Presence of anatomical variations of the circle of Willis in patients undergoing surgical treatment for ruptured intracranial aneurysms

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Abstract

Background/Aim. The presence of aneurysmal changes on the brain blood vessels has been subject to numerous research. This study investigated the relation between ruptured aneurysms and anatomical configuration of the Circle of Willis, with the purpose to obtain an insight into their mutual connection.

Methods. The analysis included 114 patients suffering from ruptured intracranial aneurysms. Preoperative cerebral angiography was performed and compared with the intraoperative findings in order to attain a precise insight into morphological changes occurring on the circle of Willis.

Results. The prevalence of asymmetrical Willis in the whole group of patients was 64%. Within the group of patients suffering from multiple aneurysms, the presence of asymmetrical Willis' circle was 75.7%. The highest incidence of the asymmetrical Circle of Willis was found among patients with aneurysmal rupture detected at the anterior communicative artery (ACoA) site (72.7% among cases with solitary and 100% among those with multiple aneurysms). Morphological changes on the A1 segment of ACoA were observed in 50 (44%) cases, with higher incidence found on the right side (69%). When comparing location of ruptured aneurysms between genders, a statistically significant prevalence of the ruptured aneurysms on ACoA was present in men, whereas women showed higher incidence of ruptured aneurysms on interior carotid artery (ICA) site (p < 0.01). The linkage between aneurysms with hypoplasia of the A1 segment of ACA and decreasing of the angle at which segments A1 and A2 join suggest the relationship between their onset, corresponding configuration type of Willis and subsequent hemodynamic changes.

Conclusion. High incidence of asymmetry of Willis circle in the group of patients with ruptured aneurysms imply association of asymmetrical configuration and disorder in haemodynamic relations with forming and rupture of intracranial aneurysms.

Key words: anatomy; central nervous system vascular malformations; circle of willis; intracranial aneurysm; aneurysm, ruptured.

Apstrakt

Uvod/Cilj. Prisustvo aneurizmatskih promena na krvnim sudovima mozga predmet je mnogih istraživanja. U ovom radu ispitivan je odnos rupturisanih aneurizma sa anatomskom konfiguracijom vilisovog prstena u cilju sagledavanja njihove međusobne povezanosti. Metode. Analizirali je bilo podvrgnuto 114 bolesnika sa rupturisanim intrakranijalnim aneurizmama. Analiziran je preoperativni angiografski nalaz i uporedavan sa intraoperativnim nalazom. Precizirane su morfološke promene na Vilisovom prstenu koje su bile predmet posmatranja. Rezultati. Zastupljenost asimetričnog Willis-ovog prstena u celokupnoj grupi bolesnika bila je 64%. U grupi bolesnika sa multiplim aneurizmama asimetričnost Willis-ovog prstena bila je zaostupljena 75.7%. Najveća zastupljenost asimetrije Willis-ovog prstena bila je u grupi bolesnika sa rupturom aneurizme na prednjoj komunikativnoj arteriji (ACoA) – 72.7% u grupi solitarnih i 100% u grupi multiplih. Morfološke promene na A1 segmentu ACoA nađene su kod 50 (44%) ispitnika, pri čemu je veća zastupljenost promena bila na desnoj strani (69%). U poređenju lokalizaciju rupturisanih aneurizma između polova, utvrđena je statistički značajna zastupljenost rupture aneurizmi na ACoA kod muškaraca i rupture aneurizmi na unutrašnjoj korotidnoj arteriji (ICA) kod žena (p < 0.01). Povezanost aneurizama sa hipoplozijom A1 segmenta ACoA i sa smanjenjem ugla šajanja A1 i A2 segmenta, jasno je ukazala na povezanost njihovog nastajanja sa odgovarajućim tipom konfiguracije Willis-ovog prstena i posledičnih hemodijnamskih promena. Zaključak. U ovom radu je zastupljenost asimetrije Willis-ovog prstena u grupi bolesnika sa rupturisanim aneurizmama ukazuje na povezanost asimetrične konfiguracije poremećenih hemodijnamskih odnosa sa formiranjem i rupturom intrakranijalnih aneurizama.
Introduction

The presence of hypoplastic segments in certain parts of Willis’ circle was established in a number of autopsies. A significant incidence of such variations of the Circle of Willis in the overall population points to an inability to define them as pathological changes, that is, anatomical variations of Willis, but rather as its types. Anatomical anomalies can be defined as rare changes appearing on the brain blood vessels which can hardly be related to the normal brain perfusion. On the other hand, redistribution of flow and involvement of the respective adaptive mechanisms of Willis, were not found to contribute to disorders in the brain perfusion needs.

Disturbed flow in certain anatomical variations of Willis’ circle might, partially, cause changes in the blood hit-wave which, accompanied with the existing weakness of the blood vessels at these sites, could represent a factor responsible for aneurysmal formation. The linkage between aneurysms and variations of Willis was investigated in a number of studies. The aim of this study was to check relevant facts delineating the linkage between aneurysms and anatomical variations of the Circle of Willis.

Methods

In the period between 2006 and 2007, an investigation was made on a series of 114 patients surgically treated for ruptured intracranial aneurysms. The patients were observed with regard to gender, age, number of aneurysms, time of rupture, location, size and the presence or absence of morphological changes in the brain blood vessels and anterior segment of the circle of Willis. Rupture had been diagnosed by means of clinical manifestation, computerized tomography finding and cerebral angiography of the brain blood vessels. A detailed analysis of cerebral angiography was performed prior to surgery to determine the relation to Willis’ elements, as well as its size and relation to the mother and surrounding blood vessels. The aneurysmal site was viewed in relation to the anterior communicative artery (ACoA), Medial carotid artery (MCA), interior carotid artery (ICA) and pericalose artery (PerA). The presence or absence of morphological changes on blood vessels were determined by means of diameter analysis, whereby symmetry/asymmetry of these changes was also considered. A diameter of a respective blood vessel was now compared with a diameter of the symmetrical blood vessel opposite it. Narrowing of the blood vessel diameter by one third or two thirds, as compared to the opposite blood vessel diameter, was denoted as ‘hypoplasia’, whereas such narrowing by less than 1/3 was marked as ‘extreme hypoplasia’. The presence of ICA angulation after PcoA separated from its supraclinoid part by less than 120°, was marked as “extreme ICA angulation”. The MCA bifurcation angle over 90° was marked as “atypical branching”. The presence or absence of these elements on one side pointed to the symmetrical of asymmetrical configuration of the Willis. The connection was monitored between the site or aneurysmal change and changes present on Willis’ circle, and the obtained findings were examined and corrected after getting an intraoperative insight. Apart from monitoring the overall group for changes on Willis’ circle, two separate groups were examined for ruptured solitary and multiple aneurysms, aimed at measuring the incidence of respective changes and possible interrelation between these and multiplicity. The results were displayed as absolute numbers and percentage. Comparing the obtained findings was completed within the respective groups with regard to the position of the aneurysm and incidence of morphological changes found on Willis’ circle. To determine the statistical significance, t test or non-parameter Mann-Whitney rank-sum test was used. Numerical parameters were presented as a mean value (X) ± standard deviation (SD).

Results

Of 114 patients, 68 (59.7%) were women and 46 (40.3%) men. Solitary aneurysms were found in 81 (71%) cases, whereas 33 (29%) subjects had multiple aneurysms. Aneurysmal rupture occurred on the average at the age of 52 ± 10.58 years, with earlier presence recorded in men (48 ± 9.74 years).

In terms of location, in the group of solitary aneurysms, ruptures were present in 40.7% of the patients at ACoA site, on the carotid artery in 27.2% (sum location of PCoA 14.8% and ICA 12.4%; in the branching of the MCA in 24.7%). In our series, aneurysms of Oer A (4.9%) and a. basilaris (2.5%) were present only in the female patients. Rupture of solitary aneurysm most often found in men was localized on ACoA (58.8%), on MCA (23.5%) and ICA (aneurysms on PCoA included) in 17.6%. In women, distribution of ruptured aneurysms greatly differed: ruptures on ACoA was present in 27.7%, on MCA in 25.5% and on ICA (aneurysms on PCoA included) in 34%. By comparing the location of ruptured aneurysms across genders, we were able to determine statistically significant prevalence of aneurysms on ACoA site in men, and aneurysmal rupture on ICA in women (p < 0.01). With regard to location and size, we found that aneurysms on ACoA site ruptured in 81.9% at the size of 3–10 mm, on MCA and ICA in 60%, whereas ruptures on PCoA occurred in 83.9%, which in total, concerning this size on ICA, was 72.7% (Table 1).

The data of patients with solitary aneurysms are shown in Table 2.

Of the total of 33 aneurysms found on ACoA segment 75.7% of morphological changes were present on A1 segment and ACoA (45.5% of various degree hypoplasias of the right A1, 27.2% of the left A1 and 3% of ACoA fenestrations) (Figure 1).

Of the total of 20 aneurysms localized on MCA 35% were found with morphologically atypical Willis’ circle (20% atypical MCA branching and 15% hypoplasia of A1 segment).

In 60% of the total of 10 aneurysms localized on ICA the presence of morphological changes on the anterior seg-

ment of Willis’ circle was detected, right-side presentation in 65% (Figure 2).

Of the total of 12 aneurysms found on the posterior communicative artery (PCoA) morphologically atypical Willis’ circle was present in 66.7%. Their right-side presentation was recorded in the same percentage (Figure 3).

A 70% of the total of four aneurysms localized on a. pericalosys (APer) was present with the morphologically atypical Willis’ circle.

The data on patients with multiple aneurysms viewed in relation to the site of ruptured aneurism are shown in Table 3.

Of 81 patients with solitary aneurysm, in 48 (59.2%) cases, certain morphological changes were found on the anterior segment of Willis’ circle. In 33 (40.7%) patients changes were registered on the A1 segment of ACoA, with more changes found on the right side.

In the group of 33 patients with multiple aneurysms, 25 (59.2%) were found with morphological changes on the anterior segment of Willis’ circle. In 17 (51.5%) changes on A1

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Table 1

<table>
<thead>
<tr>
<th>Locations of aneurysms</th>
<th>Size of aneurysms (mm)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 3</td>
<td>3–6</td>
</tr>
<tr>
<td>ACoA</td>
<td>/</td>
<td>10</td>
</tr>
<tr>
<td>MCA</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>ICA</td>
<td>/</td>
<td>2</td>
</tr>
<tr>
<td>PCoA</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>PerA</td>
<td>/</td>
<td>1</td>
</tr>
<tr>
<td>VB</td>
<td>/</td>
<td>2</td>
</tr>
<tr>
<td>Total (%)</td>
<td>3 (3.7)</td>
<td>23 (28.4)</td>
</tr>
</tbody>
</table>

ACoA – Anterior Communicative Artery; MCA – Medial Cerebral Artery; ICA – Interior Carotid Artery; PCoA – Posterior Communicative Artery; PerA – Pericalosys Artery; VB – Vertebrobasilar Artery

Table 2

<table>
<thead>
<tr>
<th>Locations of aneurysms</th>
<th>With no morphological changes</th>
<th>With morphological changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type of changes</td>
<td>left</td>
</tr>
<tr>
<td>ACoA</td>
<td>hypoplasia A1</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>a. mediana cor. call.</td>
<td>1</td>
</tr>
<tr>
<td>MCA</td>
<td>hypoplasia A1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>atypical branching of MCA</td>
<td>2</td>
</tr>
<tr>
<td>ICA</td>
<td>hypoplasia A1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>PCoA</td>
<td>/</td>
</tr>
<tr>
<td></td>
<td>prominent angulation of ICA</td>
<td>2</td>
</tr>
<tr>
<td>PCoA</td>
<td>fetal type PCoA-hypoplasia A1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>hypoplasia PCoA</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>prominent angulation of ICA</td>
<td>1</td>
</tr>
<tr>
<td>PerA</td>
<td>hypoplasia A1</td>
<td>/</td>
</tr>
<tr>
<td></td>
<td>a. pericalosis</td>
<td>1</td>
</tr>
<tr>
<td>VB</td>
<td></td>
<td>30</td>
</tr>
</tbody>
</table>

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A total number of aneurysms with left-side or right-side presentation or dominant flow did not show any difference. However, higher number of aneurysms was noticed on ACoA with dominant left-side flow (46.3%) as compared to their presence on ACoA with the dominant right-side flow.
(31%). Such presentation on ACoA is associated with higher incidence of hypoplasia of the right A1 segment, which was in our series present 60%. Some series indicated a three times more common hypoplasia of the A1 segment on the right side than on the left one. A higher incidence of aneurysms on the right MCA (31%) and right PCoA (21.8%) compared to the left MCA (24%) and left PCoA (9.3%), could be ascribed to a higher blood flow from the carotid artery towards the MCA due to a decreased flow through the hypoplastic A1 segment 8, 22–24.

Also, right-side hypoplasias of the A1 segment were present in two thirds of the cases, thus being correlated with other studies 20–22.

The linkage between A1 segment hypoplasias and aneurysmal formations on ACoA was found to be directly dependent on the hemodynamic adaptation of the ACoA to regulate the collateral flow and ensure adequate perfusion. Arterial tolerance to collateral circulation through ACoA is a diameter 0.4–0.6 mm 12, 13. An increase in diameter by 0.4–1.6 mm in the physiological conditions of a limited flow through some of the A1 segments, will supply normal flow in the distal segments 24. However, in the circumstances of hypoplasia or aplasia of some of the A1 segments, the ACoA diameter increases and shunt flow establishes 13. It is noteworthy that this process stands in direct correlation with the perfusion needs of the corresponding irrigation areas, and as such it starts immediately after embryogenesis. Once formed, shunt flow can meet perfusion needs without further structural degradation on a blood vessels joint elements. Remodelling of blood vessels to provide adequate perfusion, can be stopped at the moment of establishing suitable collateral circulation 21.

If compared with the rest of intracranial arteries, the efficacy of ACoA vasodilatation will be limited as it is the only cerebral artery developing from the plexiform blood vessel complex 26. In cases of further increase beyond the limit through the ACoA, blood flow becomes more turbulent and laminar movement ceases to exist. The ACoA-A2 joint begins to function as a stagnation point of a hemodynamic strike 13. The flow itself through norm-plastic A1 segment and enlarged ACoA increases by 50% and more (from 214 mL/min to 303 mL/min) 8. The effect of hemodynamic strike on blood vessels wall is directly dependent on the flow way and direction of the hit wave. The latter depends on the angle of A1–A2 joining, which in aneurysms on ACoA was significantly smaller and ranged between 103 and 116 degrees, whereas in norm-plastic segments it was approximately 143 degrees 13.

An increased flow through the collateral ACoA system, accompanied by diversion from the optimal bifurcation angle at the A1–A2 link, can greatly influence the increase of stress on blood vessel’s wall, thus being directly responsible, along with turbulent flow, for the forming of degenerative lesions of the intima and endothelium. The stress on the wall in the region of stationary points can under such conditions become 5–10 times higher than the normal intra-arterial stress which naturally ranges between 1.0–2.0 Pa 4, 25–29, 32, 36.

A linkage between aneurysm and hypoplasia of the A1 segment and decreasing of the A1–A2 joining angle, points clearly to the connection between their forming, corresponding configuration type of Willis and consequential hemodynamic changes.

When we investigated the location of aneurysms on ICA, separated from the aneurysms on PCoA, we noticed that 70% of them had left presentation. In 60% of the cases, morphological specificities were observed on Willis’ circle in terms of extreme angulations of the carotid artery after separation of the PCoA, and the presence of hypoplasia on the A1 segment and changes on PCoA (hypoplasia and phoetal type). Smaller ruptures on ICA (ICA – 12%, PCoA – 14%) compared to their incidence (40%), suggest a significantly lower level of stress in the region of supraclinoid part of the carotid artery, unlike the PCoA complex, or higher adaptability of the carotid artery to destructive changes in its walls and their remodeling 29. The data supporting this finding were of the 55% incidence rupture on ICA 8 mm, while the incidence of those on ACoA was 60% not bigger than 3 mm 30. The most common location on ICA is supraclinoid up to the point of PCoA separation. They belong to lateral aneurysms whose growth and rupture are contingent on the flow and radius formed by blood vessel. These are characterized by a stable intra-aneurysmal flow 31, 32, explaining the lower incidence of ruptures on ICA in relation to aneurysmal incidence. More often left-side presentation of the ruptured solitary aneurysms on ICA may be connected to a higher blood flow through the left carotid artery directly going out of the aortal arch and therefore being more prone to excessive cardiovascular mechanisms. Another assumption is that greater perfusion needs of the left brain hemisphere may influence increasing of the blood flow through the carotid artery. These assumptions call for further investigation of the blood flow of magistral blood vessels and their relationship with the cerebral perfusion.

Rupture of ICA aneurysms within multiple aneurysms is characterized by the right-side position. This finding might be in collision with the more common left-side rupture of solitary aneurysms on ICA; however, aneurysmal ruptures on the right ICA were combined with the hypoplasia of the A1 segment and aneurysms on the bifurcation of the left MCA. There is a clear indication that distribution of blood flow through the right A1 segment has direct impact on intensifying the blood flow through the right carotid artery 8, which, depending on the curve of the blood vessel, may influence aneurysmal growth and rupture.

Solitary aneurysms on PCoA ruptured more often on the right side (in nearly 67%). Morphological changes were present in the same percent in the form of hypoplasia or fetal PCoA type, and sharp angulations above the PCoA separation point. Higher right-side incidence of PCoA aneurysms correlates with more frequent changes on PCoA on the right side. The right-side incidence of changes on PCoA becomes more prominent in ruptures on PCoA within the multiple group. Aneurysms localized on PCoA belong to the group of bifurcation aneurysms, their growth and rupture being clearly connected with the distribution of blood vessels and size of

the bifurcation angle. They are characterized by circular intra-aneurysmal flow accountable for high circumferential stress, causing thus a fusiform growth of aneurysm along the length of PCoA 21,24,33.

The rupture of solitary aneurysms localized on MCA was not associated with more frequent morphological changes on the Circle of Willis. A bigger bifurcation angle on the media and the hypoplasia of the A1 segment were present in 35%, suggesting another form of hemodynamic and morphological changes was responsible for the forming and growth of aneurysms on the MCA branching.

Aneurysms localized on MCA bifurcations show certain specificities in comparison to other locations. The medial cerebral artery is formed at the earliest stage of embryogenesis from the primitive capillary plexus, and turns laterally as the embryo grows, forming a fan of blood vessels. Morphologically, it is not part of Willis' circle, but in a hemodynamic sense it is directly linked to the distribution of blood within the circle. The end part of the MCA functions as a terminal type bifurcation with the tendency of forming optimal bifurcation geometry, intended at providing minimal apical stress 8,25,27. Maintenance of the static equilibrium of the bifurcation region depends on the ratio between the flow through the afferent and its efferent vessels, and the present bifurcation angle. The tendency of optimal bifurcation geometry is for the larger branches to have smaller angles in relation to the parent vessel, while the ratio between the flow in the branches and that in the parent vessel tends to be smaller or equal to 1.0 and the angle of branching about 90° 34. Optimal bifurcation would retain its angle in the circumstances of a more intense blood flow resulting from higher blood pressure or some other hemodynamic disorders 21. This clearly suggests that inadequate bifurcation geometry was basically responsible for aneurysmal formation. Due to inadequate equilibrium between the flow in the afferent and efferent vessels, pulse opening of the bifurcation angle maintains a constant ratio between the transmural pressure in the afferent vessel and its branches. A long-term adapting to pulse bifurcation may lead to degenerative and ultrastructural changes in the vessel’s wall 15,35. With aging, as a result of dystrophic changes on the brain vessels, their elasticity decreases, and may disable compensatory pulse adaptability of the bifurcation thus impairing redistribution of the transmural pressure due to stress increase in the region of stationary point 36–42.

**Conclusion**

In the general population, the incidence and distribution of asymmetric configurations of the Circle of Willis ranges between 15 and 22%. The asymmetry of Willis in as much as 64% of the cases in this group, indicates a clear linkage between morphological changes occurring as a result of asymmetrical configuration, and disorder of hemodynamic relationships while the brain is supplied with adequate perfusion. Not only due to configuration of Willis with no visible asymmetrical morphological changes, hemodynamic load may occur within elongated and perfusion-loaded joint angles of the asymmetry of Willis. A significantly higher incidence of asymmetry in relation to aneurysmal changes on the brain blood vessels, suggest that the blood flow in the brain is adaptable to higher perfusion needs. Disorder and disturbance of dynamic stability may lead to ultrastructural changes in the walls of blood vessels as a result of higher intra-arterial flow, and possibly trigger off a cascade of mechanisms for pathological adaptation of the wall before it finally causes the forming of aneurismal changes. The notion of significantly smaller aneurysm ruptures as compared to their incidence in the overall population, make us to speculate on whether the development of aneurysmal changes on the brain blood vessels might be an attempt of a respective brain flow variations at adapting themselves to the higher perfusion needs of certain parts of the brain.

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