Angiographic analysis of the variation of arterial collaterals in moyamoya and atherosclerosis at a tertiary care center in Saudi Arabia

Ayesha Nuzhat, MD, MHPE, *Asma Al Akeel,* MD, *Maha Al Husain,* MD, SBRAD.

ABSTRACT

الأهداف: تقييم الاختلاف التشريحي لشرايين الأوعية الدموية الجانبية وانتشارها في مويامويا وتصلب الشرايين.

المنهجية: جمعت البيانات بأثر رجعي من قاعدة بيانات المرضى (العدد n=46) الذين خضعوا لتصوير الأوعية الدموية بالطرح الرقمي خلال الفترة من يناير 2010م إلى ديسمبر 2018م في قسم الأشعة ، مدينة الملك فهد الطبية، الرياض، المملكة العربية السعودية بعد موافقة مجلس المراجعة المؤسسية. حصلنا على المعلومات الديموغرافية والبيانات السريرية للمرضى مثل العمر والجنس والمسببات والعرض السريري والتدرج الوعائي باستخدام درجات سوزوكي لحالات مويامويا، والاختلاف التشريحي لشرايين الأوعية الدموية الجانبية وانتشارها وعلاجها ومتابعتها.

النتائج: وجدنا أربعة أنواع لشبكة الأوعية الدموية الجانبية لتصلب الشرايين (العدد=21) والمويامويا (العدد= 25) ؛ السّحايا الرَقيقَة، القشرية المخية، تحت العصبية، الشبكات البينية والداخلية. وقد لوحظ عدد كبير للأوعية الدموية الجانبية في المويامويا (534) من تصلب الشرايين (40). كانت الشبكة 37.1% (198 Leptomeningeal) والشبكة تحت العصبية 170 (31.8%) أكبر من قشرة المخ والأعصاب الداخلية وداخل القحف أو داخل المريء في مرضى المويامويا. في حين كانت الشبكة 25 (62.5%) والداخلية بين الأعصاب أو داخل المهاد7 (17.5%) هي السائدة في تصلب الشرايين. من بين 25 حالة مويامويا، لوحظ تصنيف سوزوكي الخامس في 5 (20%) و الرابع في 13 (52%).

الخاتمة: فهم الديناميات التي تطورت في تطور الأوعية الدموية الجانبية وبالتالي يمكن تحسين الإدارة والتشخيص.

Objectives: To evaluate the anatomical variation of arterial collaterals and their prevalence in moyamoya and atherosclerosis.

Methods: Data was collected retrospectively from patients (n=46) database who underwent digital subtraction angiography between January 2010 and December 2018 at the Radiology Department, King Fahad Medical City, Riyadh, Saudi Arabia. Demographic details and clinical data of the patients such as age, gender, etiology, clinical presentation, angiographic staging using Suzuki grading for moyamoya cases, variation of arterial collaterals, and their prevalence, treatment and follow up were obtained.

Results: Four types of collaterals network were observed in atherosclerosis (n=21) and moyamoya (n=25); the leptomeningeal, durocortical, subependymal, inner-interstriatal and intrathalamic networks. More number of collaterals were observed in the moyamoya (n=534) than atherosclerosis (n=40). Leptomeningeal network (n=198, 37.1%) and subependymal network (n=170, 31.8%) were greater than durocortical and inner-interstriatal or intrathalamic in patients with moyamoya. Whereas leptomeningeal network (n=25, 62.5%) and inner-interstriatal or intrathalamic (n=7, 17.5%) were predominant in atherosclerosis. Out of 25 cases of moyamoya, Suzuki grading V was noted in 5 (20%) and grade IV in 13 (52%).

Conclusion: Understanding the dynamics that have evolved in the development of the collaterals and therefore can improve both management and prognosis.

Keywords: moyamoya, atherosclerosis, arterial collaterals, digital subtraction angiography

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From the Department of Basic Medical Sciences, Faculty of Medicine (Nuzhat), from the Department of Radiology (Al Akeel), King Fahad Medical City; and from the Department of Radiology (Husain), Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Maha Alhusain, Medical Imaging and Radiodiagnosis, Department of Radiology, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia. E-mail: maha.alhusain@gmail.com
ORCID ID: https://orcid.org/0000-0002-2282-5439

Moyamoya is characterized by an advancing stenosis or occlusion of the terminal part of the internal carotid arteries or proximal part of the anterior and middle cerebral arteries, associated with development of intracranial arterial collaterals. The clinical presentation differs between the pediatric and adult populations, with 2 peaks of incidence at approximately 10 years and 30-40 years. The peak incidence occurs far ahead in females than in males. Adult patients mostly present with intracranial hemorrhages and ischemia, whereas transient ischemic attacks, intellectual decline, seizures and involuntary movements are more common in pediatric population in addition to brain infarctions.[1] The development of new blood collaterals is crucial for perfusion of the brain and to avert cerebral ischemia.[2] With progressive stenosis or occlusion of the main intracranial arteries, arteriogenesis is activated by fluid sheer stress facilitating endothelial monocyte invasion, release of cytokines and growth factors, proliferation of smooth muscle cells and a surge in the collaterals flow.[3]

Baltsavias et al[4] in 2015, described 4 types of anastomotic networks in moyamoya. Leptomeningeal and durocortical as the superficial meningeal networks and subependymal and inner- interstriatal networks and the inner thalamic as the deep parenchymal networks. Suzuki and Takaku, listed 6 stages of moyamoya that describes the different patterns of disease progression: Grade I = narrowing of the carotid fork; Grade II = initiation of moyamoya collaterals; Grade III = Partial stenosis of the ACA and MCA with intensification of moyamoya collaterals; Grade IV = advanced steno-occlusive changes in the ICA with small portion of ECA collaterals; Grade V= predominant ECA collaterals with further reductions in ICA collaterals; Grade VI = absence of the ACA and MCA with complete disappearance of ICA moyamoya collaterals.[5] The idiopathic disease is inherently common in East Asian countries such as Japan and Korea and relatively less common in the Middle East and Western countries. *RNF213* is the most common susceptible gene and is often reported with the *p.Arg4810Lys* founder variant in East Asian patients.[6] In Saudi Arabia, moyamoya syndrome constitutes a major risk for stroke in children reflecting commonly an underlying hematological disorder like sickle cell disease.[7] Intracranial atherosclerosis is an important etiology for ischemic stroke that contributes to collaterals formation, where well-developed collaterals precludes the severity of cerebral ischemia and represents a prognostic role in moderate and severe stenosis.

In the present study, we intend to evaluate the anatomical variation of arterial collaterals and their prevalence in moyamoya and atherosclerosis utilizing cerebral angiographic imaging.

Methods. Approval was obtained from the Institutional Review Board in King Fahad Medical City (KFMD) (IRB No-18-466). The study was carried out according to the principles of the Helsinki Declaration.

We retrospectively analyzed the collected data of patients (n=46) who underwent digital subtraction angiography between January 2010 and December 2018 at the Radiology Department, KFMC, Riyadh, Saudi Arabia. Only patients whose pretreatment DSA examinations were of sufficient quality were included in this study. Patients with vascular malformations, dissection, vasculitis and also vascular tumors were excluded.

The diagnosis of moyamoya were adapted based on the diagnostic criteria approved by the Japanese Ministry of Health and Welfare.[8]

The demographic and clinical data for these patients were detailed; including the age, gender, etiology, clinical presentation, variation of arterial collaterals and their prevalence, treatment, and follow up. Angiographic Suzuki staging[5] was determined for moyamoya cases. The vascular connections were classified according to the collaterals network namely; the leptomeningeal, durocortical, subependymal, inner-interastriatal or intrathalamic, and their detailed connections were noted.[3]

Data were entered into Excel sheet and analyzed using the Statistical Package for Social Sciences for Windows, version 22, (Armonk, NY: IBM Corp.). Descriptive statistics were calculated for demographic data as well as the collaterals networks and the detailed anatomical connections.

Results. We outlined the collateral patterns of atherosclerosis (n=21) and moyamoya patients (n=25). Females were more commonly affected than males in both groups.

Tables 1 & 2 depict demographic and clinical data and the collateral networks in the atherosclerosis patients.

Tables 3 & 4 depict demographic and clinical data and collateral networks in the moyamoya patients.

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Figures 1-4 cerebral angiographic images demonstrate examples of different collateral networks and arterial variance in moyamoya patients.

Table 1 - Demographic and clinical data of patients with atherosclerosis (N=21).

Demographic characteristics	n (%)
Gender	
Females	11 (52.0)
Males	10 (48.0)
Average age (years)	55
Min age	28
Max age	79
Infarct localization	
Multiple anterior circulation territories	3 (14.3)
MCA territory	18 (85.7)
Network of vessels observed (n=40)	
Leptomeningeal	25 (62.5)
Durocortical	2 (5.0)
Subependymal	6 (15.0)
Inner interstriatal, intrathalamic	7 (17.5)
Hemispheres (n=40)	
Right	27 (67.5)
Lateral	13 (32.5)

MCA - middle cerebral artery

Table 3 - Demographic and clinical data of patients with moyamoya (N=25).

Demographic characteristics	n (%)
Gender	
Females	19 (76.0)
Males	6 (24.0)
Average age (years)	21
Min age	3
Max age	48
Infarct localization	
Multiple anterior circulation territories	8 (32.0)
MCA territory	3 (12.0)
Not applicable	14 (56.0)
Network of vessels observed (n=40)	
Leptomeningeal	198 (37.1)
Durocortical	84 (15.7)
Subependymal	170 (31.8)
Inner interstriatal, intrathalamic	84 (15.7)
Hemispheres (n=40)	
Right	287 (53.7)
Lateral	247 (46.3)
Suzuki grading for moyamoya patients	
II	2 (8.0)
III	5 (20.0)
IV	13 (52.0)
V	5 (20.0)

MCA - middle cerebral artery

Table 2 - Vascular connections tabulated according to collateral networks in atherosclerosis.

Network	Identified vessel	Course	Recipient vessel	n (%)
Leptomeningeal	Splenial artery	Retrosplenial	Pericallosal arteries	2 (5.0)
Leptomeningeal	Parietoccipital artery	Medial and convexialparietoccipital surface	ACA distal cortical branches	2 (5.0)
Leptomeningeal	Temporal branches of PCA	Inferior temporal surface	MCA distal cortical branches	7 (17.5)
Leptomeningeal	Pcom perforators	Mesial temporal surface	Anterior choroidal artery	5 (12.5)
Leptomeningeal	Anterior choroidal artery	Choroidal segment	Temporal MCA branches	5 (12.5)
Leptomeningeal	Ophthalmic artery	Along optic nerve, perichiasmatic	Orbitofrontal and frontopolar branches of ACA	4 (10.0)
Durocortical	Anterior ethmoidal artery, posterior ethmoidal artery	Anterior falx cerberi	Orbitofrontal and frontopolar branches of ACA	1 (2.5)
Durocortical	MMA	Durocortical connection	MCA, ACA cortical branches	1 (2.5)
Subependymal	Pcom perforators	Subependymal	Medullary arteries	2 (5.0)
Subependymal	Thalamoperforators	Subependymal	Medial striate, lateral striate	2 (5.0)
Subependymal	Posterior choroidal	Choroid plexus	Pericallosal arteries	2 (5.0)
Inner interstriatal	Medial striate artery	Endostriatal network	Lateral striate	5 (12.5)
Intrathalamic	Thalamoperforators	Intrathalamic network	Adjacent thalamic territories	2 (5.0)

PCA - posterior cerebral artery, MMA - middle meningeal artery, ACA - anterior cerebral artery, MCA - middle cerebral artery

Table 4 - Vascular connections tabulated according to collateral networks in Moyamoyagroup.

Network	Identified vessel	Course	Recipient vessel	n (%)
Leptomeningeal	Splenial artery	Retrosplenial	Pericallosal arteries	33 (6.2)
Leptomeningeal	Parietoccipital artery	Medial and convexialparietoccipital surface	ACA distal cortical branches	27 (5.1)
Leptomeningeal	Temporal branches of PCA	Inferior temporal surface	MCA distal cortical branches	15 (2.8)
Leptomeningeal	Pcom perforators	Mesial temporal surface	Anterior choroidal artery	11 (2.1)
Leptomeningeal	Anterior choroidal artery	Choroidal segment	Temporal MCA branches	34 (6.4)
Leptomeningeal	Superior/ inferior hypophyseal artery	Circuminfundibular plexus	ACA at A1 or Acom level	27 (5.1)
Leptomeningeal	Inferior hypophyseal artery	Circuminfundibular plexus	ACA at A1 or Acom level	27 (5.1)
Leptomeningeal	Ophthalmic artery	Along optic nerve, perichiasmatic	Orbitofrontal and frontopolar branches of ACA	25 (4.7)
Durocortical	Anterior ethmoidal artery, Posterior ethmoidal artery	Anterior falx cerberi	Orbitofrontal and frontopolar branches of ACA	9 (1.7)
Durocortical	MMA	Durocortical connection	MCA, ACA cortical branches	25 (4.7)
Durocortical	Occipital artery	Mastoid artery	MCA, ACA cortical branches	13 (2.4)
Durocortical	STA	Durocortical connection	Orbitofrontal and frontopolar branches of ACA	21 (3.9)
Durocortical	PCA, SCA - dural branches	Durocortical connection	Cortical branches	6 (1.1)
Durocortical	Posterior meningeal artery	Durocortical connection	Occipital, temporal Cortical branches	10 (1.9)
Subependymal	Anterior choroidal artery	Ventricular branches	Medial striate, lateral striate	12 (2.2)
Subependymal	Anterior choroidal artery	Ventricular branches	Medullary arteries	13 (2.4)
Subependymal	Anterior choroidal artery	Ventricular branches	Insular branches of M2	15 (2.8)
Subependymal	Pcom perforators	Subependymal	Medullary arteries	9 (1.7)
Subependymal	Thalamoperforators	Subependymal	Medial striate, lateral striate	32 (6.0)
Subependymal	Thalamoperforators	Subependymal	Medullary arteries	34 (6.4)
Subependymal	Posterior choroidal	Choroid plexus	Pericallosal arteries	27 (5.1)
Subependymal	Posterior choroidal	Choroid plexus	Medial striate, lateral striate	27 (5.1)
Inner interstriatal	Medial striate artery	Endostriatal network	Lateral striate	45 (8.4)
Intrathalamic	Thalamoperforators	Intrathalamic network	Adjacent thalamic territories	37 (6.9)

STA - superficial temporal artery, PCA - posterior cerebral artery, MMA - middle meningeal artery, ACA - anterior cerebral artery, MCA - middle cerebral artery

Different types of collaterals networks were observed in the atherosclerosis (n=21) and moyamoya (n=25). More number of collaterals were observed in the moyamoya (n=534) than in atherosclerosis (n=40). More leptomeningeal (n=198, 37.1%) and subependymal networks (n=170, 31.8%) were observed than the durocortical and inner-interstriatal or intrathalamic networks in moyamoya, whereas leptomeningeal (n=25, 62.5%), and inner-inter striatal or intrathalamic (n=7, 17.5%) networks were predominant in patients with atherosclerosis. The right cerebral hemisphere was more commonly affected in both groups, but infarct localization in the MCA territory was greater in atherosclerosis compared to the multiple anterior circulation territories in moyamoya.

The disease showed interval progression in the majority moyamoya patients on follow up angiographic studies, whereas most atherosclerosis patients improved after either thrombolysis or angioplasty.

Discussion. More number of moyamoya patients are currently being recognized due to advances in medical imaging. This includes factors for predicting disease severity, impending hemorrhages, clinical outcomes and

potential complications through magnetic resonance angiography or conventional cerebral angiography.[9]

Peicong et al[10] in 2017 reported that infarction was very common in elderly (40.2%), many patients presented with Suzuki stage 4 or 5 (51.2%), posterior cerebral artery was involved in 22 (25.3%) and post-operative infarction or hemorrhages was 6.9%.[10] In our study, the majority of patients were referred for stroke workup in patients with atherosclerosis (n=21) and moyamoya (n=25). A greater number of collaterals were observed in the moyamoya group (n=534) than in the atherosclerosis group (n=40). The leptomeningeal network (n=198, 37.1%) and the subependymal network (n=170, 31.8%) were more predominant than

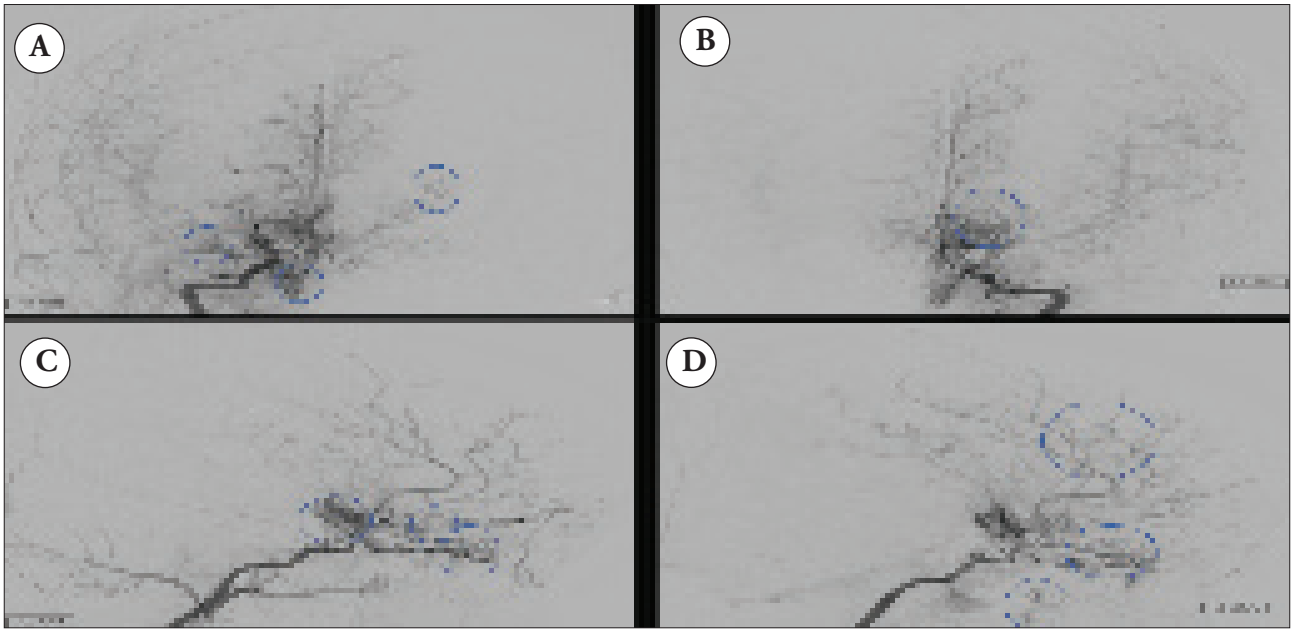

Figure 1 - Digital subtraction angiogram showing the **A & B)** frontal and **C & D)** lateral projection of after selecting the internal carotid arteries. Moyamoya collaterals originating from the lenticulostriate, anterior choroidal, hypophyseal ophthalmic and ethmoidal arteries.

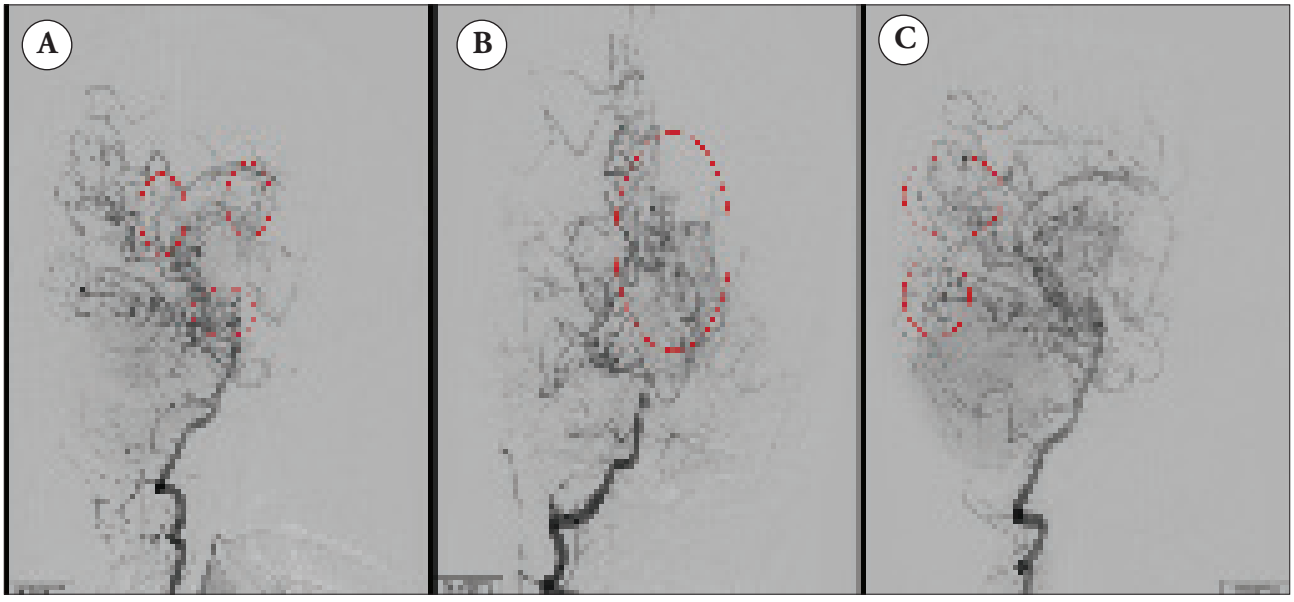

Figure 2 - Digital subtraction angiogram after selecting the **A & B)** right and **C & D)** left vertebral arteries. Moyamoya collaterals originating from the posterior communicating perforators, thalamoperforators, posterior choroidal, splenial, temporal and parieto-occipital branches.

the durocortical and inner-interstriatal or intra thalamic network in patients with moyamoya, whereas the leptomeningeal network (n=25, 62.5%) and the inner-interstriatal or intrathalamic (n=7, 17.5%) networks were more frequent in patients with atherosclerosis. Out of the 25 patients with moyamoya, Suzuki grade V was noted in 5 patients (20%), and grade IV was noted in 13 (52%) patients.

In our study, infarct localization was greater in the MCA territory in the atherosclerosis group, compared to the multiple anterior circulation territories in the moyamoya group. Although posterior circulation stroke

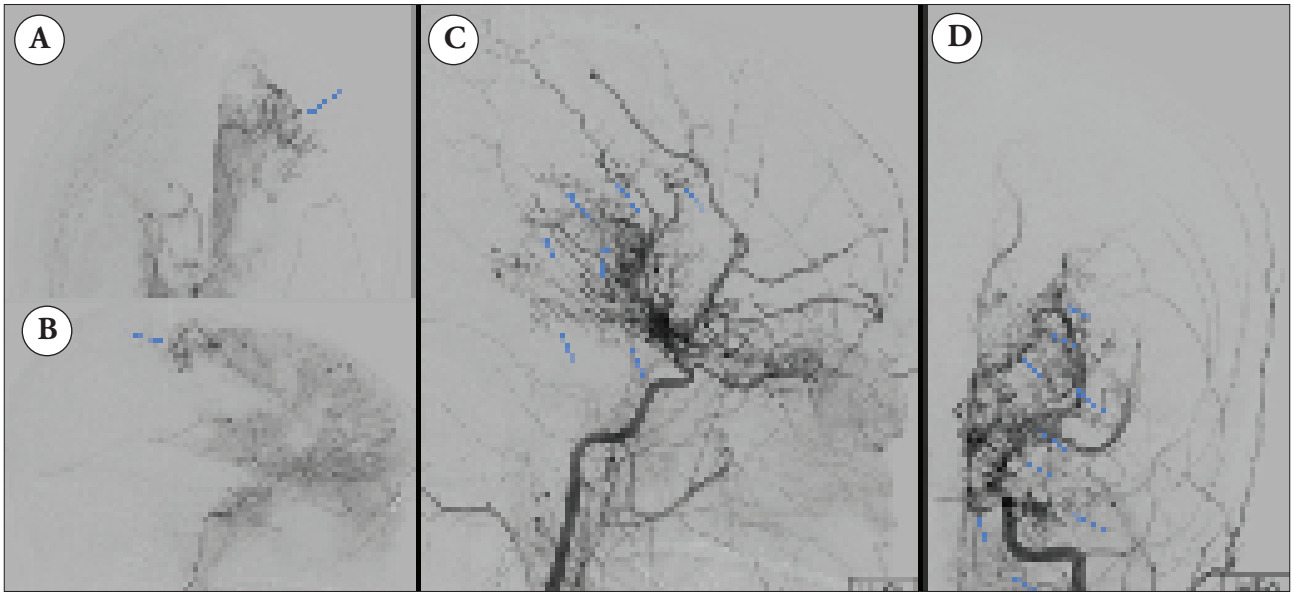

Figure 3 - Digital subtraction angiogram of the **A & B)** right internal carotid artery. The durocortical collaterals at the right parietal lobe communicating with distal anterior cerebral artery. Selective catheterization of the **C & D)** left internal carotid artery; extensive collaterals from anterior choroidal, hypophyseal, ophthalmic, ethmoidal, posterior communicating and posterior choroidal arteries. The durocortical collaterals from superficial temporal and middle meningeal arteries supplying the cortical branches of anterior and middle cerebral arteries.

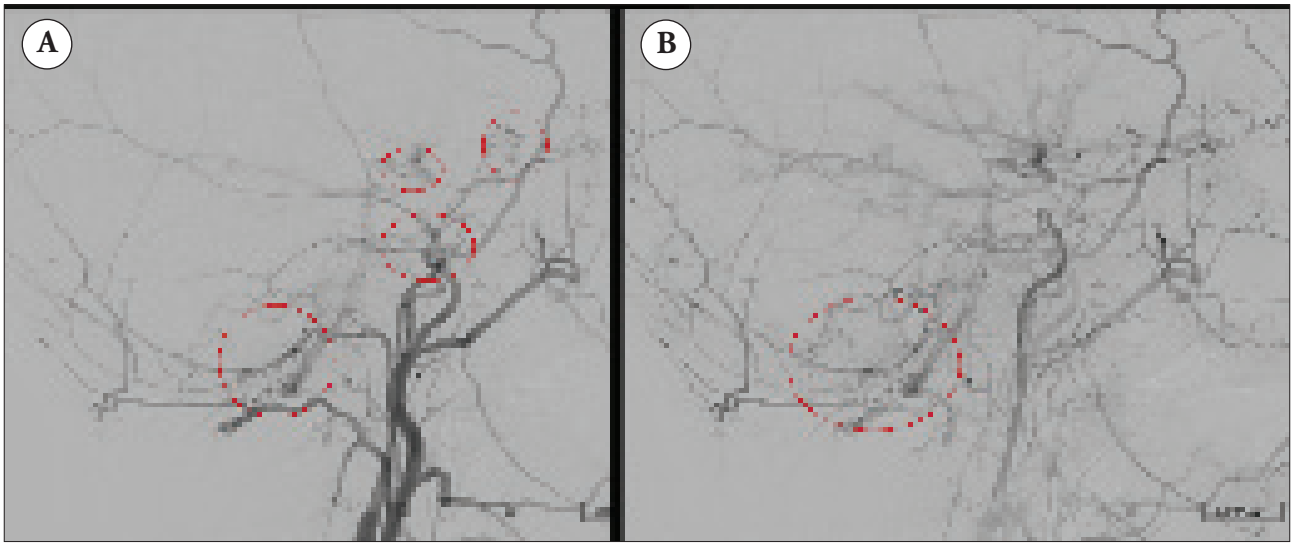

Figure 4 - Digital subtraction angiogram after selecting the left common carotid artery. **A)** The durocortical collaterals from the superficial temporal, middle meningeal and occipital arteries. **B)** The occipital artery collaterals are seen over crossing the mastoid process.

is uncommon, PCA involvement is an independent important risk factor as the leptomeningeal collateral from PCA is a significant blood flow source of collaterals.[11]

In a study conducted by Robert et al,[12] duro-pial collaterals from branches of the ECA to the territory of the ACA were observed in 5 hemispheres (6.8%) and perivascular collaterals were observed in 47 hemispheres (63.5%). Ophthalmic artery collaterals were noted in 35 patients (47.3%) and were most frequent in patients with Suzuki grades III-V.[12] In our study, the ophthalmic artery was involved in 10% (4 hemispheres) of patients in the atherosclerosis group and 4.7% (25 hemispheres) of patients in the moyamoya group.

According to Liebeskand et al,[13] collaterals circulation in atherosclerosis was satisfactorily available for analysis in 287/569 (50%) individuals with proximal arterial stenosis ranging from 50% to 99%. The extent of collateral flow correlated with the percentage of stenosis (p<0.0001), with more severe stenosis exhibiting greater compensation via collaterals. The collateral grade increased with diminished antegrade flow across the lesion (thrombolysis in myocardial ischemia) and the resultant downstream perfusion (thrombolysis in cerebral infarction) (both p<0.001). Collaterals are valuable in compensating for arterial obstruction and also serve as a marker of underlying illness. Patients with profound dynamic collaterals have smaller infarcts.[13]

The majority of patients in our study showed interval progression in the moyamoya group upon follow-up angiographic studies, whereas the atherosclerosis patients improved after thrombolysis and angioplasty. This difference is likely due to the progressive nature of moyamoya.

Study limitation. Our study is a retrospective study based on sequential conventional angiography.

The existence, timing/appearance of collateral circulation development can be observed in future prospective studies in order to prevent ischemia; also useful in planning the revascularization surgery.

In conclusion, identification of the prevalence of variant arterial collaterals in moyamoya and atherosclerosis is very useful in understanding the dynamics that have evolved in the development of the collaterals and therefore can improve both management and prognosis.

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References

1. Kim JS. Moyamoya Disease: Epidemiology, Clinical Features, and Diagnosis. *J Stroke* 2016; 18: 2-11.
2. Zhao M, Zhang D, Wang S, Zhang Y, Deng X, Zhao J. The collateral circulation in moyamoya disease: A Single-center experience in 140 pediatric patients. *Pediatr Neurol* 2017; 77: 78-83.
3. Nishijima Y, Akamatsu Y, Weinstwin PR, Liu J. Collaterals; Implications in Cerebral ischaemic diseases and Therapeutic Interventions. *Brain Research* 2015; 1623: 18-29.
4. Baltsavias G, Khan N, Valavanis A. The collateral circulation in pediatric moyamoya disease. *Childs Nerv Syst* 2015; 31: 389-398.
5. Suzuki J, Takaku A. Cerebrovascular Moyamoya Disease. Disease showing abnormal net like vessels in base of Brain. *Arch Neuro* 1969; 20: 288-299.
6. Akagawa H, Mukawa M, Nariai T, Nomura S, Aihara Y, Onda H, et al. Novel and recurrent RNF213 variants in Japanese pediatric patients with moyamoya disease. *Hum Genome Var* 2018; 5: 17060.
7. Al-Hawsawi ZM, Al-Zaid MA, Barnawi AI, Yassine SM. Fanconi anemia associated with moyamoya disease in Saudi Arabia. *Saudi Med J* 2015; 36: 233-235.
8. Fujimura M, Tominaga T. Diagnosis of moyamoya disease: international standard and regional differences. *Neurol Med Chir (Tokyo)* 2015; 55: 189-193.
9. Kim JE, Jeon JS. An update on the diagnosis and treatment of adult Moyamoya disease taking into consideration controversial issues. *Neurol Res* 2014; 36: 407-416.
10. Ge P, Zhang Q, Ye X, Liu X, Deng X, Wang R, et al. Clinical features, surgical treatment, and long-term outcome in elderly patients with moyamoya disease. *World Neurosurg* 2017; 100: 459-466.
11. Park W, Ahn JS, Lee HS, Park JC, Kwun BD. Risk factors for newly developed cerebral infarction after surgical revascularization for adults with moyamoya disease. *World Neurosurg* 2016; 92: 65-73.
12. Robert T, Cicciò G, Sylvestre P, Chiappini A, Weil AG, Smajda S, et al. Anatomic and Angiographic Analyses of Ophthalmic Artery Collaterals in Moyamoya Disease. *AJNR Am J Neuroradiol* 2018; 39: 1121-1126.
13. Liebeskind DS, Cotsonis GA, Saver JL, Lynn MJ, Cloft HJ, Chimowitz MI, et al. Collateral circulation in symptomatic intracranial atherosclerosis. *J Cereb Blood Flow Metab* 2011; 31: 1293-1301.