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Conjugate eye deviation as predictor of acute cortical and subcortical ischemic brain lesions

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ABSTRACT

Objectives: Non-enhanced computed tomography (NECT) of the brain is used to exclude intracranial hemorrhage in patients who are considered for treatment with tissue plasminogen activator due to stroke symptoms. However, early infarct signs on NECT have low sensitivity for ischemic stroke. It was hypothesized that horizontal conjugate eye deviation (average ocular gaze deviation-OGD >14°) on NECT predicts ischemic brain injury on a second detailed examination.
Patients and methods: Patients who underwent brain NECT within three hours after the onset of stroke symptoms and subsequently had brain CT scan with intravenous contrast or MRI were potential participants. OGD was measured from the cross-sectional image including both globes at their maximum diameter.
Results: 73 subjects were studied (mean age 64.2 ± 20.8 years) with a median interval (interquartile range) of 56 h (22–109.3 h) between NECT and the second examination. On NECT, 24 of 73 (32.9%) subjects had OGD >14°. Of 32 individuals with acute ischemic injury on the second examination, 19 (59.4%) had OGD >14° on NECT. OGD >14° was associated with increased risk of ischemic injury: OR = 10.5 (95% confidence interval 3.33–33.9); $P = 0.002$. OGD >14° had significantly higher sensitivity and negative predictive value than early infarct signs on NECT (59.4% vs. 21.9% and 73.5% vs. 59.7%, respectively; $P < 0.05$), and similar specificity and positive predictive value (87.8% vs. 90.2% and 79.2% vs. 63.6%; $P > 0.05$).
Conclusion: In the presence of stroke symptoms, average OGD >14° on the initial brain NECT is early predictor of ischemic brain injury.

1. Introduction

Emergency imaging of the brain is recommended for symptoms of acute stroke in order to identify contraindications for intravenous administration of recombinant tissue plasminogen activator (rtPA) or to exclude nonvascular etiology of the neurological manifestations [1]. Computed tomography (CT) scan of the brain without administration of intravenous contrast (non-enhanced CT-NECT) is the most common imaging examination performed within the first 3 h after the onset of neurological manifestations, but parenchymal injury due to acute ischemic stroke is not apparent in most cases [2,3]. Early infarct signs can be recognized by experienced radiologists in fewer than 67% of cases [1].

Horizontal conjugate eye deviation (CED) or Prevost's sign is an early clinical finding of stroke [4]. In patients with cerebral hemispheric injury (infarct or hemorrhage), CED towards the right side is associated with lesions in the internal capsule or the subcortical fronto-parietal region ipsilaterally [5]. CED towards the left side is usually related to lesions of the entire left fronto-parietal region [5]. In contrast, occlusion of the vertebrobasilar system is accompanied by CED contralateral to the brain injury [6,7].

CED is infrequent in patients undergoing NECT for disorders other than ischemic brain injury [8]. If it occurs in the presence of other diseases, the degree of eye deviation is lesser than in subjects with stroke [8]. Nevertheless, a cut-off value that would allow clear separation of these two patient groups by NECT has not

Abbreviations: CED, conjugate eye deviation; 95% CI, 95% confidence interval; CT, computed tomography; MRI, magnetic resonance imaging; NECT, non-enhanced CT; OGD, ocular gaze deviation; rtPA, recombinant tissue plasminogen activator.

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been reported. Lesley et al., have found that acute ischemic stroke involving the middle cerebral artery (MCA) territory is significantly associated with an average ocular gaze deviation (OGD) >14° [9]. In the current study, an attempt was made to confirm and extend the observation by Lesley et al., It was hypothesized that an average OGD >14° identified on a brain NECT that was performed in the context of clinical findings indicative of stroke is associated with increased risk of acute ischemic brain injury in the territories of anterior, middle or posterior cerebral arteries or in the brainstem. Thus, the main aim of this investigation was to assess the diagnostic value of average OGD as a predictor of cortical or subcortical ischemic lesions. A secondary goal was to calculate the sensitivity, specificity, positive and negative predictive values of OGD >14° and of early infarct signs on the brain NECT as tools to predict ischemic brain injury.

2. Patients and methods

2.1. Patients

We have studied prospectively consecutive patients who presented to the emergency department over a period of 12 months with one or more of the following complaints: (i) headache; (ii) confusion; (iii) loss of consciousness; or (iv) focal neurologic findings i.e., acute hemiparesis or hemiplegia, numbness, sensory loss, diplopia, blurred vision, impaired speech, aphasia. Eligible patients for participation to the study underwent NECT of the brain within three hours after the onset of symptoms followed by a second more detailed examination i.e., computed tomography scan with intravenous contrast or magnetic resonance imaging-MRI of the brain in order to rule out acute ischemic stroke [3].

Exclusion criteria for participation to the study were: (i) history of prior ischemic infarcts, intraocular lens placement, brain surgery or known disorders of the ocular motor pathways (e.g., intranuclear ophthalmoplegia, or multiple sclerosis-optic neuritis); (ii) skull bone fracture, intracranial mass, cerebral hemorrhage or increased size of the ventricular system on the initial imaging study; or (iii) an angle >10° between the optical axes of the eyes (disconjugate eye deviation). An angle between the two optical axes >10° may be the result of exophoria, exotropia or internuclear ophthalmoplegia [9]. The study protocol has been approved by the Larissa University Hospital Scientific Council and all patients have provided written informed consent for participation to the study.

2.2. Image analysis

Image analysis of brain NECT and MRI examinations was completed similar to the study by Lesley et al., using the software RadiAnt DICOM Viewer; version 1.8.6.6744 (Medixant Inc., Poznan, Poland) [9]. For the study measurements, the cross-sectional image including both globes at their maximum diameter, the lens and the midline nasal structures was selected. In a first step, OGD for each eye was calculated. A sagittal line (AB) was drawn between the midline of the nasal structures and the falx cerebri and a second line (CD) was pulled perpendicular to AB and passing through the center of each globe (Fig. 1). One more line was drawn through the longitudinal axis of each lens (EF and GH). The OGD for each eye was defined as the acute angle between lines CD and EF or GH. The OGD was positive if the eye deviated to the right and negative if it deviated to the left. The average OGD was calculated as:

Average OGD = [|right eye OGD| + |left eye OGD|]/2.

The angle between the two optical axes was also measured in order to recognize disconjugate eye deviation:

Angle between the two optical axis = |right eye OGD − left eye OGD|.

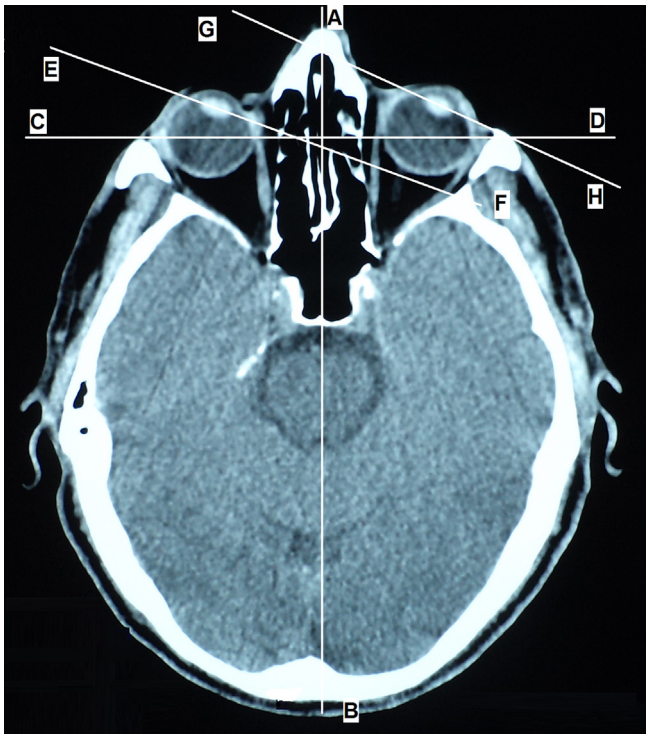

Fig. 1. A sagittal line (AB) was drawn between the midline of the nasal structures and the falx cerebri and a second line (CD) was pulled perpendicular to AB and passing through the center of each globe. A third line (EF or GH) was drawn through the longitudinal axis of each lens. The OGD for each eye was defined as the acute angle between lines CD and EF or GH.

If this angle was <10°, the patient by definition had conjugate visual axes; if the angle was ≥10°, the optical axes were disconjugate and the respective subject was excluded from further analysis [9]. Minor early signs of acute ischemic injury (early infarct signs) other than CED i.e., obscuration of lentiform nucleus, loss of insular ribbon, cortical ribbon sign, effacement of the cerebral sulci, loss of differentiation between gray and white matter, hyperdensity of middle cerebral artery or "dot" sign were also recorded.

2.3. Data analysis

X^2 test was used to compare patients with an average OGD >14° to those with an average OGD ≤14° regarding frequency of acute ischemic injury on the second detailed examination (CT scan with intravenous contrast or MRI of the brain). Odds ratio and 95% confidence interval (CI) for identifying ischemic brain injury on the second examination among patients with an average OGD >14° on NECT as compared to participants with OGD ≤14° was calculated by univariate logistic regression analysis. Odds ratio and 95% CI was recalculated after patients with ischemic lesions only in the cortex were excluded.

Sensitivity, specificity, positive and negative predictive values of an average OGD >14° in predicting findings of acute ischemic stroke on the second exam were calculated. Sensitivity, specificity, positive and negative predictive values were also calculated for minor early signs other than CED as predictors of acute ischemic stroke were also calculated. Average OGD >14° and minor early signs of ischemia were compared regarding sensitivity, specificity, positive and negative predictive values using McNemar's test.