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Comprehensive Analysis of Basal Ganglia Densities in Acute Middle Cerebral Artery Ischemia on Computed Tomography

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Abstract

To present a new objective radiological criterion that can detect early cerebral ischemia by analyzing the density changes in the basal ganglia, which are well-characterized anatomical structures in non-contrast brain tomography of patients with acute ischemic stroke confirmed by diffusion-weighted magnetic resonance imaging. Patients who underwent brain tomography and diffusion-weighted imaging due to a suspected acute ischemic stroke with normal tomography findings were included in the study. Ischemic cases were included in the acute ischemic stroke group, and those that were not diagnosed with ischemia were included in the control group. The densities of the thalamus and basal ganglia were measured in all patients. In the control group, the left basal ganglia and thalamus densities were higher compared to the right side. In the acute ischemic stroke group, the densities of the lentiform and caudate nucleus were significantly higher on the non-ischemic side than on the ischemic side. The acute ischemic stroke group had a lower symmetrical agreement in terms of the densities of the basal ganglia and thalamus compared to the control group. In acute ischemic cases, density changes in the basal ganglia and thalamus are promising indicators that can be used in radiological diagnosis in the early period and at the time of non-contrast brain tomography.

Key words: *Stroke, Brain tomography, Emergency medicine.*

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Introduction

Acute ischemic stroke (AIS) is one of the most important causes of morbidity and mortality in developed countries (1). In the diagnostic management of AIS, non-contrast brain computed tomography (CT) maintains its place as the basic and first-line radiological method (2). Brain computed tomography is a fast imaging method that can be accessed in many centers and directly affects diagnosis. The first imaging method used in patients with suspected AIS is non-contrast brain CT, which is extremely successful in preventing hemorrhagic cerebrovascular events (CVEs), including very small brainstem hemorrhages. However, the success of CT in the diagnosis of AIS in the hyperacute period is much lower than that of hemorrhagic processes. Therefore, diffusion-weighted magnetic resonance imaging (DW-MRI), which allows for the diagnosis of acute infarction within minutes, is considered to be the most sensitive and specific radiological modality in the diagnosis of AIS (3, 4). In addition, in the early ischemic CVE process, in which significant ischemic changes are not yet visible on non-contrast brain CT, findings that may offer an idea about the presence or localization of ischemia in the irrigation areas of the middle cerebral artery (MCA) have been previously described (5, 6). These findings include the hyperdense MCA sign, obscured lentiform nucleus sign, and insular ribbon sign (7). However, these findings are subjective and require a high level of practitioner experience to achieve an accurate diagnosis.

This study aimed to present a new objective radiological criterion that can detect early cerebral ischemia by analyzing density changes in the basal ganglia, which are anatomical structures that can be well characterized on CT, in patients with ischemic CVE confirmed by DW-MRI.

Materials and Methods

Local ethics committee approval was obtained for the study (decision no: 359, date 25/11/2020). This retrospective study involved the examination of the images obtained from the hospital radiological picture archiving and communication system (PACS) belonging to patients older than 18 years, who underwent non-contrast brain CT and DW-MRI imaging after being admitted to the emergency department with a suspicion of acute ischemic CVE between August 1, 2020 and December 30, 2020. The radiological images were analyzed by a radiologist with ten years of neuroradiology experience. The first brain CT images of the patients following their presentation were evaluated. The patients with significant signs of ischemia on brain CT were excluded from the study. In patients without significant ischemia findings on CT, the bilateral thalamus, lentiform nucleus and caudate nucleus densities were measured and recorded in Hounsfield units (HU). Then, the DW-MRI images of these patients at the time of the same admission were analyzed. The patients with no signs of acute ischemia on DW-MRI were included in the control group, and those with ischemia in the right or left unilateral MCA irrigation area on the DW-MRI images were evaluated as the AIS group.

Brain CT Technique

The brain CT images were acquired using a 128-slice, Optima CT660 CT device (General Electric Medical Systems, Milwaukee, WI, USA). During imaging, the patients were in a supine position. Sedation or contrast agent injection was not used for the examinations. The routine brain CT axial images were obtained according to following parameters: slice thickness, 5 mm; interval, 5 mm; kV, 120; mA, 150-200; pitch, 0.531; rotation time, 0.5 s; collimation, 40 mm; matrix, 512; FOV, 20 cm.

DW-MRI Technique

For the routine examination protocol, the b-value was taken as 1000 s/mm^2 and the slice thickness as 5 mm.

Density Measurement Technique

In axial CT sections, at the lateral ventricular level, thalamus density (TD), lentiform nucleus density (LND), and caudate nucleus density (CND) were measured for both sides using the same size regions of interest. Figure 1 presents the measurements of density values in the basal ganglia and thalamus in a patient without AIS. Figure 2 shows the images obtained from a patient with acute ischemia detected on DW-MRI and apparent diffusion coefficient (ADC) despite the absence of a significant ischemia finding in the first non-contrast brain CT image taken in the same plane due to the suspicion of AIS. Basal ganglia density measurements made on the CT images of the same patient are given in Figure 3.

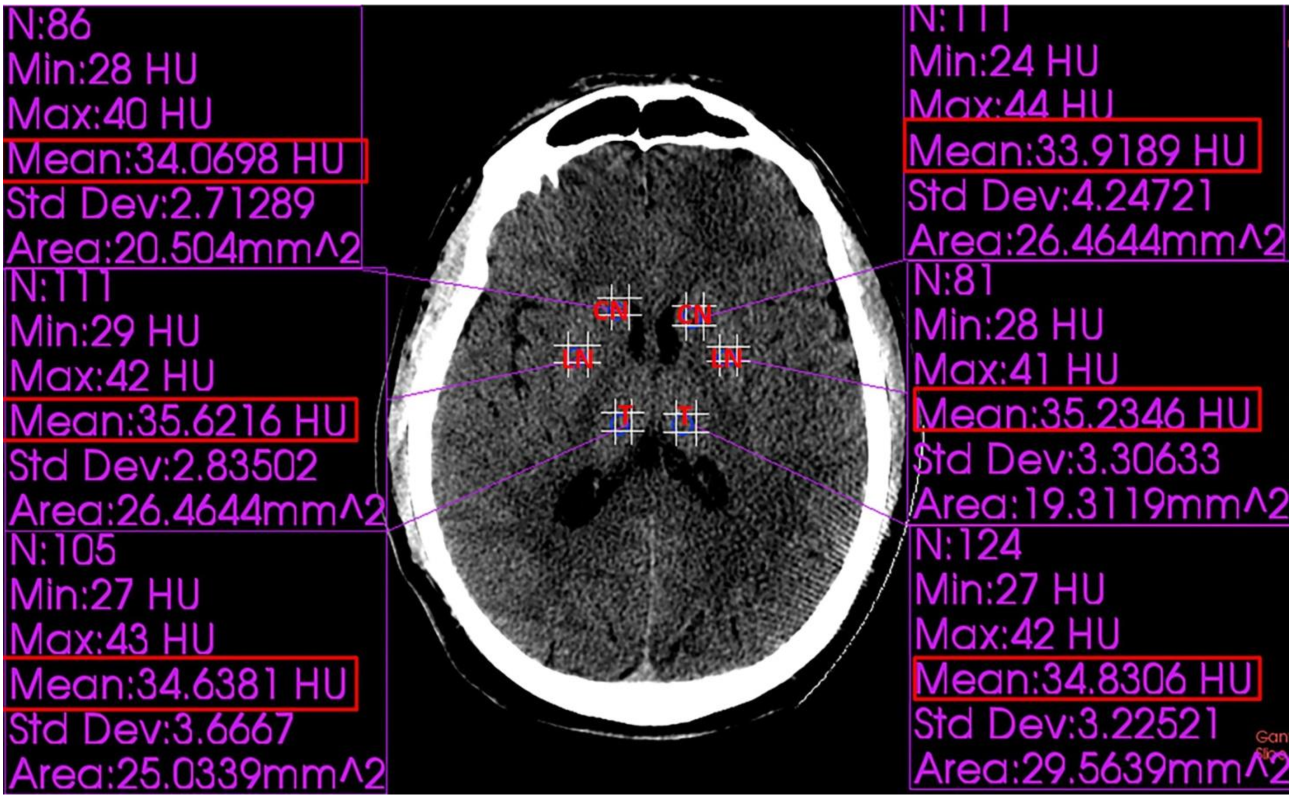

Figure 1: Measurement of density values in the basal ganglia and thalamus in a patient without ischemic CVE.

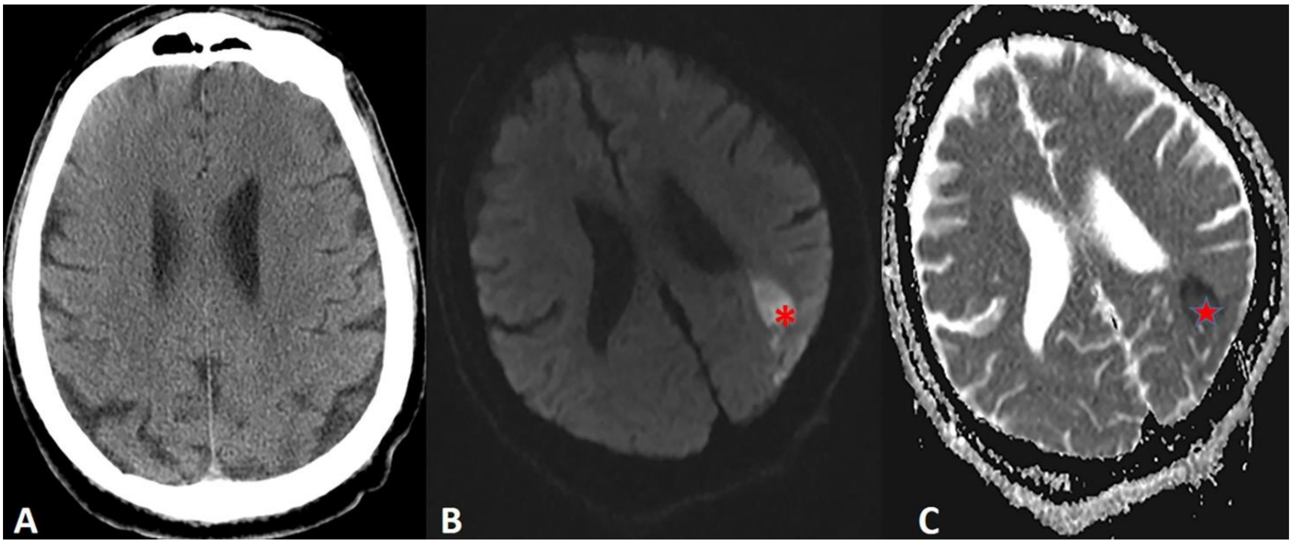

Figure 2: In the patient with suspected AIS (A); No significant ischemia findings on CT, (B); Parenchymal hyperintensity due to ischemia is shown in DWI (asterisk), (C); Signal loss supporting ischemia is shown on ADC images (star).

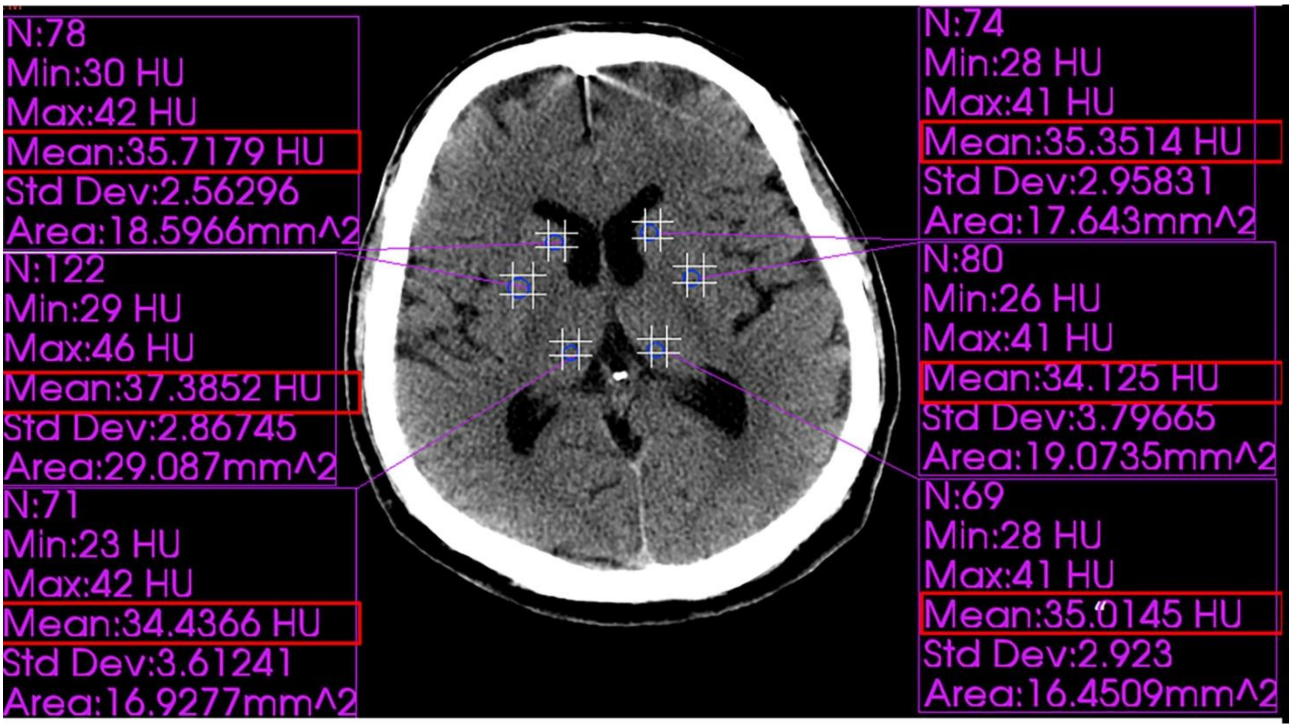

Figure 3: Measurement of the basal ganglia and thalamus densities at the lateral ventricular level on the CT images of the patient whose CT, DW-MRI and ADC images are given in Figure 2. The patient has an ischemic area on the left and the left LND is 3.2 HU, as being lower than the contralateral measurement.

Statistical Analysis

In this study, statistical analyses were performed using SPSS (Version 22.0, SPSS Inc, Chicago, IL, USA, License: Hitit University) software package. Descriptive statistics were presented with mean ± standard deviation and median (min-max) values in accordance with the data distribution. Categorical data were presented as numbers and percentages (%). The distribution of normality was analyzed using the Kolmogorov-Smirnov test. In the comparison of numerical variables between two independent groups, the independent-samples t-test (Student's t-test) was used for normally distributed data. For continuous variables, the paired t-test was used for data showing a normal distribution in dependent two-group comparisons, and the Wilcoxon signed-rank test was conducted for data that did not show a normal distribution. Relationships between categorical variables were investigated using the chi-square test. The agreement between the measurements was evaluated with the intraclass correlation coefficient (ICC). In addition, the Bland-Altman plots were constructed with 95% limits of agreement to visually show the agreement between the two measurements. p <0.05 was taken as the statistical significance level.

Results

There were a total of 104 patients in the sample. Fifty-three (51%) of the patients were in the control group and 51 (49%) were in the AIS group. Fifty-one (49%) of the participants were male and 53 (51%) were female. The mean age was 71.07±9.04 (59-95) years. The mean age of the patients in the control group was 70.96±9.94 years and that of the patients in the AIS group was 71.18±8.10 years, indicating no statistically significant difference (p=0.905). In the control group, 47.2% (n=25) of the patients were male and 52.8% (n=28) were female. In the AIS group, 51% (n=26) of the patients were men and 49% (n=25) were women. The gender ratios were statistically similar between the two groups (p=0.698).

In the control group, the left TD, LND and CND measurements of the patients were statistically significantly different from the right-side measurements (p=0.001, p<0.001, and p<0.001, respectively, Table 1). Figure 4 presents the distribution of the right and left measurements of the TD, LND and CND parameters in the control group.

Table 1: Comparison of the TD, LND and CND values between the right and left sides in the control group and between the ischemic and non-ischemic sides in the AIS group.

	Control group			**AIS group**		
	Right (n=53)	**Left (n=53)**	***p* value**	**Ischemic (n=51)**	**Non-ischemic (n=51)**	***p* value**
	Mean±SD	**Mean±SD**		**Mean±SD**	**Mean±SD**	
TD	33.74±2.62	33.96±2.59	**0.001****	36.64±2.54	37.03±2.46	0.179*
LND	34.87±3.05	35.13±2.98	**<0.001****	36.75±2.98	38.92±2.77	**<0.001****
CND	34.84±3.00	35.15±3.03	**<0.001****	37.01±3.04	37.78±3.45	**0.014****

TD, Thalamus density; LND, Lentiform nucleus density; CND, Caudate nucleus density.
*Paired t-test.
**Wilcoxon signed-rank test.

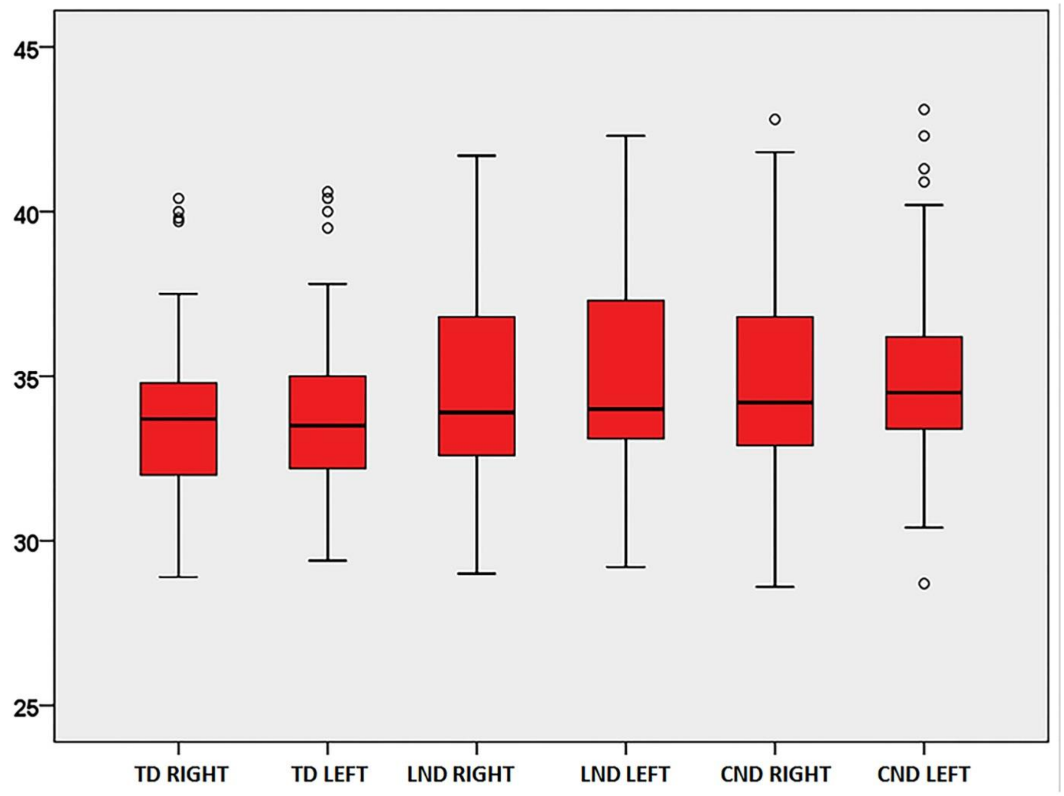

Figure 4: Distribution of the right and left measurements of the TD, LND and CND parameters in the control group.

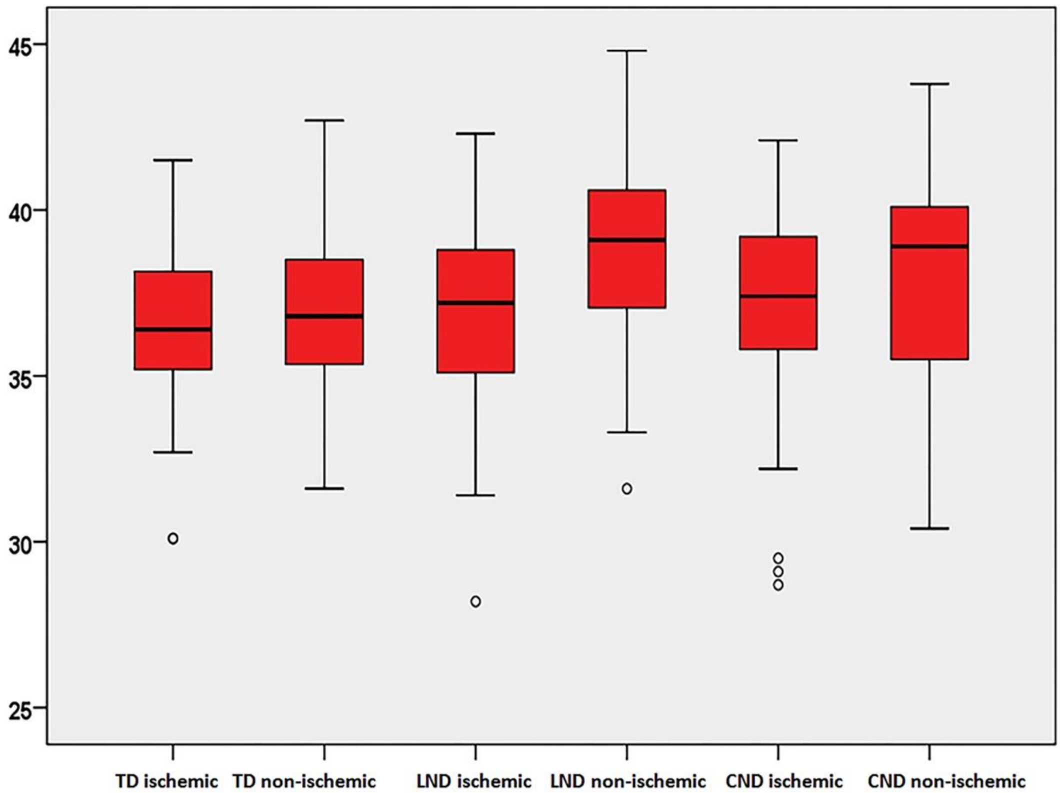

Figure 5: Distribution of the ischemia and non-ischemic side measurements of the TD, LND and CND parameters in the AIS group.

The TD measurement values on the ischemic and non-ischemic sides of the patients in the AIS group were not statistically significantly different (p=0.179, Table 1). However, the LND and CND measurements of these patients were statistically significantly higher in the non-ischemic side compared to the ischemic side (p < 0.001 and p=0.014, respectively, Table 1). Figure 5 shows the distribution of the measurements of the TD, LND and CND parameters among the patients with and without ischemia in the AIS group. According to the ICC values, there was an excellent agreement between the TD, LND and CND measurements on the right and left sides of the 53 patients in the control group [0.971 (0.946-0.984), 0.986 (0.961-0.994), and 0.969 (0.936-0.984), respectively, Table 2]. For the 51 patients in the AIS group, the ICC values revealed a moderate agreement between the TD, LND and CND measurements of the ischemic and non-ischemic sides [0.656 (0.469-0.788), 0.511 (0.042-0.753), and 0.642 (0.447-0.779), respectively, Table 3].

Table 2: Analysis of agreement in the TD, LND and CND measurements between the left and right sides for the control group.

Control group	**ICC (95% CI)**	***p* value**
TD right-left	0.971 (0.946-0.984)	**<0.001**
LND right-left	0.986 (0.961-0.994)	**<0.001**
CND right-left	0.969 (0.936-0.984)	**<0.001**

TD, Thalamus density; LND, Lentiform nucleus density; CND, Caudate nucleus density; ICC indicates intraclass correlation cofficient; 95% CI, Confidence interval.

Table 3: Analysis of agreement in the TD, LND and CND measurements the ischemic and non-ischemic sides for the AIS group.

AIS group	**ICC (95% CI)**	***p* value**
TD ischemic- non-ischemic	0.656 (0.469-0.788)	**<0.001**
LND ischemic-non-ischemic	0.511 (0.042-0.753)	**<0.001**
CND ischemic-non-ischemic	0.642 (0.447-0.779)	**<0.001**

TD, Thalamus density; LND, Lentiform nucleus density; CND, Caudate nucleus density; ICC indicates intraclass correlation cofficient; 95% CI, Confidence interval.

Figures 6 and 7 show the Bland-Altman plots that were constructed with 95% limits of agreement to visually demonstrate the agreement between the TD, LND and CND measurements in the control and AIS groups.

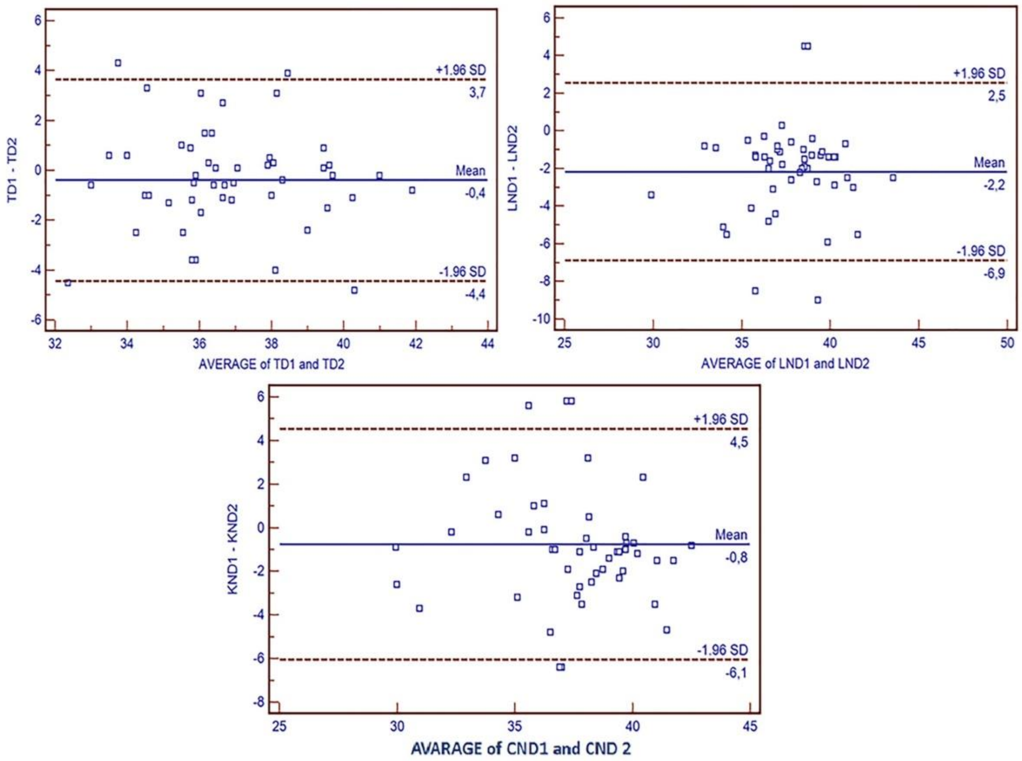

Figure 6: Bland-Altman plots constructed with 95% limits of agreement to visually demonstrate the agreement between the TD, LND and CND measurements in the control group.

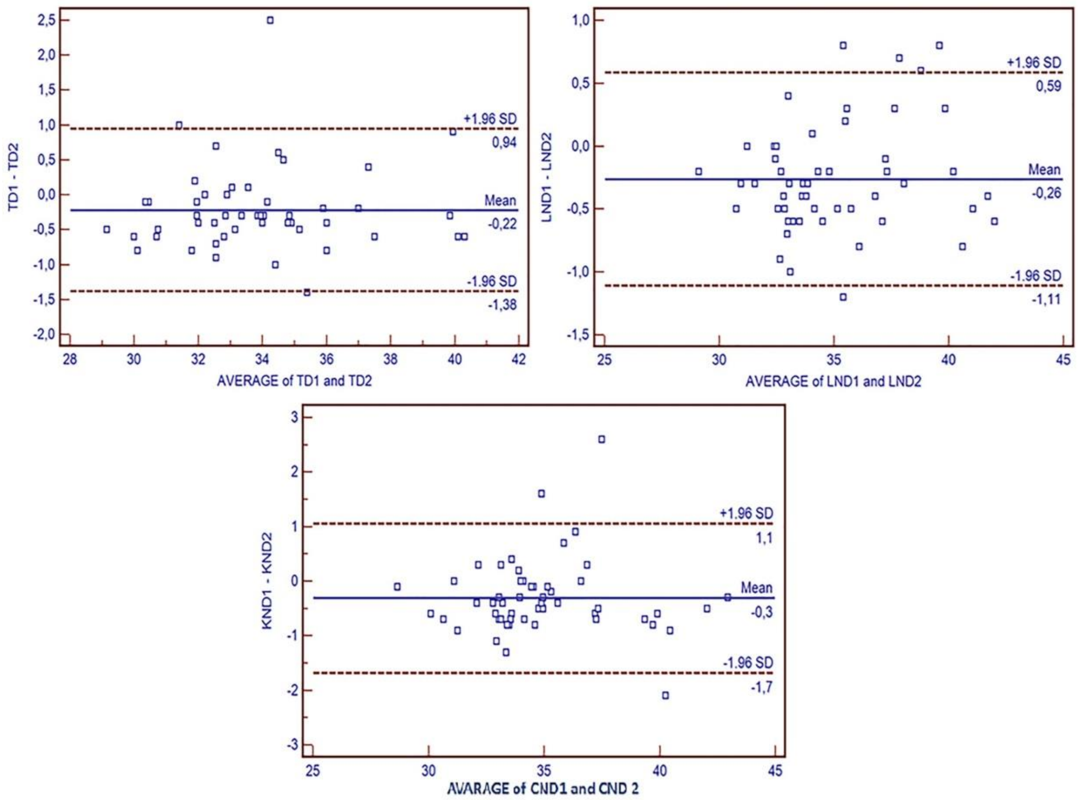

Figure 7: Bland-Altman plots constructed with 95% limits of agreement to visually demonstrate the agreement between the TD, LND and CND measurements in the AIS group.

Discussion

Acute ischemic stroke is the most common cause of mortality following cardiovascular diseases and cancer (8, 9). If AIS can be recognized within the first three hours, thrombolytic therapy can be performed and extremely successful clinical results can be achieved (9). Although there are high-sensitivity neurological examination findings for this important clinical situation, most are not specific (10). The first radiological tool used in the diagnostic management of these cases is non-contrast brain CT, which can successfully exclude possible intracranial hemorrhage and tumor presence (11, 12). Today, the CT device has taken its place in almost all centers with emergency departments (9). Typical and distinct ischemia findings in brain CT often occur after the first six hours, and some radiological markers that may be significant in terms of ischemia can sometimes be identified during this period (9). The hyperdense MCA sign, hypoattenuation in LN, insular ribbon sign, loss of gray-white matter distinction, and obscured sulcus are among the main early markers (6, 13). DW-MRI is a highly sensitive radiological modality that can reveal acute ischemia within minutes or hours (14). However, MRI is still not as common as CT in many centers. It is also clear that a high level of experience is required for the recognition of early MRI ischemia markers that can be easily identified in CT. Therefore, after the first CT examination, which is considered to be normal in the presence of AIS suspicion, the patient is frequently referred for a DW-MRI examination in the same center if equipped or a different center. This situation not only causes delays in diagnosis but also leads to difficulties in terms of cost effectiveness. In our study, we investigated the efficacy of an objective method that can provide ease of application, different from the subjective markers previously described, in patients with suspected AIS, which is a common disease that warrants an early diagnosis.

The basal ganglia and the thalamus are symmetrical deep gray matter elements located at the base of the forebrain and have wide and complex relationships with the cerebral cortex and other brain structures (15). The thalamus, CN and LN are structures that can be well characterized in the axial plane in cross-sectional radiological images. The arterial supply of the basal ganglia is mainly provided by the anterior cerebral artery (ACA) and the lenticulostriate arteries originating from MCA (16). Therefore, it should be known that changes secondary to ischemia may occur in these structures in occlusive diseases of ACA and MCA. Thus, in our study, we also examined the effect of MCA with a large cerebral irrigation area on the density differences of arterial supply loss in ischemic events and investigated its contribution to clinical practice.

In our study, the patient group with MCA ischemia was examined. Lateral lenticulostriate arteries originating from the MCA supply the lentiform nucleus. Therefore; density changes in LND are the most important variable for our study. However, the caudate nucleus is supplied by the medial lenticulostriate arteries. However, ACA, like MCA, originates from the internal carotid artery. Therefore, it can be thought that it may also be affected in proximal MCA ischemia. The thalamus is supplied by arteries originating from the posterior circulation. Therefore, we do not expect significant statistical results in TD variability. However, in our study; TD variability, which are important and easily identifiable anatomical structures, was also evaluated.

Contrary to what was expected in our study, the left side TD, LND and CND values of the patients in the control group were statistically significantly higher than their right side measurements. Although the basal ganglia and the thalamus are known to be symmetrical anatomical structures, this situation may be a result of variability in vascularization. Considering that the mean age of the patients in the control group was 70.96 ± 9.94 years, we believe that potential carotid system stenosis or asymmetric atherosclerotic changes may have led to individual density differences. Nevertheless, for the 53 patients in this group the TD, LND and CND values had an excellent agreement between the right and left side measurements while there was a moderate agreement between the ischemic and non-ischemic side measurements of TD, LND and CND among the 51 patients in the AIS group. This indicates that in patients without occlusive acute cerebrovascular pathologies, the difference in density caused by other factors affecting arterial supply is much less than in the patient group with AIS. Supporting this, while the highest mean density among TD, LND and CND was found to be 0.31 in our control group (CND mean right-left density difference), the mean density difference in the patient group reached 2.17 (LN mean ischemic-non-ischemic side density difference). However, it was an expected result that TD did not show a significant difference in density between the ischemic and non-ischemic sides. In light of these findings, we can state that there was a significant decrease in the LND and CND values on the ischemic side. This was a trial study investigating the use of basal ganglion
density differences in routine non-contrast brain CT examinations on anatomical structures that can be easily demonstrated as an objective and quantitative marker of acute ischemia, regardless of the experience of the practitioner. Although the data obtained indicated that especially LND and CND significantly decreased on the ischemic side in the patients with AIS, the study also had important limitations. As discussed above, TD, LND and KND are in different densities compared to their symmetry in the control group. The reason for this can be considered as atherosclerosis, which is the most common and basic pathological process associated with cardiovascular system diseases (17). In asymptomatic and apparently healthy individuals, atherosclerosis occurs earliest and most commonly in the peripheral arteries and carotid system. Asymptomatic carotid arterial stenosis is a common vascular pathology associated with atherosclerosis, and its incidence increases in parallel to age (18, 19).

It can be easily stated that this vascular disease, which occurs in an asymptomatic patient group, will adversely affect arterial supply to cerebral structures. Therefore, the density analysis of twin intracranial structures that show symmetry would not offer reliable results beyond doubt without performing a carotid Doppler examination and excluding the possibility of carotid artery stenosis. In future similar studies, creating patient groups from individuals that are known not to have carotid system stenosis may provide more accurate results. It should also be noted that diagnostic algorithms for a common public health problem such as AIS have been created over numerous studies conducted with large patient groups over many years. Our study was conducted over a short period of time with a limited number of patients, and therefore we consider that more objective results can be revealed by future studies with larger patient groups.

Conclusion

In light of the data revealed by our study, in acute ischemic cases, density changes in the basal ganglia and thalamus are promising for use in radiological diagnosis in the early period at the time of non-contrast brain tomography, which can also eliminate the need for DW-MRI. Similar studies to be conducted with larger and selected patient groups can present further data that will show that this method can make serious contributions to clinical practice in future.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgement

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References

1. Lövblad K-O, Baird AE. Computed tomography in acute ischemic stroke. Neuroradiology. 2010;52(3):175-87.

2. Jensen-Kondering U, Riedel C, Jansen O. Hyperdense artery sign on computed tomography in acute ischemic stroke. World J Radiol. 2010;2(9):354.

3. Latchaw RE, Alberts MJ, Lev MH, et al. Recommendations for imaging of acute ischemic stroke: a scientific statement from the American Heart Association. Stroke. 2009;40(11):3646-78.

4. Fiebach J, Schellinger P, Jansen O, et al. CT and diffusion-weighted MR imaging in randomized order: diffusion-weighted imaging results in higher accuracy and lower interrater Basal Ganglia Densities in Acute Cerebral Ischemia variability in the diagnosis of hyperacute ischemic stroke. Stroke. 2002;33(9):2206-10.

5. Taşdemir N, Tamam Y, Tabak V, et al. A The Assessment of Early Stage Computed Tomography Findings in Acute Ischemic Stroke. Dicle Med J. 2008;35(1):50-7.

6. Moulin T, Cattin F, Crepin-Leblond T, et al. Early CT signs in acute middle cerebral artery infarction: predictive value for subsequent infarct locations and outcome. Neurology. 1996;47(2):366-75.

7. Olcay HÖ, Çevik Y, Emektar E. Evaluation of Radiological Imaging Findings and Affecting Factors in Patients with Acute Ischemic Stroke. Ankara Med J. 2018;18(4):492-9.

8. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasogen activator for acute ischemic stroke. N Engl J Med. 1995;333(24):1581-7.

9. Teksam M, Cakir B, Coskun M. CT perfusion imaging in the early diagnosis of acute stroke. Diagn Interv Radiol. 2005;11(4):202.

10. Mayer TE, Hamann GF, Baranczyk J, et al. Dynamic CT perfusion imaging of acute stroke. AJNR Am J Neuroradiol. 2000;21(8):1441-9.

11. Wardlaw J. Overview of Cochrane thrombolysis meta-analysis. Neurology. 2001;57(suppl 2):S69-S76.

12. Prokop M. Multislice CT angiography. Eur J Radiol. 2000;36(2):86-96.

13. von Kummer R, Meyding-Lamade U, Forsting M, Rosin L, et al. Sensitivity and prognostic value of early CT in occlusion of the middle cerebral artery trunk. AJNR Am J Neuroradiol. 1994;15(1):9-15.

14. Eastwood JD, Lev MH, Provenzale JM. Perfusion CT with iodinated contrast material. AJR Am J Roentgenol. 2003;180(1):3-12.

15. Hegde AN, Mohan S, Lath N, et al. Differential diagnosis for bilateral abnormalities of the basal ganglia and thalamus. Radiographics. 2011;31(1):5-30.

16. Osborn A. Diagnostic Neuroradiology. 1st Mosby-Year Book; 1994.

17. Song P, Fang Z, Wang H, et al. Global and regional prevalence, burden, and risk factors for carotid atherosclerosis: a systematic review, meta-analysis, and modelling study. Lancet Glob Health. 2020;8(5):e721-e9.

18. de Weerd M, Greving JP, de Jong AW, et al. Prevalence of asymptomatic carotid artery stenosis according to age and sex: systematic review and metaregression analysis. Stroke. 2009;40(4):1105-13.

19. Cina C, Safar H, Maggisano R, et al. Prevalence and progression of internal carotid artery stenosis in patients with peripheral arterial occlusive disease. J Vasc Surg. 2002;36(1):75-82.