The online version of this article is located at http://www.minervamedica.it

Journal of Neurosurgical Sciences 2016 ????;60 (??):000-000

ORIGINAL ARTICLE

The determination and comparison of the vascular configurations of the posterior cerebral and posterior communicating arteries by two different techniques

Hayri KERTMEN [1], Bora GÜRER [1], Kutluay ULUÇ [1], Erhan TURKOGLU [1]
Ulas CIKLA [1], Shahriar SALAMAT [2], Mustafa K. BAŞKAYA [1]

[1]Department of Neurological Surgery, School of Medicine and Public Health, University of Wisconsin, Madison, WI, USA; [2]Department of Pathology and Laboratory Medicine, School of Medicine and Public Health, University of Wisconsin, Madison, WI, USA

Corresponding author: Mustafa K. Başkaya, Department of Neurological Surgery, University of Wisconsin, School of Medicine CSC, K4/822, 600 Highland Avenue, Madison, WI 53792, USA. E-mail: m.baskaya@neurosurgery.wisc.edu

ABSTRACT

BACKGROUND. Although configurations of the posterior cerebral artery (PCA) and posterior communicating artery (PComA) have been extensively studied, reported rates of adult (AC), fetal (FC) and transitional configurations (TC) vary widely due to techniques used. A histological technique was applied to measure the circumference of the arteries and this was compared with caliper measurements taken from the same arteries.

METHODS. Ninety-five brains were examined. The external diameters of all pre-communicating, post-communicating PCAs and PComAs were measured under operating microscope with a micrometer caliper. After measurements, all arteries were prepared for histology, sections were stained with Verhoff's elastic technique and the circumferences were measured using the light microscope. In the caliper group, AC was found in 77.2%, FC was found in 17.3% and TC was found in 5.5% of the right hemispheres, while on the left AC was found in 81.7%, FC in 18.3% and no TC was found. In the histology group, AC was found in 78.3% and FC was found in 21.7% of the right, while on the left AC was found in 81.7% and FC was found in 18.3% of cases. No TC was found in any hemisphere. There was no statistical significance between the two groups.

RESULTS. Results of the present study reveal several important findings. When the PComA was absent in one hemisphere, the PComA was FC on the contralateral hemisphere.

CONCLUSIONS. Transitional configuration was found in a very small number of cases in the caliper group compared to previous studies, and no TC was found in the histology group.

(*Cite this article as:* Kertmen H, Gürer B, Uluç K, Turkoglu E, Cikla U, Salamat S, *et al.* The determination and comparison of the vascular configurations of the posterior cerebral and posterior communicating arteries by two different techniques. J Neurosurg Sci 2016;60:000-000)

Key words: Posterior cerebral artery - Intracranial aneurysm - Surgical procedures, operative.

Since the first description of the circulus arteriosus cerebri (CAC) by Thomas Willis in 1662, many anatomical variations of the posterior circulation have been described.[1] The posterior cerebral artery (PCA) is usually divided into four segments. The posterior communicating artery (PComA) makes the distinction between the P1 (precommunicating) and the P2 (postcommunicating) segments. In the adult human brain, three configurations of the PCA/PComA have been described; adult, fetal and transitional.[1-7] The most common configuration is the adult configuration (AC), in which the diameter of the P1 is greater than that of the PComA (P1>PComA). In the fetal configuration (FC), the diameter of the P1 segment is smaller than the diameter of PComA (P1<PComA). In transitional configuration (TC), the diameter of the P1 is

expected to be equal to the diameter of the PComA (P1=PComA).

Reported incidence of the AC, FC, TC varies significantly between previous studies due to different measurement techniques.[1, 3, 5-18] Therefore, there is a need for a more accurate and objective measurement method. The aim of the present study was to determine and to compare the vascular configurations of the posterior circulation using two different methods of external measurement of vascular diameter versus measuring the vessel circumference in histologic preparation.

Materials and methods

Ninety-five cadaveric brains ranging between 13 and 95 years of age were examined. None of the specimens included in the study had any macroscopic evidence of cerebrovascular disease.

The brains were removed from the cranium by the standard method of extraction. Brains were fixed in 10% buffered formalin for 10 to 14 days. The CAC together with the basilar artery, and its main branches were carefully removed from the brain using arachnoidal dissection under operative microscope (Leica, Wild M 695, Leica Microsystems Inc. Wetzlar, Germany). Posterior part of the CAC was then photographed (Figure 1A).

1) Caliper group: the external diameters of the P1 and P2 segments of the PCA and PComA were measured 3 mm away from the P1-PComA junction with a micrometer caliper (Fisher Scientific, Pittsburgh, PA, USA) under an operating microscope (Figure 1B). The caliper was standardized according to the manufacturer's instructions. The measurements were taken three times on each segment and the average diameter was recorded in millimeters.

2) Histology group: following caliper measurements vessels on the right side were marked with Indian ink. The portion of arterial circle including the ICA, PComA, P1 and P2 segments were placed in a tissue cassette and processed for paraffin embedment using the standard methods. Following processing P1, P2 and PComA were separated and placed in paraffin in a vertical plane for embedding. Five µm thick paraffin sections were taken from all vessels and stained with Verhoff's elastic technique.[19] Using the light microscope at 2X magnification vessels were captured in cross section by digital means. Subsequently the circumferences of the internal elastic laminae were measured in millimeters using Image-Pro program (Image-Pro Plus Version 5.0.1 For Windows 2000 & XP Professional Copyright 1993, 2004 Media Cybernetics, Inc., Silver Spring, Maryland, USA) (Figure 2A, B). The circumferences of the P1s and PComAs were measured and the vascular configurations were determined as AC if P1>PComA, FC if P1<PComA and TC if P1=PComA. Vessels with measurements differing less than 10% were considered equal.

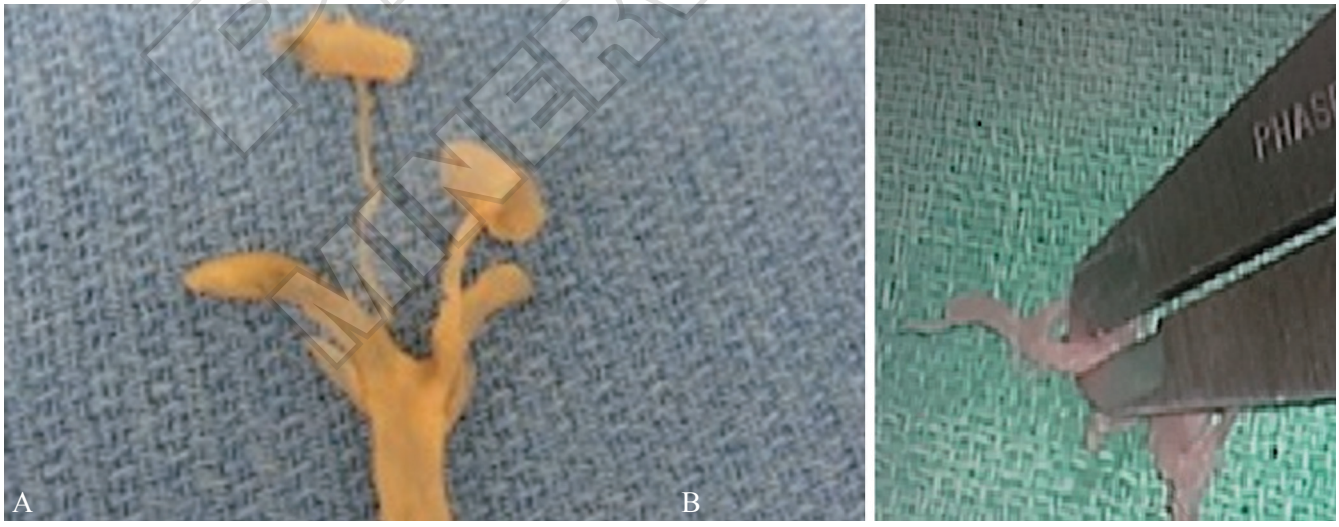

Figure 1.—A) Posterior part of the arterial circle/circulus arteriosus cerebri following removal from the brain. In this case a bilateral adult configuration is shown; B) caliper being used to measure vascular diameter.

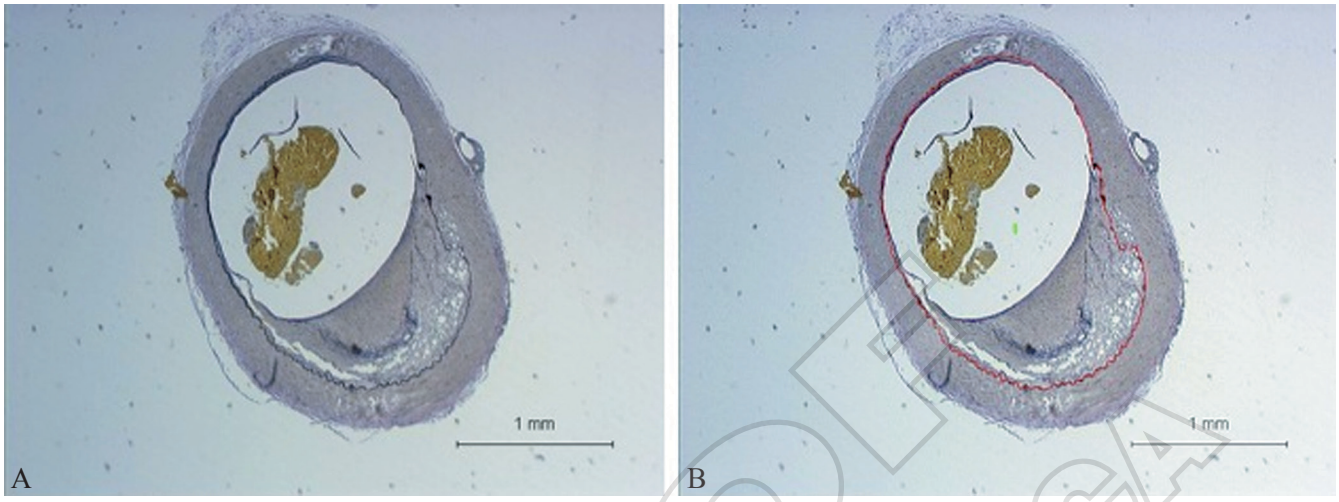

Figure 2.—A) Photomicrograph of a histological section stained with Verhoff's elastic (X2 obj); B) using Image-Pro program the red ink delineates and measure the vascular internal elastic lamina/diameter. (X2 obj).

As mentioned previously, the external diameters of the vessels were measured in the caliper group while in the histology group we measured internal luminal circumference using the internal elastic lamina. Due to this difference, we compared our methods by expressing our findings in form of ratios between vascular sizes.

Statistical analysis

The data analysis was performed using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, USA). Whether the distributions of continuous variables were normal or not was determined by Shapiro Wilk test. Data were shown as mean±SD or median (minimum-maximum), where applicable. The mean differences between both the "caliper" and "histology" groups and also left and right sides were evaluated by Paired Samples t test. Otherwise Wilcoxon Sign Rank test was applied for comparisons of the median values. The differences in the prevalence of types of classification between "caliper group" and "histology group" were analysed by Marginal Homogeneity or McNemar test, where appropriate. A "P" value less than 0.05 was considered statistically significant.

Results

The subject population consisted of 49 men (51.6%) and 46 women (48.4%). The mean age was 63.5 years.

1) Caliper group: On the right, the mean diameters for P1 was 1.86 mm (0.26-3.44 mm), for P2, 2.02 mm (1.0-3.30 mm) and for PComA, 1.09 mm (0.12-2.55 mm) (Table I). AC was found in 71 (77.2%), FC in 16 (17.3%) and TC in 5 (5.5%) of all right hemispheres. PComA was absent on the right in 3 specimens. On the left the mean diameter for P1 was 1.82 mm (0.46-3.61 mm), for P2, 2.06 mm (0.82-3.47 mm) and for PComA, 1.05 mm (0.15-2.55 mm) (Table I) (Figure 3). Adult configuration was found in 72 (77.4%) and FC in 21 (22.6 %) of the left hemispheres in the caliper group. PComA was absent in 2 specimens on the left. Also, there were no cases with TC on the left.

In the caliper group, 58 (61%) of brains had bilateral AC and 7 (7.3%) had bilateral FC (Table 2). When the PComA was absent in one hemisphere, the contralateral hemispheres had FC. There was no statistically significant difference between the diameters of the right and left P1, P2 and PComA in the caliper group (Table III).

2) Histology group: on the right, the mean circumference for P1 was 5.48 mm (1.03-12.96 mm), for P2, 5.83 mm (1.08-11.80 mm) and for PComA, 3.33 mm (0.47-9.22 mm) (Table I). Adult configuration was found in 72 (78.3%) and FC was found in 20 (21.7%) of right hemispheres. No TC was found on the right. Similar to the caliper group, the right PComA was absent in 3 (3.3%) cases. On the left, the mean circumference for P1 was 5.63 mm (0.51-12.01 mm), for P2, 5.88 mm (0.77-11.53 mm) and for PComA, 2.79 mm (0.73-10.87 mm)

TABLE I.—*The values of the diameters (for the caliper group) and the circumferences (for the histology group) of the arteries of the posterior circulation.*

Variable	Mean (mm)	SD	Min (mm)	Max (mm)
Caliper group				
R P1	1.86	0.67	0.26	3.44
R P2	2.02	0.44	1.00	3.30
R PComA	1.09	0.56	0.12	2.55
L P1	1.82	0.62	0.46	3.61
L P2	2.06	0.53	0.82	3.47
L PComA	1.05	0.60	0.15	2.55
Histology group				
R P1	5.48	2.13	1.03	12.96
R P2	5.83	1.73	1.08	11.80
R PComA	3.33	1.97	0.47	9.22
L P1	5.63	2.23	0.51	12.01
L P2	5.88	1.78	0.77	11.53
L PComA	2.79	1.68	0.73	10.87

SD: standard deviation: Min: minimum; Max: maximum; R: right; P1: precommunicating posterior cerebral artery; P2: postcommunicating posterior cerebral artery; PComA: posterior communicating artery; L: left.

TABLE II.—*The percentages of distributions of the configurations in both study groups.*

	Caliper group	Histology group
AC		
Bilateral	58 (61%)	61 (64.2%)
R only[+]	13 (13.6%)	13 (13.6%)
L only[+]	14 (14.7%)	13 (13.6%)
FC		
Bilateral	7 (7.3%)	5 (5.2%)
R only[++]	10 (10.5%)	13 (13.6%)
L only[++]	15 (15.7%)	12 (12.6%)
TC		
Bilateral	None	None
R only	5 (5.2%)[+++]	None
L only	None	None

[+] The contralateral hemisphere was not adult configuration.
[++] The contralateral hemisphere was not fetal configuration.
[+++] All contralateral hemispheres were adult configuration.
AC: adult configuration; FC: fetal configuration; TC: transitional configuration; R: right; L: left.

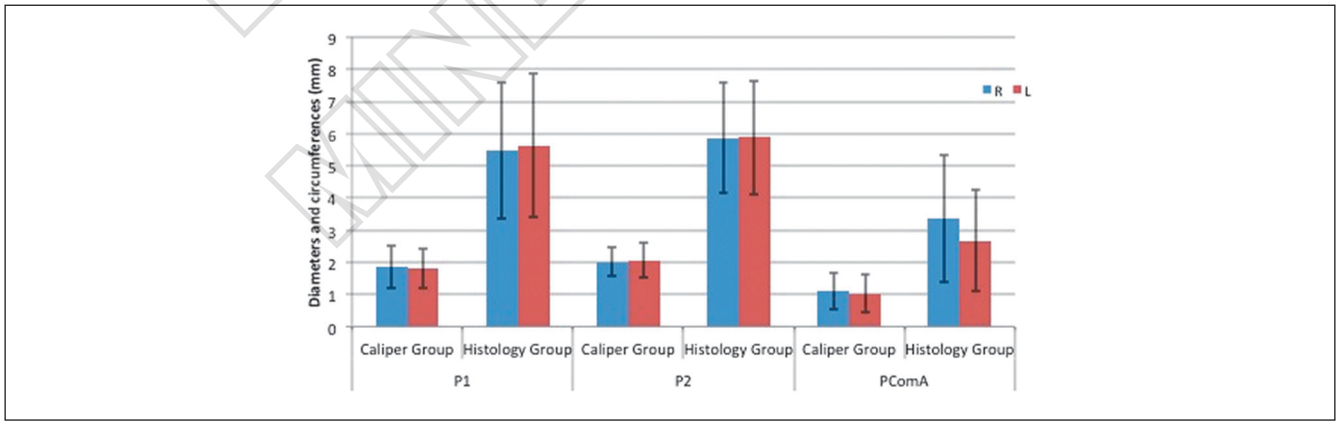

Figure 3.—Bar-graphs revealing the mean diameters and circumferences of the study groups.

TABLE III.—*Diameters and circumferences of P1. P2 and PComAs in the right and left hemispheres.*

Variable	Mean (mm)	SD	Min.	Max	P value
P1 (caliper group)					0.549[a]
R	1.86	0.67	0.26	3.44	
L	1.82	0.62	0.46	3.61	
P2 (caliper group)					0.366[a]
R	2.02	0.44	1.00	3.30	
L	2.06	0.53	0.82	3.47	
PComA (caliper group)					0.293[b]
R	1.10	0.56	0.12	2.55	
L	1.02	0.59	0.15	2.55	
P1 (histology group)					0.713[b]
R	5.48	2.13	1.03	12.96	
L	5.63	2.23	0.51	12.01	
P2 (histology group)					0.404[b]
R	5.86	1.71	1.08	11.80	
L	5.88	1.78	0.77	11.53	
PComA (histology group)					0.004[b]
R	3.35	1.97	0.47	9.22	
L	2.67	1.57	0.73	10.87	

[a]paired samples t test; [b]Wilcoxon Sign Rank test.
SD: standard deviation; Min: minimum; Max: maximum; R: right; P1: precommunicating posterior cerebral artery; P2: postcommunicating posterior cerebral artery; PComA: posterior communicating artery; L: left.

TABLE IV.—*Configuration distribution in the right and left hemispheres.*

Histology Group	Caliper group				P value
	AC	FC	TC	Total	
R					0.180[a]
AC	66 (%71.8)	4 (%4.3)	2 (%2.2)	72 (%78.3)	
FC	5 (%5.4)	12 (%13.0)	3 (%3.3)	20 (%21.7)	
TC	-	-	-	-	
Total	71 (%77.2)	16 (%17.3)	5 (%5.5)	92 (%100.0)	
L					0.344[b]
AC	69 (%74.2)	7 (%7.5)	-	76 (%81.7)	
FC	3 (%3.2)	14 (%15.1)	-	17 (%18.3)	
TC	-	-	-	-	
Total	72 (%77.4)	21 (%22.6)	-	93 (%100.0)	

[a]Marginal homogeneity test; [b]McNemar test.
AC: adult configuration; FC: fetal configuration; TC: transitional configuration; R: right; L: left.

(Table I). Adult configuration was found in 76 (81.7%) and FC was found in 17 (18.3%) cases on the left. The left PComA was absent in two cases. In this group, 61 (64.2%) of the brains had bilateral AC, and 5 (5.2%) of the brains had bilateral FC. TC was not found in the histology group (Table II). When PComA was absent in one hemisphere, the contralateral hemispheres had FC in the histology group as well. There was no statistically significant difference between the size of right and left P1s and P2s in the histology group. However, right PComAs were larger than left PComAs (p=0.004) (Table III).

Comparison of both groups

On the right, there were 71 (77.2%) AC in the caliper group; however, when these were examined histologically, 5 (5.7%) vessels were found to have larger PComA and were thus FC. In the histology group, 72 (78.3 %) AC were identified on the right, of which 4 (4.3 %) were interpreted as FC in the caliper group. On the right, 5 TC (5.5 %) were identified in the caliper group and none in the histology group. Two of these TCs were interpreted as AC and three were FC in the

TABLE V.—*The evaluation of the P1/P2 and P1/PComA values in both study groups.*

Variable	Mean	SD	Min.	Max.	P value[a]
R P1/P2 (%)					0.573
Caliper group	94.64	33.35	9.96	171.70	
Histology group	100.75	59.42	15.68	590.74	
R P1/PComA (%)					0.153
Caliper group	248.08	218.51	14.29	1516.67	
Histology group	258.27	225.05	19.62	1489.86	
L P1/P2 (%)					0.116
Caliper group	92.01	32.99	21.30	185.19	
Histology group	106.76	88.61	7.62	841.56	
L P1/PComA (%)					0.004
Caliper group	249.41	171.71	24.21	953.33	
Histology group	279.06	192.71	8.56	1225.51	

[a]Wilcoxon Sign Rank test
SD: standard deviation; Min: minimum; Max: maximum; R: right; P1: precommunicating posterior cerebral artery; P2: postcommunicating posterior cerebral artery; PComA: posterior communicating artery; L: left.

histology group. Comparison between the caliper and the histology groups was not statistically significant (P=0.180) (Table IV).

On the left, 72 (77.4%) AC were identified in the caliper group. However, histologically, 3 (5.7%) vessels were interpreted FC. No TC was found on the left in the both groups. There was no statistical significance between the histology and clipper groups (P=0.344) (Table IV).

Due to varied method (diameter versus circumference) between the groups, we compared ratios of the right P1/P2, right P1/PComA, left P1/P2 and left P1/PComA. On the left side P1/PComA ratio was larger in the histology group when compared with the caliper group (P=0.004) (Table V). There was no statistically significance difference determined among other comparisons. There was no TC identified with histological measurement on both sides. When one hemisphere had no PComA, the contralateral hemispheres had FC both in the histology and caliper groups.

Discussion

Embryological development of the posterior part of the CAC is complex.[20] In the fourth month of gestation the formation of the CAC is completed and all arterial segments of the CAC are thin and equal in diameter.[1, 4, 21, 22] As of the fourth month of gestation variation in diameter of the posterior arteries of the CAC begins

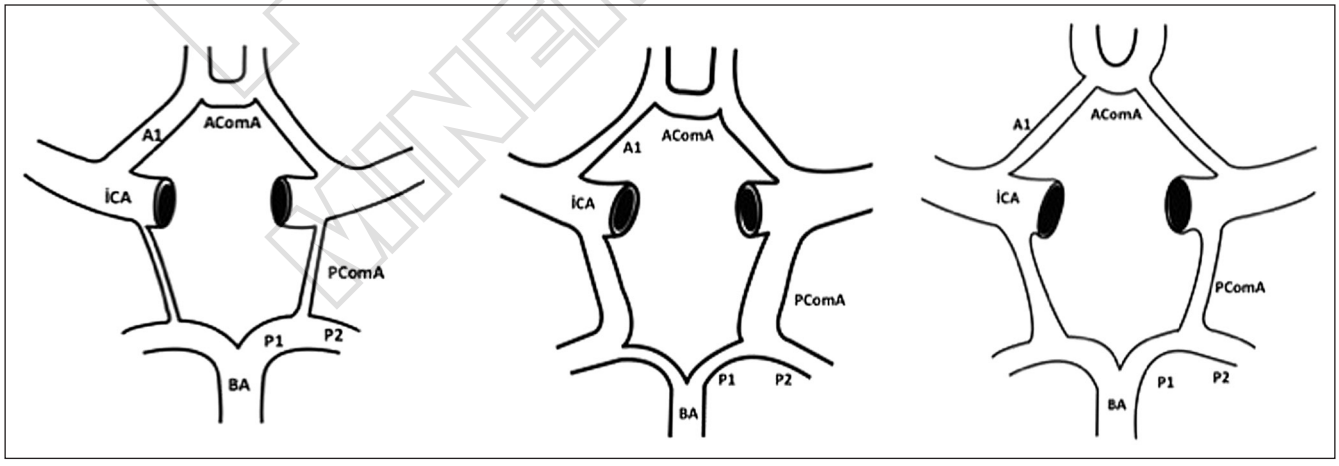

Figure 4.—Schematic drawings representing the three main anatomical variations of the posterior circulation: adult configuration (A), fetal configuration (B), transitional configuration (C).

TABLE VI.—*Past published studies.*

Author, year	N.	Population	Method	AC (%)	FC (%)	TC (%)
Alpers, 1959 [24]	350	Autopsy, normal adult brains	Under surgical microscope, outer diameter	76.5	14.6	8.9
Alpers, 1963 [8]	194	Autopsy, serebral softening	Under surgical microscope, outer diameter	not mentioned	29	not mentioned
Saeki, 1977 [7]	50	Autopsy, normal adult brains	Under surgical microscope, outer diameter	54	46	0
Zeal, 1978 [18]	50	Autopsy, normal adult brains	Under surgical microscope, outer diameter	58	40	2
Kamath, 1981 [25]	100	Autopsy, normal adult brains	Under surgical microscope, outer diameter	73.5	25	1.5
Bisaria, 1984 [9]	126	not mentioned	not mentioned	not mentioned	31.7	not mentioned
Pedroza, 1987 [5]	50	Autopsy, normal adult brains	Under surgical microscope, outer diameter	not mentioned	22	not mentioned
Van Overbeeke, 1991 [1]	53	Autopsy, fetuses and neonates	Under surgical microscope, outer diameter	18	9	73

AC: adult configuration; FC: embryonic configuration; TC: transitional configuration.

to appear, especially at the level of PComA. However the CAC remains symmetrical in most cases.[4, 21] In adult population there are three main anatomical variations. In AC, the diameter of P1 is larger than PComA (Figure 4A). In FC, the diameter of P1 is smaller than PComA (Figure 4B). In TC, the diameter of P1 is equal to the PComA (Figure 4C).

Although variations of the PCA and PComA have been studied extensively, conflicting results have been obtained due to the different measurement methods used (Table VI). In Padget's work,[16] AC was found in less than 50% of cases. Different studies have reported variable AC ratios ranging between 54% and 93.3%.[2, 6, 7, 18] The reported ratios of FC also vary from as low as 4.4% to as much as 40%.[2, 5, 7-14, 17, 18] that of TC also vary from 2.2% to 18%.[2, 3, 6, 10, 14] It is clear that, there is no concordance between ratios of the posterior circulation configurations in previously reported studies. There are several factors, which may have contributed to these discrepancies. Foremost, majority of measurements in these studies were performed with calipers with or without operative microscopic magnification. As shown in Figure-1b this method is quite crude and operator dependent. Moreover, due to lack of blood flow and turgor within the lumen of vessel in the *post-mortem* brain, in non-perfused brains, distortions and subjective changes in the diameter and the shape of the vessels can occur. On the other hand in *post-mortem* studies that utilized vascular perfusion with colored-silicone the entire vessel length may not have filled with the same amount of silicone and thus the vascular expansion could have been variable. In addition, in the caliper method, measurement is subject to inconsistencies due to the force of handling. Therefore, finding a more accurate, sensitive and objective method of lumenal measurement is desired.

The internal elastic lamina exists in all the arteries of the CAC, runs along the internal circumference of each vessel and essentially defines the lumenal size. Therefore, in *post-mortem* studies, Verhoff's elastic stain that outlines the thin band of the internal elastic lamina provides a reliable outline for measuring the circumferences of the arteries even if there is *post-mortem* distortion.[23]

In our study, we used two different methods to evaluate the anatomical variations of the posterior part of the CAC. First we measured the external diameters with a micrometer caliper under operating microscope as performed in the past studies. Subsequently, we measured the circumferences of the internal elastic laminas of the same arteries under the light microscope with Verhoff's elastic stain. We then compared both measurement methods. We considered vessels to be of equal size when measurements fell within a 10% range.

Five TC were identified all on the right side in the caliper group. Interestingly no TC was found with histological method. This finding may suggest that TC may be a false statement since with more sensitive measurement, such as histological method, the diameters of P1 and PComA may not be determined as equal.

Another important finding of the present study is that when PComA was absent on one side, the contralateral hemisphere contained FC in both caliper and histology groups.

Conclusions

The main aim of the present report is to describe the anatomical variations in the posterior circulation using two different methods of measurement. Although our results revealed no statistically significant difference between the two methods, there were significant find-

ings; first, when PComA was absent in one hemisphere, the contralateral hemispheres had FC. Second, presence of TC was not confirmed with histological method. These findings may suggest non-existence of TC.

References

1. Van Overbeeke JJ, Hillen B, Tulleken CA. A comparative study of the circle of Willis in fetal and adult life. The configuration of the posterior bifurcation of the posterior communicating artery. J Anat 1991;176:45-54.
2. De Silva KR, Silva TR, Gunasekera WS, Jayesekera RW. Variation in the origin of the posterior cerebral artery in adult Sri Lankans. Neurol India 2009;57:46-9.
3. Khamlichi A, Azouzi M, Bellakhdar F, Ouhcein A, Lahlaidi A. Anatomic configuration of the circle of Willis in the adult studied by injection technics. Apropos of 100 brains. Neurochirurgie 1985;31:287-93.
4. Lazorthes G, Gouazé A, Santini JJ, Lazorthes Y, Laffont J. Le modelage du polygone de Willis. Rôle des compressions des voies arterielles d'apport dans les mouvements de la colonne cervicale et de l'extrémité céphalique. Neurochirurgie 1971;17:361-78.
5. Pedroza A, Dujovny M, Artero JC, Umansky F, Berman SK, Diaz FG, Ausman JI, Mirchandani HG. Microanatomy of the posterior communicating artery. Neurosurgery 1987;20:228-35.
6. Riggs He, Rupp C. Variation in form of circle of Willis. The relation of the variations to collateral circulation: Anatomic analysis. Arch Neurol 1963;8:8-14.
7. Saeki N, Rhoton AL Jr. Microsurgical anatomy of the upper basilar artery and the posterior circle of Willis. J Neurosurg 1977;46:563-78.
8. Alpers BJ, Berry RG. Circle of Willis in cerebral vascular disorders. The anatomical structure. Arch Neurol 1963;8:398-402.
9. Bisaria KK. Anomalies of the posterior communicating artery and their potential clinical significance. J Neurosurg 1984;60:572-76.
10. Hasabe K. Arterien der Hirnbasis. In: Anatomie der Japaner. Kyoto:Maruzen, 1928, pp 111-24.
11. Kameyama M, Okinaka SH. Collateral circulation of the brain with special reference to atherosclerosis of the major cervical and cerebral arteries. Neurology 1963;13:279-86.
12. Kleiss E. Die verschiedenen Formen des Circulus arteriosus cerebralis Willisii. Anatomischer Anzeiger 1942;92:216-30.
13. McCormick WF. Vascular disorders of nervous tissue: Anomalies malformations and aneurysms. In: Structure and Function of Nervous Tissue. New York: Academic Press, 1969, pp 537-96.
14. Mitterwallner, FV. Variationsstatistischen Untersuchungen an den basalen Hirngefassen. Acta Anatomica 1955;24:51-88.
15. Padget DH. The circle of Willis. It's embryology and anatomy. In: Intracranial Arterial Aneurysms. New York: Comstock Publishing Co, 1947, pp 67-90.
16. Padget DH. The development of cranial arteries in the human embryo. In: Contributions to embryology. Washington: Technical Press, 1948, pp 205-61.
17. Tulleken CA, Luiten ML, The basilar artery bifurcation: Microscopical anatomy. Acta Neurochir 1987;85:50-5.
18. Zeal AA, Rhoton AL Jr. Microsurgical anatomy of the posterior cerebral artery. J Neurosurg 1978;48:534-59.
19. Carson FL, Hladik C. Histotechnology: A Self-Instructional Text. Chicago: ASCP Press, 1990, pp 147-49.
20. Vasović LP. The tenth vascular component in a rare form of the cerebral arterial circle of fetuses. Cells Tissues Organs 2004;178:231-8.
21. Guerin J, Gouazé A, Lazorthes G. Le polygone de Willis de l'enfant et les facteurs de son modelage. Neurochirurgie 1976;22:217-26.
22. Milenković Z, Vuèetić R, Puzić M. Asymmetry and anomalies of the circle of Willis in fetal brain. Microsurgical study and functional remarks. Surg Neurol 1985;24:563-70.
23. Gartner LP, Hiatt JL. Color Text Book Of Histology. 2nd Ed. Saunders, 2001, pp 239.
24. Alpers BJ, Berry RG, Paddison RM. Anatomical studies of the circle of Willis in normal brain. AMA Arch Neurol Psychiatry 1959;81:409-18.
25. Kamath S. Observations on the length and diameter of vessels forming the circle of Willis. J Anat 1981;133:419-23.

Acknowledgments.—The authors are grateful to the decedents and their families who through their generous donations made this study possible. We are also recognizing the expert skills of Ms. Angie Hayward HTCM for her expert preparation of tissues in this study.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Article first published online: March 18, 2014. - Manuscript accepted: March 13, 2014. - Manuscript revised: February 26, 2014. - Manuscript received: December 9, 2013.