Quantification of hyperdense middle cerebral artery sign by multidetector computed tomography (MDCT)

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Resumen
Objetivos. Obtener una cuantificación absoluta y relativa de la densidad en el signo de la arteria cerebral media (ACM) con el fin de lograr un valor objetivo para el diagnóstico temprano de isquemia cerebral aguda con TCMD.

Materiales y Métodos. Se incluyeron 40 pacientes, 20 con sospecha de isquemia cerebral aguda (edad media 73,4 años) y 20 pacientes controles (edad media 71,2 años, p=0,63), que se realizaron TC cerebral con un equipo de 64 filas de detectores. La cuantificación absoluta se realizó midiendo la densidad en UH en el segmento de la ACM visualmente de mayor densidad. También se midió la densidad en el mismo segmento de la ACM contralateral para calcular la diferencia entre ambas arterias (cuantificación relativa).

Resultados. En pacientes casos, la densidad media de la ACM afectada (62,5 UH, IC 99%: 46,2 – 78,7) fue mayor que la de la ACM contralateral (39,3 UH, IC 99%: 33,3-45,3) (p=0,0004) y también fue mayor en comparación con la ACM en pacientes controles (44,7 UH, IC 99%: 37,4-45,3) (p=0,0045). En la cuantificación relativa, la diferencia media entre la densidad de la ACM afectada y la de ACM contralateral en los pacientes casos fue de 23,2 UH (IC 95%: 11,7-34,7), mientras que, en pacientes controles, la diferencia media entre la densidad de la ACM derecha y la ACM izquierda fue 5,2 UH (IC 95%: 2,4-8,4) (diferencia: 17,8 UH, p = 0.0045).

Conclusión. Mostramos diferencias significativas (absolutas y relativas) en la densidad de la ACM en pacientes con sospecha de isquemia cerebral aguda en comparación con sujetos normales.

Palabras clave. Accidente cerebro vascular. Arteria cerebral media. Tomografía computada multidetector.

INTRODUCTION

Computed tomography (CT) and magnetic resonance imaging (MRI) play a central role in the management of acute stroke. CT perfusion, diffusion-weighted imaging, and perfusion MRI may help to improve identification of patients who are candidates for thrombolytic therapy [1,2]. However, because of better availability, ease of use and short examination time, CT is still --and is likely to remain--the method of choice in the initial differential diagnosis of stroke.

During the first hours of an acute stroke, CT findings may be subtle or even undetectable, even when a large territory is involved. However, many signs have been described as markers of early acute stroke on CT: 1) basal ganglia hypodensity, 2) hypoattenuation of the insular ribbon, 3) effacement of convexity sulci, and 4) the hyperdense middle cerebral artery.
Quantification of hyperdense middle cerebral artery sign (HMCAS). In recent years, recognition of the early signs of stroke has become more important with the advent of systemic thrombolytic therapy. Increased attenuation of the middle cerebral artery (MCA) was first described in the early 1980s, corresponding to the presence of an occlusive thrombus within the involved vessel. This finding has been observed within 90 minutes of symptom onset. In addition, some authors have reported that the presence of this sign has an independent prognostic value in terms of subsequent morbidity and mortality. Some authors have reported that the specificity of HMCAS in identifying MCA occlusion approaches 100%, whereas its sensitivity is lower.

However, false positives have been noted in patients with a high hematocrit or calcified atherosclerotic disease. Furthermore, with the new multidetector CT scanners, a reduction of partial volume effects has been achieved due to thinner slice thickness. This determines an apparent relative vascular hyperdensity.

Fig. 1: (a) Brain MDCT axial image of a 68-year-old male patient showing right MCA hyperdensity. (b) Zoomed-in image showing absolute quantification of density of both MCAs by a single pixel ROI. The difference between the affected MCA and the contralateral MCA is 16 HU.

Fig. 2: (a) Brain MDCT axial image of a 69-year-old female patient showing both MCAs with normal density. (b) Zoomed-in image showing similar attenuation values in both MCAs.
The aim of this study is to obtain absolute and relative quantification values of density in the middle cerebral artery (MCA) sign, in order to obtain an objective value for an early diagnosis of acute ischemic stroke using multidetector CT.

MATERIALS AND METHODS

The project was approved by the Institutional Review Board. A prospective study was performed, from November 2007 to March 2010, in 32 patients who underwent brain CT scan on the same day as stroke was clinically suspected. Twelve patients with intraparenchymal hematoma on CT were excluded. Of the remaining 20 patients, 16 (80%) were males and 4 (20%) were females. The mean age in this group was 73.4 years (range 60-82). We also reviewed selected studies of 20 patients with an age range between 60 and 80 years who attended our site to have a brain CT scan performed for other reasons during the same period. In this control group, 12 patients (60%) were males and 8 (40%) were females, and the mean age was 71.2 years (range 62-79). All patients underwent non-contrast brain CT scans with a 64-row multidetector scanner (Brilliance 64; Philips Medical Systems, Cleveland, OH). The following technical parameters were used for data acquisition: collimation, 64 x 0.625 mm; 2-mm reconstruction slice thickness; table increment, 1 mm; matrix, 512 x 512; pitch 0.45; 140 kV; 300 mA; gantry rotation time, 0.75 sec.

The affected side was defined as the one where the HMCAS was subjectively observed. Absolute quantification was performed by measuring vascular attenuation in HU on axial CT slices using one-pixel regions of interests (ROIs) in the visually MCA’s densest segment. Using the same methodology, density was also measured in the same segment of the contralateral MCA (not affected). For relative quantification, density in the same segment of the contralateral MCA was measured to calculate the difference between both arteries (Fig. 1). In controls, density measure-
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Measurements were taken from an arbitrary portion of the M1 segment of the MCAs on both sides, with the aim of obtaining an absolute and relative quantification of attenuation (Fig. 2). All measurements were made by two observers with different levels of experience, a neuroradiologist (F.M.) and a third-year resident in Radiology (C.A.).

Statistical analyses were performed using Student’s t test to calculate differences between groups, when the study variable showed normal distribution. Differences with p values < 0.05 were considered statistically significant. Interobserver variability in measurements of MCA attenuation was assessed by calculating the Spearman’s correlation coefficient and the agreement interval by the Bland-Altman method.

Fig. 8: Progression of ischemic stroke in a 71-year-old patient. (a) Brain MDCT performed 6 hours after the onset of symptoms. Coronal reconstruction shows hyperdensity of the left MCA and subtle hypodensity of ipsilateral basal ganglia. (b) Follow-up MDCT performed 24 hours after the onset of symptoms, showing persistent left MCA sign and extensive area of infarction in the MCA territory.

Fig. 9: Brain MDCT, axial slice in a 64-year-old patient. Sylvian cisterns are narrow and impair proper identification of the MCA. In these cases, an increased slice thickness improves visualization of the right HMCAS (arrow).

Fig. 10: Seventy-year-old patient with right motor deficit and left HMCAS on brain MDCT. For tortuous vessel courses, maximum intensity projection (MIP) reconstructions allow more apparent visualization of the sign.
RESULTS

There were no significant differences ($p = 0.63$) in age between the group of cases with suspected stroke (mean 73.4 years; range 60-82) and controls (mean 71.2 years; range 62-79).

When absolute quantification was performed, in cases, the mean density of the affected MCA was 62.5 HU (99% CI: 46.2 to 78.7), while that of the healthy contralateral MCA was 39.3 HU (99% CI: 33.3 to 45.3), with a significant difference of 23.2 HU ($p<0.0004$) (Fig. 3). The mean density of MCAs in controls was 44.7 HU (99% CI: 37.4 to 52), significantly lower than the density of the affected MCA in cases, with a difference of 17.8 HU ($p = 0.0045$) (Fig. 4).

In relative quantification, the mean difference between density of the affected MCA and that of contralateral MCA in cases (Fig. 5) was 23.2 HU (95% CI: 11.7 to 34.7), while in controls the mean difference between the right MCA density and the left MCA density was 5.2 HU (95% CI: 2.4 to 8.4). The difference between cases and controls was significant with a $p$ value = 0.0032 (95% CI: 6.8 to 28.8).

In the assessment of interobserver variability, the coefficient of correlation was $r=0.87$ with 95% limits of agreement between -8.4 to 6.3 HU.
Fig. 13: Differential diagnosis: atheromatous plaques. (a) Seventy-year-old patient with hyperdensity of the left MCA on CT scan. An assessment of the vessel on the orthogonal plane by multiplanar reconstruction allows visualization of eccentric hyperdensity of lumen (arrow), which is typical of calcified atheroma plaques. (b) A 75-year-old patient with right MCA MCA hyperdensity on CT scan. In the orthogonal plane, hyperdensity involves the whole vessel lumen (arrow), which is indicative of a vascular thrombus. This differential diagnosis cannot be made only by density measurement, as there are fibrous atheromatous plaques that are usually less than 100 HU and vascular thrombi of over 100 HU, which indicates an overlap of attenuation values and the impossibility of determining a cut-off value.
DISCUSSION

According to the literature, the HMCAS is observed in 30% of patients experiencing a vascular event in the territory of the MCA. In most studies, this sign is qualitatively reported, and no HU values are mentioned. However, Koo et al. found as positive a value above 43 HU in attenuation of the affected MCA. Schuknecht et al. subsequently focused on the same issue, but did not report comparative values between both MCAs. Recently, Abul-Kasim et al. considered MCA attenuation above 50 HU and MCA ratio (affected MCA/healthy MCA) above 1.4 as cut-off values defining the limit between the presence and absence of HMCAS.

After performing densitometric measurements, we obtained a significant difference when comparing HU values in the affected MCA in patients with acute stroke to those in the contralateral MCA and in controls (Figs. 6 and 7). Abul-Kasim et al. reported objective and subjective findings in cases of acute stroke with HMCAS. The values they found in 39 patients were slightly lower on the affected side (60.5 HU) than ours (62.5 HU). When using the affected MCA/healthy MCA density ratio, the mean value was 1.5. In our cases, the mean difference between density of the affected MCA and that of the healthy MCA was 23.2 HU, while in controls the difference was only 5.2 HU. To our knowledge, this is the first report of a quantitative assessment of the HMCAS in a prospective series of patients, evaluated with a multidetector CT scanner, with results that are in general agreement with those obtained by Abul-Kasim et al.

Other authors emphasize that the presence of HMCAS has a prognostic value in the evaluation of patients after thrombolysis. Kharitonova et al. observed in 1905 patients that HMCAS disappeared after IV thrombolysis in half of cases, and these patients had a much better prognosis than those with persistent HMCAS on CT scans (Fig. 8). Therefore, given the existence of an alternative treatment approach, the observer’s experience is not the main factor to ensure an accurate diagnosis (Figs. 9 and 10). Identification of which signs are most important to be recognized and the clarification of their definition are the two factors with major implications for diagnostic accuracy. In our study, vascular density was evaluated and quantified by two observers with different levels of experience in neuroradiological imaging (a senior physician and a resident) and a high degree of correlation and agreement was achieved.

Therefore, based on the therapeutic and prognostic implications of this sign, its identification by physicians with little experience is of paramount importance, as many of these patients are seen at emergency departments by junior physicians and/or residents. Most of the times, they perform a brain CT scan in patients with acute ischemic stroke. Quantitative assessment would provide objective data to support visual inspection, not matter how accurate and detailed visual inspection might be (Fig. 11).

A combined qualitative and quantitative assessment makes it possible to rule out other differential diagnoses that could lead to false positive HMCAS, such as high hematocrit or calcified atherosclerotic plaques. In the first case, increased density is generalized and both middle cerebral arteries often show high attenuation (Fig. 12). In the presence of atheromatous disease, calcified plaques are usually eccentric. This is better appreciated on multiplanar reconstructions orthogonal to the major axis of the vessel involved (Fig. 13).

Limitations to our study include the small sample size, although the interobserver correlation was very good. However, we included a group of controls with no vascular involvement, which provides further information and makes results stronger. An additional limitation is the inclusion of patients with different times of progression on the same day of the cerebrovascular event. The agreement between the few studies on quantitative assessment of HMCAS reported in the literature and our findings is promising. Hyperdense MCA may be objectively detected by multidetector CT by measuring MCA density and comparing it with that of the healthy contralateral MCA. We think that the incorporation of routine reading of CT scans in this group of patients at emergency departments with subjective and objective (quantification) assessments would further increase the final outcome accuracy and precision and provide the clinical neurologist with necessary radiological data to make a decision on the therapeutic approach.

References

6. Koo CK, Teasdale E, Muir KW. What Constitutes a True