = 0.0055, PR = 1.36, 95% CI: 1.09 to the location of cerebral aneurysms 48% more frequently after the carotid siphon (p = 0.0336, RC = 1.48, 95% CI: 1.03–2.13), and to larger lesions. For each increase of 1° in the anterior angle, there is an increase in aneurysm size of 1001 mm (p = 0.015). These findings may mean that carotid siphons with more intense curvatures would lead to greater changes in the shear force of the wall and greater damping of the vector force in a hammer water pulse. These changes in blood flow would lead to increased hemodynamic stress in the carotid siphon, with a consequent higher frequency of aneurysm in this topography and the formation of smaller lesions and with a lower risk of rupture, due to the decrease in the vector force in a hammer water pulse toward the aneurysmal domus [49].

Then, the change of direction of blood flow at the points of curvature of the carotid siphon occur in detriment of the deceleration of the linear velocity of blood flow and the loss of the linear vector force of the water hammer pulse. This deceleration would occur with a change from laminar to turbulent flow in the proximity of the curvatures, with lower intensity and greater oscillations of the shear stress of the wall. On the other hand, decreasing the force of the linear vector toward the aneurysmal sac would reduce the size of the aneurysms and the risk of rupture. Still a greater swirling flow would lead to greater initial endothelial lesion for the aneurysmal formations. Thus, more obtuse anterior angles, with less laminar flow deceleration and less generation of turbulent flow in the vicinity of the carotid siphon, were statistically associated with larger aneurysms, greater risk of rupture and a higher incidence of aneurysm after the carotid siphon; whereas, more acute anterior angles, with greater deceleration of the laminar flow and greater generation of swirling flow in the siphon, were shown to be associated to smaller aneurysms, lower risk of rupture, and a higher incidence of aneurysm in the carotid siphon [49].

High-velocity laminar flow due to a nontortuous carotid siphon would lead to hemodynamic consequences for the other curvatures and bifurcations of the cranial circulation after the carotid siphon, explaining the higher incidence of postsiphon aneurysms and a higher risk of rupture at these sites in patients with higher angles. Stratified analysis of the subgroups by location revealed that aneurysms located in the anterior communicating artery in patients with anterior angle greater than 15.40° presented an 84% greater chance of rupture (p = 0.049), suggesting that the hemodynamic effects resulting from the anatomy of the siphon can persist anatomically after the siphon [49].

These studies have contributed to a better understanding of the geometric risk factors, but little is known about the anatomical changes in the carotid siphon and, consequently, the repercussions of the hemodynamic changes that the mechanisms of neurosurgical interventions could entail. Devices, such as intracranial stents and detachable coils, and even clips of aneurysms can modify the morphology of the carotid siphon and the knowledge of these

consequences could be used to obtain better therapeutic results. This becomes even more important considering that one-third of intracranial aneurysms are located in the carotid siphon [4, 32].

1.5. Flow diverter stents

The microsurgical access of carotid siphon aneurysms can often be considered of high technical complexity. In this way, endovascular treatment has become popular as a safe and effective alternative [32–34].

In the last 10 years, a new device for the treatment of intracranial aneurysms has been presenting promising results, the intracranial flow diverter stents (FDS). They are cylinders with walls formed by braided metallic wires configuring extremely diminutive fenestrations. When implanted in the wall of the parental artery, the small fenestrations allow the passage of blood to the penetrating branches, avoiding neurological deficits, but blocking the blood flow into the aneurysmal sac, and leading to thrombosis and subsequent progressive reduction of its volume [32, 33, 41, 43].

It is nowadays believed that such stents, by virtue of their structural conformation of braided wires, would perfectly fit the anatomy of the vessel in which it was implanted [32].

The rupture of intracranial aneurysms continues to be one of the neurosurgical diseases with the highest morbidity and mortality. Despite advances in the knowledge of the causes and evolution of these lesions, the understanding of all etiological mechanisms remains a challenge for modern neurosurgery.

Recently, hemodynamic studies of the interaction between blood flow and the endothelial wall have received increased attention as an important element in the genesis, development, and rupture of cerebral aneurysms [19, 20, 39]. In this context, studies of carotid siphon interactions are especially important because of the anatomical peculiarities of this region and considering that about one-third of all intracranial aneurysms are located there [1, 18, 21].

Studies such as those by Lin et al., Bogunović et al., and Takeuchi et al. showed that vessels with more intense curvatures are related to greater oscillation and decrease of wall shear force [21–23]. The change in direction of blood flow caused by the carotid siphon curvatures would be related to the transformation of the originally linear flow into turbulent flow. This transformation of the flow pattern would decrease and oscillate wall shear stress, which would precipitate the first endothelial changes in the genesis of aneurysm formation or stenoses [24, 25]. Jou et al., using 3D reconstructions of 25 patients with paraclinoid aneurysms, identified that the mean wall shear stress is inversely dependent on the size of the aneurysmal sac and that ruptured aneurysms present a lower mean wall shear stress near the aneurysmal cervix [39]. Zhang et al., also using 3D reconstructions, hemodynamic studies, and the anatomical classification of Zhang, showed that stenotic lesions tend to appear soon after intense carotid siphon curvatures, also evidencing that siphons that present more pronounced curvatures, such as type C, have statistically more stenoses than siphons with softer curvatures [29]. Piccinelli et al. analyzed individually the aneurysm curves of the carotid siphon and showed that ruptured aneurysms are statistically more present in carotid siphon curves of smaller

diameter and shorter length, being preferentially located in the external wall of the curvature [27]. Recently, Lauric et al. compared demographic data with 3D angiogram and showed that women have carotid siphons with curvatures greater than men and patients with aneurysms on siphon also present larger curvatures [40]. Lauric et al. evidenced that men generally have carotid siphons with less prominent curvatures than women [40].

In one of the first studies to evaluate geometric and anatomical changes in the carotid siphons after FDS release in the treatment of the aneurysm in this region and its repercussions Waihrich et al. observed that FDS release led to a morphological change in the carotid siphon, characterized by a progressive and statistically significant increase ($p < 0.001$) in the anterior and posterior angles independently of the angiographic result in the O'Kelly-Marotta scale [35, 50]. In addition, the multivariate analysis showed that there is an increase in the frequency of D results progressively in the quartiles of the anterior angle increase, inferring that there is a greater possibility of radiological cure (result D) in larger increases of anterior angle. Despite the progressive increase of the posterior angle after the FDS release, the statistical relation between this increase and the D result by the multivariate analysis was not observed. Probably, this result was due to the smaller magnitude of the posterior angle increase, both after stent implantation (from 3.97° ± 25.06° to 22.05° ± 25.18° vs. 71.98° ± 31.27° to 79, 43° ± 31.80°), and in relation to the result D with non-D (from 8.34° ± 22.21° to 26.78° ± 24.40° vs. 74.67° ± 25.35° to 81.08° ± 33.58°) [36–38, 50].

The FDS technology is based on increasing blood flow resistance in the aneurysm neck, reducing the inflow and outflow of blood into and out of the aneurysmal sac, and stagnating and thrombosing the blood into the aneurysm. However, changes in carotid siphon geometry may be related to a higher probability of cure. It is possible that the increase of the angle and the reduction of the anterior angle curvature lead to a reduction of the hemodynamic stress in the region, that is, the morphological changes would increase the intensity and reduce the oscillation of the wall shear force, contributing to better final results.

The age, in patients under 60 years, also proved to be an independent variable for a greater chance of cure. Lin et al. evidenced in their study that carotid siphons with greater tortuosity present greater technical difficulty for the release of FDS [21]. In fact, patients older than 60 years presented a higher statistical proportion of the more tortuous types of siphons (types S and C, with $p < 0.001$) and statistically lower values of both the anterior angle (6.06° ± 28.49° vs. 18.07° ± 20.26°, $p < 0.001$), and posterior (71.00° ± 37.68° vs. 80.80° ± 27.14°, $p = 0.025$), evidencing the presence of more tortuous siphons in this population [50]. Another important point is that large and giant aneurysms present greater technical difficulty in their treatment and, in addition, often require more time to thrombose completely [6, 42].

2. Cervical internal carotid artery aneurysm

Aneurysms of the extracranial carotid artery (ECAA) are rare, and little is known about its natural history, the etiology is diverse, and most ECAA are asymptomatic and do not grow over time but may progress into a pulsatile mass, cranial nerve compression, or cause a stroke.

Patients with an asymptomatic ECAA have a rate of ischemic stroke in the aneurysm territory of 1.1 per 100 patient years. For patients with an increasing ECAA diameter, intervention may be considered, while in patients with small non-growing asymptomatic ECAA, a conservative approach seems justified [45].

The main cause of the ECAA is atherosclerotic disease, followed by trauma and most aneurysms in 608 on a total of 1239 patients were located in the internal carotid artery, i.e., its cervical extracranial portion in a study by Welleweerd et al. invasive treatment for extracranial carotid artery aneurysms pertains to only 0.6–3.8% of all extracranial carotid interventions. The best medical treatment comprises antithrombotic treatment and regular follow-up. Traditional surgical treatment has been associated with the risk of stroke and cranial nerve damage; whereas, endovascular ECAA repair has only been described in small case series. However, early mortality and number of strokes is low in surgical and endovascular treatment even in the long-term follow-up, supporting the assumption that invasive treatment could prevent stroke [44].

3. Conclusion

The morphological analysis of the anatomy of the carotid siphon revealed a directly proportional relation between the anterior carotid siphon angle and larger aneurysms, a higher risk of rupture, and the location of the aneurysms distal to the carotid siphon.

The use of flow redirecting stents to treat aneurysms in the carotid siphon caused morphological changes characterized by increased anterior and posterior angles. Specifically, the anterior angle increase was associated with better angiographic results, i.e., aneurysmal occlusion at 6 months.

About ECAA treatment, a better knowledge about the natural history and risk of complications of the different treatments is needed in order to get a consensus, the early and long-term outcome of invasive treatment are favorable, despite some cranial nerve damage be possible after surgery.

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