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Research Paper

Hyperdense Middle Cerebral Artery: Quantification of CT Density in Stroke and Non-Stroke Patients

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ABSTRACT:

BACKGROUND:

The hyperdense middle cerebral artery sign (HMCAS), often linked to thrombosis of the M1 MCA segment, is the appearance of increased attenuation of the proximal middle cerebral artery (MCA). It may be the sole diagnostic feature on computed tomography (CT) in the early stages following an ischemic stroke.

OBJECTIVE:

To evaluate the CT density number of hyperdense MCA presented with hyperacute and acute stroke and comparing the measurements with those of non-stroke patients with hyperdense MCA on the baseline non-enhanced brain CT.

METHODS:

This study is a comparative cross sectional study that included two groups; group A: patients aged ≥35 years with clinical diagnosis of hyperacute (first 6 hours) or acute (6 hours-4 days) stroke who were referred to the CT unit and group (B): patients aged ≥35 years referred to the CT unit for various indication with no clinical evidence of stroke who were labeled by two radiologists as normal brain CT. The study carried out in the CT unit at Al-Imamein AL-Kadhimein Medical City through the period 2016-2017.

RESULTS:

This study showed that there is a statistically significant difference between the mean density of the dense MCA at the site of stroke (48 HU) when compared to the contralateral MCA (39.7 HU) with average difference in density value of 8.3 HU ($p<0.001$), the same applies when tested against the dense MCAS in the non-stroke group (42.2 HU) with average difference of 5.8 HU ($p<0.002$). However, no significant difference was found when testing the density in the non-stroke group against that of the contralateral MCAS in stroke group ($p=0.2$). Moreover, significant variation was observed between the density ratio of stroke and non-stroke patients (1.29 vs 1.02, $p=0.009$). A cutoff MCA density of 41.7 HU was proposed to the predict pathological state.

CONCLUSION:

Hyperdense MCA is associated with acute ischemic stroke exhibit higher CT attenuation value that of contralateral normal vessel or dense MCAS in healthy individuals. ACT density value of >41.7 HU is suggested as the best limit to mark the distinction.

KEYWORDS: Hyperdense middle cerebral artery, stroke, CT density.

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INTRODUCTION:

Stroke is a main source of death and disability in the world. According to the World Health Organization, 20 million people suffer ill effects of stroke, of these more than 5 million die and another 5 million people are permanently disabled. Stroke is a global health problem and is one of the main causes of mortality and morbidity in adult [(1)]. The use of computed tomography (CT) for brain imaging has revolutionized the way that patients with acute stroke are treated. Ischemia is the primary cause of acute stroke (80%). Thrombolytic treatment is now possible when hemorrhagic stroke can be visually distinguished from ischemic stroke [(2)]. Most hospitals in affluent nations offer thrombolytic therapy, with the goal of improving

clinical and functional results by achieving early revascularization in a subset of patients[3]. The most popular imaging technologies are single-photon emission computed tomography (SPECT), PET tomography, magnetic resonance imaging (MRI), and computed tomography (CT). While PET and SPECT give a means of imaging the physiological and functional features of the brain, CT and MRI provide physical imaging of the brain. Among them, the most common methods for identifying stroke are CT and MRI. [4,5].

Hyperdensity sign of middle cerebral artery

One of the first indicators of an ischemic cerebrovascular accident (CVA) is the hyperdense artery sign (HAS), which appears on a non-enhanced CT brain scan and is thought to be a significant radiological marker in the diagnosis of acute arterial thrombotic occlusion. The term "hyperdense middle cerebral artery (MCA) sign" describes the appearance of high attenuation of the proximal section of MCA, which is typically linked to thrombosis of the M1 MCA segment. Following an ischemic stroke, this may be the only early diagnostic sign on CT. [6]. Presence of hyperdensity within the Sylvian fissure of branches of MCA (known as M2 segment), is referred to as dot sign and this indicates an embolic occlusion in distal MCA and this is associated with good prognosis as compared to the hyper density of the M1-segment. HAS of MCA was discovered 25 years ago [7]. Authors have since noted that the sign is very specific for cerebral artery thrombus and that it indicates a poor prognosis for intravenous thrombolysis in cases of acute stroke [8]. Additionally, the size and location of the intravascular hyperdensity affect the outcome. The smaller, peripherally situated variation of the HAS, known as the MCA dot sign, is linked to a better intravenous thrombolysis outcome than HAS [9,10].

The study objective was to evaluate the CT density number of hyperdense MCA in patients presented with hyperacute and acute stroke and comparing the measurements with those of non-stroke patients with hyperdense MCA on the baseline non-enhanced brain CT.

METHODS:

This study is a comparison cross sectional study carried out in the CT Unit at Al-Imamein Al-Kadhimein Medical City through the period 2016-2017. The study included two groups; group (A): patients aged ≥35 years with clinical diagnosis of hyperacute (first 6 hours) or acute (6 hours-4 days) stroke who were referred to the CT unit, group (B): patients aged ≥35 years referred to the CT unit for various indications with no clinical evidence of stroke who were labelled by the two radiologists as normal brain CT and found subjectively to have dense MCA.

Exclusion criteria

1. Evidence of stroke at territories other than MCA (for group A).
2. Previous history of stroke.
3. Heavily calcified MCA.
4. Recent thrombolytic therapy.
5. Intra-parenchymal hemorrhage.
6. Stroke patient with no evidence of dense MCA.

After obtaining a complete medical history, the researchers filled out a prepared questionnaire that they devised in order to gather data. The following were included in the questionnaire:

1. Patients age.
2. Clinical presentations of stroke patients.
3. Clinical history of stroke patients (past medical history, drug history)
4. Indication for CT scan in group B patients.
5. MCA density at both sides.
6. MCA density ratio.

The CT examination was performed by multi-detector CT 256 Slice Siemens Company (Somatom Definition Edge) and examination by using Axial section and protocol include:

Total mAs 1318, Total DLP 367 mGycm

Scan	Kv	mAs/ref.
Patient position H-SP		
Topogram	1 120	35mA
Head	2 100	261/425

Slice thickness 5.0 mm Acq. 128x 0.6mm

CT density measurements

At an axial CT section selected to include (if applicable) the M1 segment of both MCAs. In stroke patients, the CT density measurement of the affected side was performed at the most visually dense portion of the vessel and for the contralateral MCA it was taken at a location approximately comparable to the affected side. In non-stroke group, the CT density of M1 segment of MCA was measured at the most visually dense part on both sides. The density measurement was accomplished by placing circular region of interest (ROI) within the confines of the vessels avoiding the arterial walls. Three density measurements were taken and the average value recorded for the right and left sides in both stroke and non-stroke patients. The CT density ratio between right and left sides was estimated for group B while for group A, the density ratio was calculated by measuring the CT density of the affected side and dividing it by the density of the contralateral side.

Ethical considerations

Research approval was taken from Institutional Review Board, College of Medicine, Al-Nahrain University, and a verbal informed consent was taken from patients or their relatives.

Statistical analysis

The statistical package for social sciences (SPSS) version 22 computerized statistical software was used to enter all patient data. Descriptive statistics are displayed as percentages, frequencies, and mean ± standard deviation. A one-way ANOVA analysis was utilized to compare more than two means, and an independent sample t-test was employed to compare two means. ROC curve analysis was used to accomplish the density and density ratio measurement in stroke diagnosis at CT scan and estimate cutoff values. The significance level (p value) for each statistical test is set at ≤0.05.

RESULTS:

The current study included 60 patients with dense MCA as detected by native CT scan. The patients were classified into two groups: group A included 30 patients who were presented with symptoms and signs of unilateral ischemic stroke at the territory of MCA and the diagnosis was confirmed by CT scan of the brain with subjective dense MCA, and group B, which included 30 patients who did not have any symptoms and signs of ischemic stroke but were found to have dense MCA upon CT scan of the head performed for other reasons.

The mean age of group A patients was 59.6±12 years with range (35-85 years); (90%, N=27) were presented with acute stroke while 10% (N=3) of them were presented with hyper acute stroke (Table 1).

The mean MCA density at ischemic site of group A patients was 48±6.2 HU (range 39.9-64.7), while mean MCA density at contralateral side (non-ischemic side) of group A patients was 39.7±7.4 (HU) (range 30.3-51.7 HU). The average difference in density value between each side was 8.3±1.2 HU. There was a highly significant difference in MCA density between ischemic side and contralateral side (P<0.001) (Table 2).

Table 1: Presentation and clinical history of group A patients.

Variable		Mean±SD	
Age (years)		59.6±12.0	
		No.	%
Presentation	Acute	27	90.0
	Hyperacute	3	10.0
Total		30	100.0

Table 2: MCA density mean and range of both MCA in group A patients.

Variable	Ischemic side Mean±SD (Range)	Contralateral side Mean±SD (Range)	P value*
Average MCA (HU)	48±6.2 (39.9-64.7)	39.7±7.4 (30.3-51.7)	<0.001

*Independent sample t-test

Group B included 30 non-stroke patients. The mean age of group B patients was 58.6±11.9 years with range (36-77 years); All of the 30 patients in group B had bilateral dense MCA as assessed visually by the researcher, thus there was a total of 60 dense MCAs (100%).

The mean of right MCA density for group B patients was 42±6.5 (HU) with range of 30.3-51.7 (HU), while the mean of left MCA density of group B patients was 42.5±6.0 (HU) with range of 32.2-57.2 (HU). The mean CT number of the two sides was 42.2±5.3 HU. The average difference in density value between each side was 0.5±0.05 (HU). No significant difference in MCA mean was observed between left and right sides for group B patients (Table 3).

Table 3: MCA means distribution according to right and left side for group B patients.

Variable	Right MCA Mean±SD (Range)	Left MCA Mean±SD (Range)	P value*
Average MCA (HU)	42±6.5 (30.3-51.7)	42.5±6 (32.2-57.2)	0.7

The mean density ratio of group A patients, was 1.29±0.38 with range of 1.02-2.7, while the mean of density ratio of group B patients was 1.1±0.07 with range of 1-1.26 with highly significant difference in the density ratio mean between two study groups (Table 4).

Table 4: MCA ratio means distribution according to study groups.

Variable	Group A Mean±SD (Range)	Group B Mean±SD (Range)	P value*
MCA ratio	1.29±0.38 (1.02-2.7)	1.1±0.07 (1-1.26)	0.009

Average MCA mean density (HU) at ischemic side of group A patients was significantly higher than MCA mean density at contralateral side of group A patients and MCA mean density of group B patients (48 vs. 39.7 vs. 42.2) (HU), P <0.001, P = 0.002 respectively). The MCA mean density at contralateral site of group A was not significantly different from MCA mean density of group B patients (P = 0.2) (Table 5).

Table 5: Average MCA mean density according to study groups.

Study groups	Average MCA (HU) Mean±SD
Ischemic site	48.0±6.2
Contralateral site	39.7±7.4
Non-stroke	42.2±5.3
P value *	<0.001
Post hoc Tukey test	**P value**
Ischemic site vs. Contralateral site	<0.001
Ischemic site vs. Non-stroke	0.002
Contralateral site vs. Non-stroke	0.2

*One way ANOVA analysis

The acceptable cut off points and the corresponding validity test values for MCA density in prediction of stroke is shown in table (6) and figure 14, cutoff MCA density of 41.7 HU had a reasonable sensitivity but low specificity (93.3% sensitivity and 50% specificity).

Table 6: Coordinates of the ROC Curve of MCA density regarding stroke and non-stroke patients.

Cutoff point (MCA)	Sensitivity	Specificity
41.5	93.3%	47.7%
41.7	93.3%	50%
42	90%	50%
43	83.3%	57.7%
44	70%	60%

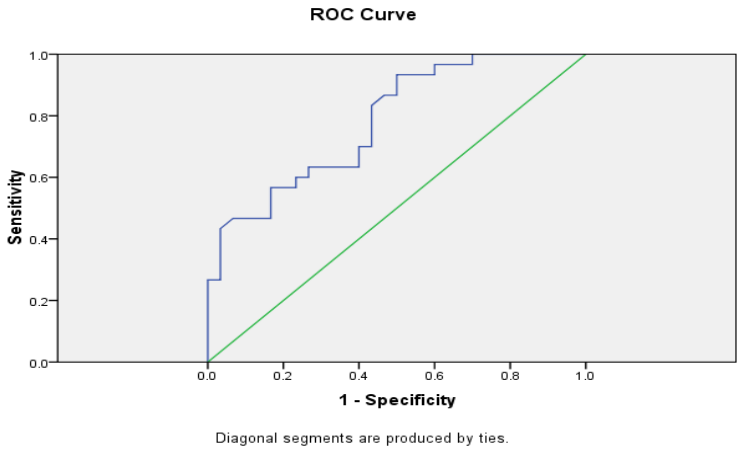

Figure 1: ROC curve for MCA density prediction of stroke (AUC=0.78).

The best cutoff points and the corresponding validity tests values for MCA density ratio in prediction of stroke is shown in table (7) and figure 15, A cutoff MCA density ratio of 1.11 had minimal acceptable validity results (56.7% sensitivity and 60% specificity).

Table 7: Coordinates of the ROC Curve of MCA density ratio regarding stroke and non-stroke patients.

Cutoff point (MCA)	Sensitivity	Specificity
1.08	60%	47.7%
1.09	56.7%	47.7%
1.1	56.7%	50%
1.11	56.7%	60%
1.12	50%	60%

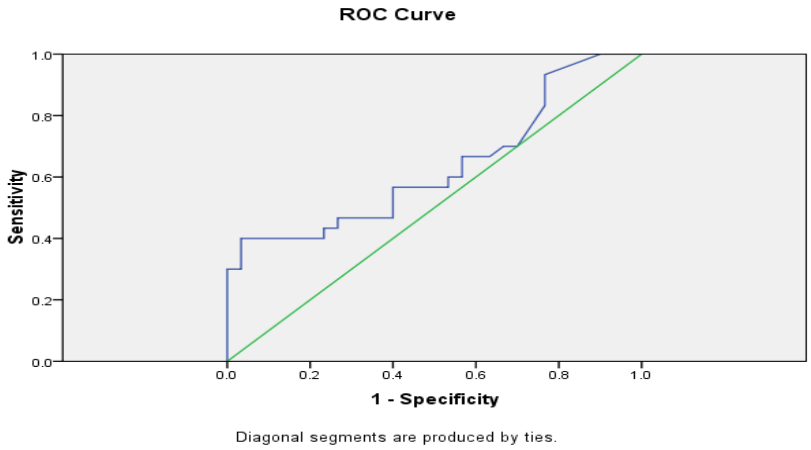

Figure 2: ROC curve for MCA density ratio prediction of stroke (AUC=0.63)

DISCUSSION:

This study showed that there is a statistically significant difference between the mean density of the dense MCA at the site of stroke when compared to the contralateral MCA, the same apply when tested against the dense MCAs in the non-stroke group. However, no significant difference was found when testing the density in the non-stroke group against that of the contralateral MCAs in stroke group. Moreover, significant variation was observed between the

density ratio of stroke and non-stroke patients. A cutoff MCA density of 41.7 HU was proposed to predict pathological state, these findings had been proposed by one of the earliest studies in this regard by Tomsick et al., who stated that this prediction required that the artery appears brighter than the adjacent brain and other intracerebral vessels, speculating that the sign of dense MCA, as an early sign of vascular occlusion is present in acute MCA infarction secondary to thrombosis, embolism or subintimal hemorrhage [(11)]. It wasn't until 2000 that Koo et al. looked into what they called "a true hyperdense MCA sign" and suggested that a CT density number of 43 HU be taken into consideration when diagnosing thrombosis [(12)].

When comparing the density of the MCA on the stroke side with the vessel on the current study, a notable difference was discovered.

Non-stroke side or of the control group and a cutoff value of 41.7 was generated using ROC curve. These findings are consistent with those of Koo et al., [(12)] and several more recent studies by Demirtaş et al., in 2021 who found obvious difference in the density of the MCA between abnormal and normal sides and they reported a variable cutoff value of to be predictive of MCA thrombosis/occlusion [(13)]. However, the cutoff value in the current study is considered minimal acceptable and further studies are recommended to confirm its significance in the clinical practice. The present study calculated the density difference and have found an average value of 8.3 HU when relating the dense MCA at stroke side against that on the contralateral side, on the other hand, the difference was less drastic when comparing the dense MCA in normal subjects on either side (0.5 HU). Ernst et al., [(14)] in a study conducted in 2014, have found that the non-affected MCA average density was 42 HU, which is comparable to that of our study, however, the density mean of the affected vessels was 62 HU and this subsequently resulted in higher average difference of 23 HU.

The density ratio mean of stroke patients measured by CT scan in the present study was significantly higher than mean density ratio for non-stroke patients, this is similar to the result of previous study by Topcuoglu et al., [(15)], which reported a mean SDS density of "44.5±5.7 HU" on the affected ischemic side. At the same time, they suggested that the findings of hyperdense artery may have a diagnostic and prognostic use in patients where CT angiography cannot be performed; however, a quantitative assessment instead of qualitative evaluation would be more useful to clinical correlation as the limited sensitivity and specificity of the suggested value prohibits its use as a reference value.

The combination of visual and quantitative evaluation together would confidently help eliminating other differential diagnoses that may be the cause of false positive dense MCA when assessed subjectively alone, such as the high hematocrit or the presence of calcified atheroma. Nevertheless, some clues exist to suggest these diagnoses, as the increment in density is often bilateral in case of polycythemia while in the condition of atherosclerosis, calcified plaques are frequently eccentric in location beside several other vessels may exhibit the high-density appearance as well [(16)]. According the above-mentioned results, our study recommended to use the CT attenuation number together with visual assessment of the MCA in suspected stroke patients at the emergency departments as both qualitative and quantitative evaluation would increase the accuracy of the final diagnosis

CONCLUSION:

hyperdense MCA associated with acute ischemic stroke exhibit higher CT attenuation value that of contralateral normal vessel or dense MCAs in healthy individuals. A CT density value of >41.7 HU is suggested as the best limit to mark the distinction.

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Author contribution

Tariq S. Fakher: data collection and Statistical analysis

Rana M Farhan: Literature Review

Noor A. Hummadi: editing and patients follow up.

Wasan I. Al-Saadi: Discussion of results

Conflict of interest

None

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