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Morphometry of the Middle Cerebral Arteries: A Radio-Anatomical Study Based on Computed Tomography Angiography Findings

Morfometría de las Arterias Cerebrales Medias: Un Estudio Anátomo-Radiológico Basado en los Hallazgos de la Angiografía por Tomografía Computada

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SUMMARY: Middle cerebral artery (MCA), which has the largest irrigation area of the arteries that feed the brain, is an important artery whose microanatomy should be well known because of its vascular variation. In pathologies which are known to affect the cerebrovascular system such as type 2 diabetes mellitus (T2DM) and hypertension, morphometric characteristics of MCA gain importance. The aim of this study is to compare the morphometric characteristics of M1 segment of MCA in T2DM and hypertensive patients with those of healthy control group by using computed tomographic angiography (CTA). The study was carried out with retrospective morphometric analysis of CTA images of 200 individuals between 40 and 65 years of age. The individuals were grouped in four as hypertensive patients (group 1), patients with T2DM (group 2), patients with hypertension and T2DM (group 3) and healthy control group (group 4). Length and diameter measurements of M1 segment were performed and recorded by using 3D CTA images. While statistically significant difference was found between bilateral M1 segment diameters of both women and men ($p<0.05$), no statistically significant difference was found between segment lengths ($p>0.05$). As a result of the post hoc analysis performed, it was concluded that right and left M1 segment diameter of group 1, group 2 and group 3 was found to be different from group 4 in both sexes ($p<0.05$). We believe that this study will both be a guide in radio-anatomic assessments to be performed and also increase microanatomic level of information in the surgical treatment of the artery by showing the morphometric changes that occur in M1 segment of MCA in T2DM diseases.

KEY WORDS: Middle cerebral artery; Computed tomographic angiography; Type 2 Diabetes Mellitus; Hypertension.

INTRODUCTION

Middle cerebral artery (MCA), which is the thickest branch of internal carotid artery (ICA), is also an important artery associated with 20-43 % of all intracranial haemorrhages. While an occlusion in MCA is known to be the most common cause of ischemic stroke, the blockage of M1 segment of MCA may cause severe damage to the brain, and even death (Shi *et al*., 2010). It is reported that 86.2 % of MCA's aneurisms occur in M1 segment of the artery (Brzegowy *et al*., 2018).

Although MCA infarction isn't a rare condition, it is seen only in 0.9 % of acute stroke disease (Akiyama *et al*., 2001). However, studies have reported that when the irrigation area of MCA is considered, 30-66 % probability of death is reported (Hacke *et al*., 1996; Gurol & St Louis, 2008). In the case of a malignant MCA, this rate can go up to 80 % (Vahedi *et al*., 2007).

MCA, which has the largest irrigation area of the three main arteries known to feed the brain, is also the continuation of ICA in terms of calibration and course. The fact that it supplies blood to a large part of the brain, including a part of the frontal lobe and the lateral surface of the temporal and parietal lobes, causes serious clinical pictures in aneurysm

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(Shi *et al*., 2010). Good micro-anatomical knowledge is required to be successful in the surgical treatment of the pathologies of this artery, which has a large irrigation area. The most important reason for this is the fact that MCA is the structure with the most vascular variation among cerebral arteries. Surgeons' knowing these vascular variations well can provide benefits such as correcting ischemia resulting from stroke, restoring perfusion and saving the patient from neurological deficits by minimizing ischemic brain damage (Gurol & St Louis, 2008; Shi *et al*., 2010). Although there are many branching, variation, anomaly and duplication studies on MCA in the literature, the fact that chronic diseases of participants have been ignored in these studies draws attention as an important deficiency. This situation limits learning the effects of chronic diseases on MCA in literature. A great majority of the studies conducted are radiological studies in addition to cadaveric and experimental studies (Akiyama *et al*., 2001; Vahedi *et al*., 2007; Kahilogullari *et al*., 2012; Ciftci *et al*., 2022). Today, due to its advantage of being a non-invasive method, computed tomographic angiography (CTA) is an up-to-date tool used in endovascular treatments and intracranial assessment. CTA is advantageous compared to cadaver based anatomical studies in terms of creating a larger data base and allowing more precise measurements (Brzegowy *et al*., 2018). Hypertension, which is known as a major risk factor for stroke, has been reported to cause cerebrovascular changes, arterial wall thickening and endothelial damage. These changes trigger or accelerate atherosclerosis formation by changing cerebral blood flow (Chobanian, 1992; Faraco & Iadecola, 2013). It is reported that there are frequent diabetic cerebrovascular disorders in the chronic period of type 2 diabetes mellitus (T2DM), which is a common heterogeneous metabolic associated with chronic complications such as nephropathy, angiopathy, retinopathy and peripheral neuropathy. Nutrition of the brain is also affected by recurrent hypoglycaemia attacks and poor metabolic control (American Diabetes Association, 2006).

Pathologies such as T2DM and hypertension are important pathologies which increase the tension of the vascular wall and consequently predispose to stroke (Dolan *et al*., 2013; Chi & Lu, 2017). In the literature review conducted, no studies were found evaluating the MCA morphology of T2DM and hypertensive patients. This study aims to compare the morphometric characteristics of M1 segment of MCA in patients with T2DM and hypertension by using CTA images.

MATERIAL AND METHOD

Patient Population. The study protocol was approved by of the Local Clinical Research Ethics Committee (2020/1377). The study was conducted between 2014 and 2020 by performing retrospective morphometric analyses of CTA images of 200 individuals aged between 40 and 65 who referred to the University Faculty of Medicine Radiology Department. Axial, sagittal and coronal sections were used in the measurements taken from CTA. Images of the participants who had aneurysm in brain arteries, those who had temporary ischemic attack, embolism, endovascular treatment history, those who were using cigarette or alcohol, those who had hyperlipidemia, those younger than 40 and older than 65, those who had a diagnosis of hypertension and T2DM for less than 5 years and more than 10 years were excluded from the study. Images with artefact were not included in the study. The individuals included in the study were grouped in four;

Group 1: Hypertensive patients (n=45)
Group 2: Patients with T2DM (n=45)
Group 3: Patients with T2DM and hypertension (n=45)
Group 4: Healthy control group (Individuals who met the inclusion criteria, who did not have a diagnosis of T2DM or hypertension), (n=65)

Imaging method: Images were obtained from Somatom Definition Flash, Simens Healthcare, Forchheim, Germany double source spiral CTA. The device was 256 section multislice CT. Its dose is 120 kv 35 mA. Section thickness of the device is 0,6 mm, and the amount of contrast material is 100 ml. For CTA scanning, parameters were adjusted as 120 kv for tube voltage for Simens, 200 mA for tube voltage, 64¥0.6 mm for collimation, 500 ms for gantry turnaround time, 0.6 mm for section thickness.

The patient was laid on the table in supine position with the head in the front and the arms on the sides. The scanning area was set from vertex to mentum. A single section was placed on the reference image from the 'region of interest' design to aorta by using the 'Bolus tracking' method and the threshold was adjusted as 100 HU to start imaging. 80-100 ml low osmolarity non-ionic contrast material was injected to the median cubital vein with an automatic pump with an injection rate of 4-5 mL/sec and following the contrast material, 40 ml physiological saline solution was injected for homogeneous distribution.

MCA has 4 main segments:

M1 (sphenoidal) segment: It is parallel to sphenoid canal, it has a posterior course.
M2 (insular) segment: It progresses in insula.
M3 (opercular) segment: It progresses over frontal, parietal and temporal opercula.

M4 (cortical) segment: It progresses in lateral fissure and spreads to the cortex in the lateral side of frontal, parietal and temporal lobes. MCA has central (perforating) and cortical branches throughout the course mentioned above (Brzegowy *et al*., 2018).

The following parameters were measured bilaterally by performing vascular analysis and using 3D images so that vascular residue does not affect measurement:

1. Length of M1 measured bilaterally from the internal carotid artery division to the M1 bifurcation,
2. Diameter of M1 in the middle section of the artery. Figure 1 shows measurement parameters.

In the literature, it is stated that the normal limit of the length value of the M1 segment of the MCA is 15-17 mm, while the normal limit of the diameter measurement is 2.4-4.6 mm (Özsoy *et al*., 2007).

Ethical consideration. Malatya Clinical Researches Ethical Board (2020/1377).

Data Analysis. The data were transferred to the screen for radiological analysis. All radiological measurements determined were performed and recorded by a single specialist radiologist. The images taken were started to be evaluated from axial sections. They were then analysed in each of the three planes (axial, sagittal, coronal) by using maximum intensity projection images.

Statistical Analysis. The compliance of data to normal distribution was examined with Kolmogorov Smirnov test and it was found that the data were not normally distributed. For data which were not normally distributed, median and minimum (min) and maximum (max) values were given. Mann Whitney U test was applied to the data to compare the parameters of male and female patients in the same group. Kruskall Wallis H test was applied to the data to compare the parameters of the patients between the groups. Post Hoc Mann Whitney U test and paired comparisons were conducted to find out from which groups the difference between the groups originated from. Post Hoc test was given as Model Viewer table. $p<0.05$ values were considered as statistically significant. IBM SPSS Statistics 22.0 for Windows program was used in statistical analyses.

RESULTS

85 women (42.5 %) and 115 men (57.5 %) were included in the study; mean age of women was found as 57.25±1.1, while mean age of men was found as 59.39±0.7.

In our study, the normal limit of MCA M1 segment length measurement was 23 % on the right and 22 % on the left; The normal limit of the diameter measurement was determined as 79 % on the right and 80 % on the left (Table I).

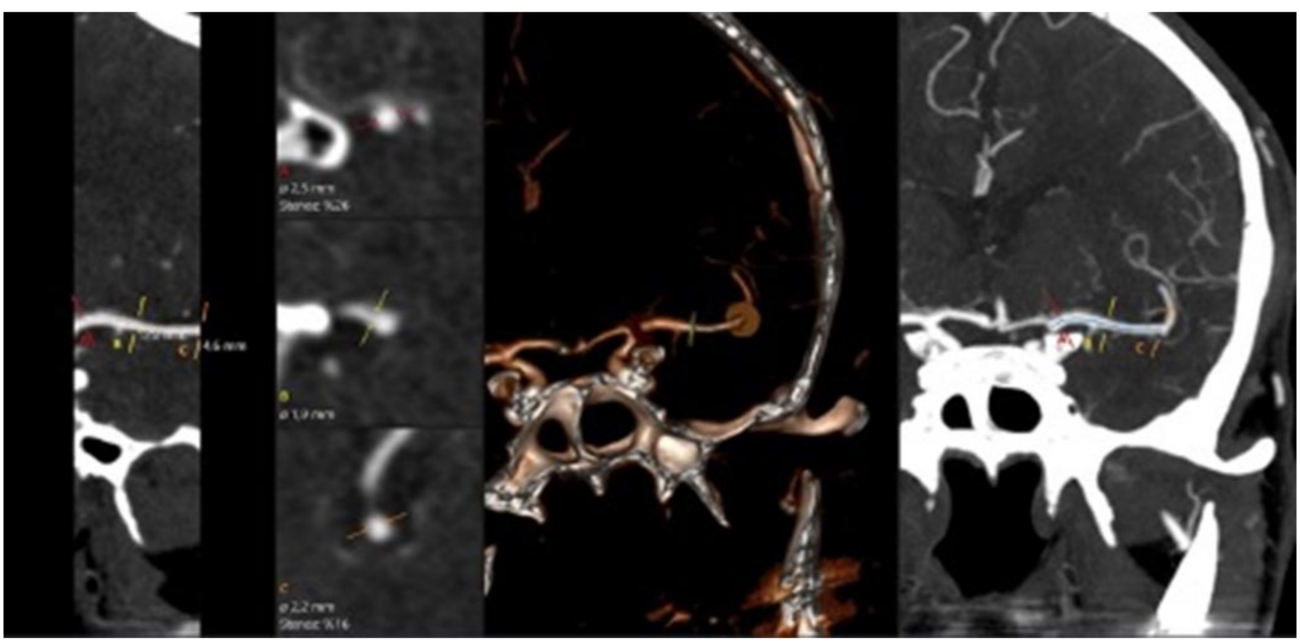

Fig. 1. M1 Segment of MCA (A: Starting point of M1 segment, B: midpoint of M1 C: End of M1 segment).

Table I. Occurrence of the value ranges of the diameter and segment lengths of the M1 segment of the MCA

	Parameters (mm)	Right M1 Segment	Left M1 Segment
LENGTH	<15	%31	%29
	15-17	%23	%22
	>17	%47	%49
D_AMAT ERS	<2,4	%21	%20
	2,4-4,6	%79	%80
	>4,6	-	-

In CTA assessments, M1 segment diameter of right MCA was found to be larger in men when compared with women in Group 4 (p<0.05) (Table II).

According to the results of Kruskal Wallis test used for the M1 segment diameter and segment length measurements of MCA between groups in female and male patients, statistically significant difference was found in bilateral MCA M1 segment diameter measurement in the comparison of female and male patients between the groups (p<0.05), while no statistically significant difference was found in segment length (p>0.05) (Table III).

In parameters which were found to be statistically significant in terms of the result of Kruskal Wallis test, Mann-Whitney U test was conducted as post hoc test to find out which group the difference resulted from. According to the analysis results, difference was found between group 1 and group 2 and group 4 in right MCA M1segment diameter measurements of male patients, while difference was found between group 3 and group 2 and group 4 in left MCA M1segment diameter measurements. In female patients, difference was found between group 3, group 2, group 1 and group 4 in right MCA M1segment diameter measurements and between group 3 and group 2 and group 4 in left MCA M1 segment diameter measurements (p<0.05) (Fig. 2).

Table II. Comparison of M1 segment diameter and segment length measurements of MCA in male and female patients according to groups.

Groups	**Parameters (mm)**	**Female**	**Male**	**p**
		Median (min - max)	Median (min - max)	
Group 1	Right M1 Dia.	2.6 (2-3.2)	2.8 (2-3.2)	0.277
	Left M1 Dia.	2.6 (2.3-7.1)	2.7 (1.9-3.4)	0.548
	Right M1 Len.	15 (2.6-22.6)	16 (11.4- 24.2)	0.208
	Left M1 Len.	15,8 (2.4-23.4)	16.3 (8- 22.7)	0.524
Group 2	Right M1 Dia.	2.4 (2.1-2.9)	2.4 (2- 3.1)	1
	Left M1 Dia.	2.5 (1.9 - 2.7)	2.5 (2.2- 3.1)	0.405
	Right M1 Len.	15.5 (12.2 - 18.6)	16.7 (11.3- 21.9)	0.315
	Left M1 Len.	17.1 (10.1- 24.4)	16.8 (12- 22.5)	0.840
Group 3	Right M1 Dia.	2.4 (1.6- 3.2)	2.5 (2- 3)	0.139
	Left M1 Dia.	2.5 (1.6- 3)	2.5 (1.9- 3.3)	0.086
	Right M1 Len.	14.9 (10.2- 21.2)	15.9 (7.2- 26.4)	0.250
	Left M1 Len.	16.1 (8.7- 18.5)	14.8 (5- 23.4)	0.751
Group 4	Right M1 Dia.	3 (2.5- 3.4)	2.6 (2.2- 3.5)	**0.004***
	Left M1 Dia.	3 (2.5- 3.7)	2.7 (2.4- 3.3)	0.081
	Right M1 Len.	16.9 (7.6- 19.9)	16.8 (12.4- 22.1)	0.524
	Left M1 Len.	16.8 (9.7- 19.4)	17.6 (14.1- 21.1)	0.251

* = Significant differences at the p<0.05 level; M1 Dia. = Arteria cerebri media; M1 Len. = Arteria cerebri media)

Table III. Comparison of M1 segment diameter and segment length measurements of MCA between groups.

	Parameters (mm)	**Group 1**	**Group 2**	**Group 3**	**Group 4**	p
		Median (min-max)	Median (min-max)	Median (min-max)	Median (min.-max)	
Male	Right M1 Dia.	2.8 (2-3.2)	2.4 (2-3.1)	2.5 (2- 3)	2.9 (2.2-3.5)	**<0.001***
	Left M1 Dia.	2.7 (1.9-3.4)	2.5 (2.2-3.1)	2.5 (1.9- 3.3)	2.9 (2.4-3.3)	**0.005***
	Right M1 Len.	16 (11.4-24.2)	16.7 (11.3-21.9)	15.9 (7.2- 26.4)	16.8 (12.4-22.1)	0.407
	Left M1 Len.	16.3 (8-22.7)	16.8(12-22.5)	14.8 (5- 23.4)	17.6 (14.1-21.1)	0.101
Female	Right M1 Dia.	2.6 (2-3.2)	2.4 (2.1-2.9)	2.4 (1.6- 3.2)	3 (2.5-3.4)	**<0.001***
	Left M1 Dia.	2.6 (2.3-7.1)	2.5 (1.9-2.7)	2.5 (1.6- 3)	3 (2.5-3.7)	**<0.001***
	Right M1 Len.	15 (2.6-22,6)	15.5 (12.2-18)	14.9 (10.2- 21)	16.9 (7.6-19.9)	0.537
	Left M1 Len.	15.8 (2.4-23)	17.1 (10.1-24)	15.1 (8.7-18.5)	16.8 (9.7-19.4)	0.539

*: Significant differences at the p<0.05 level; M1 Dia. = Arteria cerebri media diamater; M1 Len. = Arteria cerebri media length.

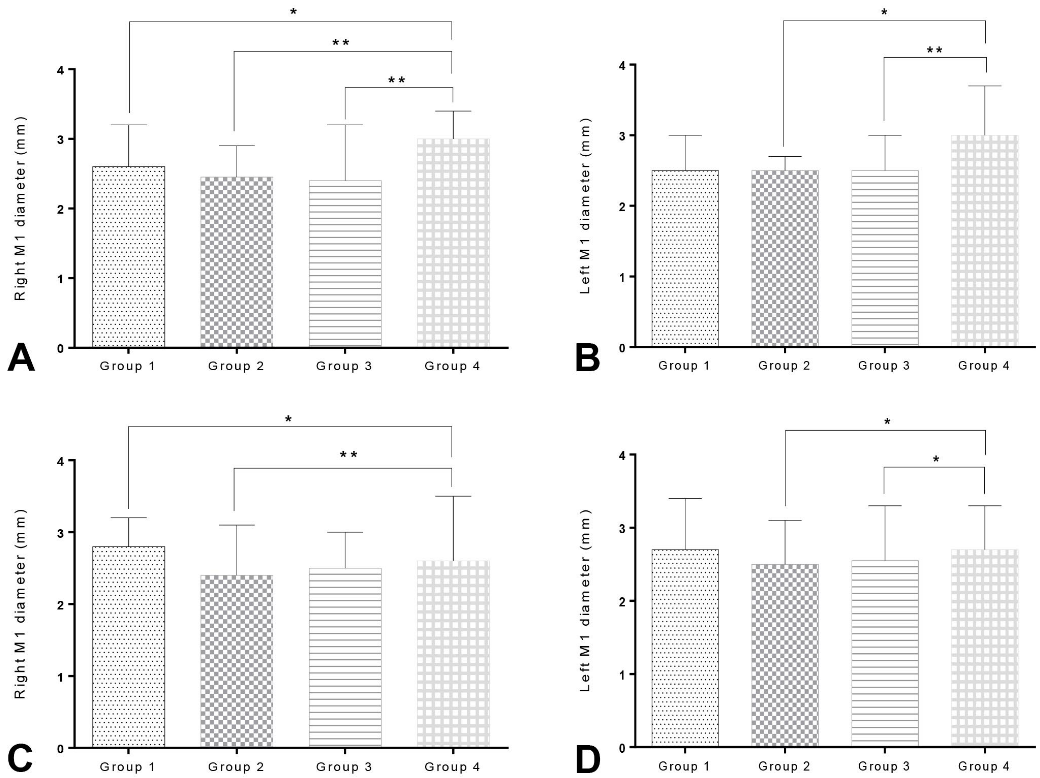

Fig. 2. Post-Hoc test results of vessel diameter in male and female patients (*: Significant differences at the p<0.05 level, **: Significant differences at the p<0.01 level; M1 diameter: right Arteria Cerebri Media; A and B = female patients; C and D = male patients.

DISCUSSION

The aim of this study was to find out whether there were differences between MCA M1segment diameter and length measurements of hypertensive patients (Group 1), T2DM patients (Group 2), patients with hypertension and T2DM (Group 3) and healthy control group (Group 4). In retrospective morphometric assessments between groups on CTA images of individuals, it was found that there were no statistically significant differences between the bilateral M1 segment diameters of both women and men. As a result of the post hoc analysis performed to find out which group the difference resulted from, it was concluded that right and left M1 segment diameters of group 1, group 2 and group 3 were different from those of group 4 in both sexes. Malignant MCA infarct is an important clinical picture of cerebral circulation that causes death in 70-80 % of the cases; moreover, it is associated with long term disability in survivors. Since aneurysms are frequently seen in areas with branching in MCA, it is important to have information about different artery models, especially for aneurysm-related surgeries.

Hypertension causes hypertrophic formation in cerebral veins, leading to an increase in vascular wall volume, an increase in wall thickness and a decrease in vascular lumen. Hypertension may also cause hardening of the large arteries in the brain, leading to cognitive disorders (Faraco & Iadecola, 2013).

Although there are limited number of studies comparing hypertensive and normotensive individuals, increase in lumen diameter and wall-to-lumen ratio in MCA associated with high blood pressure has been reported in hypertensive rat models (Rigsby *et al*., 2007). Another experimental study which reported that chronic hypertension causes vascular remodelling in artery wall during the process also supports this information (Pires *et al*., 2010).

In our study, it was concluded that bilateral M1 diameters of hypertensive patients was statistically narrower than those of the control group. This information supports the literature reviewed. It was concluded that M1 diameter of group 3 was narrower when compared with that of group 4. Although M1 length measurement of group 3 was shorter than the other groups, this difference was not statistically significant. In literature, short M1 segment of MCA is reported as an important condition that increases the risk of aneurysm (Zurada *et al*., 2010).

The International Diabetes Federation estimated that 1 in 11 adults aged 20–79 years (415 million adults) had diabetes mellitus globally in 2015. Over 90 % of diabetes mellitus cases are T2DM (International Diabetes Federation, 2015). Studies which report that the probability of T2DM associated vascular diseases to cause mortality and morbidity was 80 %, T2DM increased the risk of stroke 1.5-3 times and increased short and long term mortality after stroke show the importance of vascular remodelling in T2DM (He *et al*., 2010).

In their study, Tchistiakova *et al*. (2014), used magnetic resonance imaging technique to find out how T2DM and hypertension together affected brain vascularization and concluded that in T2DM and hypertension comorbidity, especially hypertension could increase tendency for cerebrovascular event. Huang *et al*. (2020), reported that when compared with healthy individuals, T2DM patients had higher plaque prevalence, maximum plaque length, maximum wall thickness and maximum lumen stenosis.

Patients with T2DM have increased incidence of atherosclerotic cardiovascular, peripheral arterial and cerebrovascular disease. Comorbidity of hypertension is frequent in patients with T2DM and this can affect cerebrovascular anatomy (Deng *et al*., 2012). It is thought that insufficient hypertensive control accompanying T2DM makes macro and micro vascular complications more severe and vascular and structural anomalies worse. However, it was concluded in our study that there were no statistically significant differences in diameter and segment length of M1 in group 2 and group 3. This result may show that our patients have sufficient hypertension control.

In our study, it was concluded that in addition to having narrower M1 segment diameter than the control group, group 2 and group 3 also had narrower M1 segment diameter than group 1, which consisted of only hypertensive individuals. We believe that this situation is a result of the fact that the damage of T2DM to vascular structures is more severe when compared with hypertension.

Elevated HT rates in both men and women are closely associated with increased obesity rates. Currently, up to 70 % of essential HT cases are associated with T2DM. T2DM affects vascularity in cerebral vessels and causes important conditions such as stroke (Faulkner & Belin de Chantemèle, 2018). In our study, the rate of CVO in the Group 3 group was found to be 32 %.

CONCLUSION

In the literature, morphometric studies on MCA focus on radiological imaging studies in the presence of plaque or symptomatic sclerosis and it can be seen that there is a deficiency in comparing the length and diameter of M1 segment of MCA with healthy control group in conditions such as hypertension and T2DM. Cerebrovascular Event (CVO) rates of the patients were found to be 23 % in Group 1, 27 % in Group 2, and 32 % in Group 3.

As a result of our study, it was concluded that the diameter of M1 segment of MCA was narrower in female and male hypertensive and T2DM patients when compared with healthy control group, while there were no differences in length. We believe that the results found will be a guide while evaluating the changes in MCA in hypertension and T2DM diseases and will increase the level of micro-anatomic information on surgical treatment of this artery.

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RESUMEN: La arteria cerebral media (ACM), que otorga la mayor área de irrigación de las arterias que alimentan el cerebro, es un vaso importante cuya microanatomía debe ser bien conocida por su variación vascular. En patologías que afectan al sistema cerebrovascular, como la diabetes mellitus tipo 2 (DM2) y la hipertensión, las características morfométricas de la ACM cobran importancia. El objetivo de este estudio fue comparar las características morfométricas del segmento M1 de la ACM en pacientes con DM2 e hipertensos con las del grupo control sano mediante el uso de angiografía por tomografía computada (TC). El estudio fue realizado através de análisis morfométrico retrospectivo de imágenes de TC de 200 individuos entre 40 y 65 años de edad. Los individuos fueron divididos en cuatro grupos, como pacientes hipertensos (grupo 1), pacientes con DM2 (grupo 2), pacientes con hipertensión y DM2 (grupo 3) y grupo control sano (grupo 4). Las mediciones de longitud y diámetro del segmento M1 se realizaron y registraron utilizando imágenes 3D TC. Si bien se encontraron diferencias estadísticamente significativas entre los diámetros bilaterales de los segmentos M1 de mujeres y hombres (p<0,05), no se encontraron diferencias estadísticamente significativas entre las longitudes de los segmentos (p>0,05). Como resultado del análisis *post hoc* realizado, se concluyó que el diámetro de los segmentos

M1 derecho e izquierdo del grupo 1, grupo 2 y grupo 3 fue diferente del grupo 4 en ambos sexos (p<0.05). Creemos que este estudio será una guía en las evaluaciones anátomo-radiológicas y también mejorará el nivel de información microanatómica en el tratamiento quirúrgico al mostrar los cambios morfométricos que ocurren en el segmento M1 de la ACM en las enfermedades con DM2.

PALABRAS CLAVE: Arteria cerebral media; Angiografía por tomografía computarizada; Diabetes mellitus tipo 2; Hipertensión.

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