Differential Diagnosis of Ischemic Vertigo by Optical Coherence Tomography

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Cite this article as: *Kocak MN, Ates O, Ondas O, Kaya Z. Differential Diagnosis of Ischemic Vertigo by Optical Coherence Tomography. Eurasian J Med 2020; 52(3): 288-91.*

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Received: July 22, 2020
Accepted: September 9, 2020

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DOI 10.5152/eurasianjmed.2020.20188

ABSTRACT

Objective: This study aimed to evaluate the differences in the mean retinal nerve fiber layer (RNFL) thickness using optical coherence tomography (OCT) in patients with early stage central vertigo with or without vertebrobasilar stenosis detected by Doppler ultrasound.

Materials and Methods: A total of 50 patients with ischemic vertigo and 50 healthy individuals were included in the study. The distinction between central and peripheral vertigo was determined by physical and neurological examinations and the Dix-Hallpike maneuver. For all patients, the mean RNFL thickness was determined using OCT performed by 2 independent ophthalmologists.

Results: There were no significant differences between the groups in terms of age and sex distribution ($p>0.05$). On average, in superior, inferior, and temporal quadrants, there was a statistically significant difference between the control and patient groups ($p<0.001$).

Conclusion: The retina may be affected in patients with ischemic vertigo because of atherosclerotic ischemic lesions in the carotid and vertebral arteries. Neuroimaging methods and OCT were evaluated together to develop a new diagnostic approach. With OCT, which is a non-invasive method, early and more objective differential diagnosis will be possible.

Keywords: Vertigo, tomography, retina

Introduction

Vertigo, an illusion of motion, is caused by asymmetry of the vestibular system as a result of damage or dysfunction of the central vestibular structures in the inner ear maze, vestibular nerve, or brain stem. The dominant symptom of vestibular dysfunction is vertigo [1]. Vertigo is a symptom and not a diagnosis. Severe vertigo can result from both central and peripheral lesions. Some patients with vertigo complain that they feel they are spinning, whereas others feel that the environment is spinning.

Peripheral vestibular lesions affect the labyrinth of the inner ear or the vestibular portion of the vestibulocochlear (VIII) nerve. Unlike central vertigo, vertigo caused by peripheral lesions tends to be intermittent, disrupts functionality, and the attacks are shorter in duration. Nystagmus, which is the rhythmic oscillation of the eyes, is always present in peripheral vertigo and is usually unidirectional and never vertical. Peripheral lesions are usually associated with inner ear symptoms, such as hearing loss and tinnitus or additional symptoms, such as vestibulocochlear (VIII) nerve dysfunction [2].

Vertigo of the central nervous system origin is usually caused by lesions affecting the brain stem vestibular nuclei or lesions that affect its connections. Rarely, central vertigo may occur as a symptom of complex partial seizures or may be because of a cerebral cortical lesion. The etiology of central vertigo frequently involves stroke, intracranial tumors, metabolic disorders, and paroxysmal or degenerative diseases. Approximately 20% of ischemic strokes include posterior circulation strokes. The most common symptom in posterior circulation strokes is central vertigo [3].

Central vertigo can occur with or without nystagmus. If nystagmus is present, it may be vertical, unidirectional, or multifaceted and may have different characteristics in the two eyes. Vertical nystagmus is the oscillation of the eye in a vertical plane. Vertigo caused by central lesions

may be accompanied by brain stem or cerebellar symptoms, such as motor or sensory deficits, hyperreflexia, extensor plantar response, dysarthria, or extremity ataxia. Early diagnosis and treatment of central vertigo is important as otherwise it may have serious consequences [2].

Despite modern imaging techniques, misdiagnosis of stroke cases presenting to the emergency department with vertigo is still high [4, 5]. Approximately 20% of ischemic events occur in the posterior circulation (vertebrobasilar) area, and vertigo is one of the most common symptoms of vertebrobasilar diseases. The results of posterior circulation strokes are more severe than those of anterior circulation strokes. In the presence of isolated vertigo, neuroimaging should be performed considering the underlying posterior circulation infarction [6, 7].

The ophthalmic artery, which is the first major branch of the internal carotid artery, is branched at the level of the anterior clinoid process and initially enters the intracranial pathway and then enters the optic canal. The most important ocular branch of the ophthalmic artery is the central retinal artery. Therefore, the retinal nerve fiber layers (RNFLs) may also be affected in patients with ischemic vertigo because of atherosclerotic ischemic lesions in the carotid and vertebral arteries.

Many anastomoses between the internal and external carotid arteries occur at the level of the ophthalmic artery. After the ophthalmic artery, the posterior communicating artery branch emerges from the internal carotid artery and joins the posterior cerebral artery [8]. The arterial supply of the inner ear is shown in Figure 1.

RNFL thickness is a sensitive indicator of the optic nerve health and nerve damage. Optical coherence tomography (OCT), a non-invasive technique for cross-sectional tomography of the retina and optic nerve, is used to measure RNFL thickness. RNFL thickness measurement is valuable for the early detection of optic neuropathies and for monitoring glaucoma progression.

Main Points

- Currently, there is no effective method in neuroimaging in the diagnosis of central vertigo due to labyrinth ischemia.
- In the OCT method, the differential diagnosis is made by measuring the thickness of the retinal nerve sheath.
- OCT, which is a noninvasive imaging method, is useful in the differential diagnosis of central vertigo of ischemic origin.

Using OCT, this study aimed to evaluate the mean RNFL thickness differences between patients with early stage central vertigo, with or without vertebrobasilar stenosis detected by Doppler ultrasound.

Because the retina may also be affected in patients with ischemic vertigo caused by atherosclerotic ischemic lesions in the carotid and vertebral arteries, early and more objective differential diagnosis will be possible with OCT, which is a non-invasive method. In this study, we aimed to investigate the sequelae level and prognosis of central vertigo and its correlation with OCT findings, a non-invasive neuroimaging method, and offer a new diagnostic approach for ischemic vertigo.

Materials and Methods

Ethical Committee Approval

Approval for this study was obtained from the ethics committee of Ataturk University Medical Faculty. All the participants were given detailed information concerning the purpose and procedures of the study in accordance with the Declaration of Helsinki and provided informed consent before their participation in this prospective study.

Participants

A total of 50 patients with ischemic vertigo and 50 healthy individuals were included in the study. All patients attending the Ataturk University Medical Centre of Neurology between March 2017 and July 2019 were included in this study.

Study Design

In our study, the distinction between central and peripheral vertigo was made by physical and neurological examinations and the Dix-Hallpike maneuver. Peripheral vertigos were excluded. Laboratory tests and metabolic values, carotid and vertebral artery Doppler results, and cranial magnetic resonance imaging (MRI) and/or computed tomography (CT) scans for differential diagnosis in patients with central vertigo were examined. Patients with central vertigo of ischemic origin were identified and included in our study. OCT findings of these patients were compared with the degree of atherosclerotic stenosis in the carotid and vertebral artery Doppler and infarct areas on the cranial MRIs.

Laboratory Investigations

In the laboratory analysis, blood tests were performed for differential diagnosis; vitamin B12 levels, thyroid function tests, liver enzymes for the suspicion of Wilson's disease, ceruloplasmin and copper levels, α-fetoprotein and immunoglobulin levels for ataxia telangiectasia, and auto-antibody levels in case of suspected autoimmune disease were investigated. Cerebrospinal fluid analysis was performed for the presence of demyelinating diseases and infection.

Differential Diagnoses

Posterior fossa tumors and malformations, cerebellar infarction and bleeding, degenerative dis-

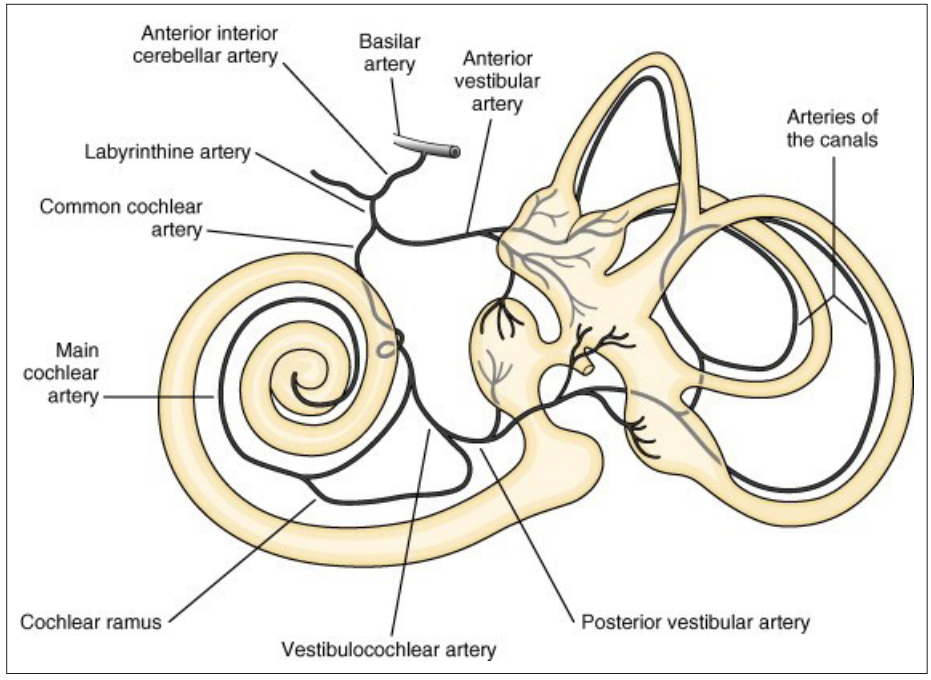

Figure 1. Arterial supply of the inner ear. (From Schuknecht HF: Pathology of the Ear. Philadelphia, Lea & Febiger, 1993, p 64.) Copyright© 1993 Philadelphia, Lea & Febiger

eases, multiple sclerosis, and Meniere's disease were investigated using CT and MRI.

In the physical examination of vertigo, balance and gait tests and cranial nerve examinations were performed. The differential diagnosis of central and peripheral vertigo was made according to the Dix-Hallpike maneuver.

Ophthalmologic Examinations

All the patients underwent an ophthalmologic examination, including best corrected visual acuity (BCVA) (logarithm of the minimum angle of resolution [logMAR]), slit-lamp biomicroscopy, intraocular pressure (IOP), dilated funduscopy with 90-D fundus lens, OCT, fundus photography, and fundus fluorescein angiography. After mydriasis induction with tropicamide eye drops, the ophthalmologic examinations were performed by the same retina specialists. Patients with ophthalmologic or systemic diseases other than ischemic vertigo were excluded from the study.

OCT

Using the OCT device (RTVue SD-OCT; Optovue, Inc, Fremont, CA, USA), macular thickness mapping and peripapillary RNFL thickness measurements were performed in all the eyes by 2 independent ophthalmologists with D status. The optic nerve head map protocol was used in this study. This device has a light source of 840-nm wavelength. Each eye was examined after pupillary dilatation. The circumpapillary RNFL thickness was measured in 4 quadrants (temporal, nasal, superior, and lower) for all patients. Global RNFL thickness was obtained by calculating the average of a total of 3,608 RNFL thicknesses.

Statistical Analysis

Statistical analyses were performed using Windows Statistical Package for the Social Sciences (Version 11.5; SPSS, Inc., Chicago, IL, USA). Statistical significance was calculated using the independent samples Student t-test. All the results were expressed as mean and standard deviation (SD) (mean±SD); $p<0.05$ was considered as statistically significant.

Results

Examination Outcomes

In the control group, 29 (58%) were women, 21 (42%) were men, and average age was 60.7±2.8 years. Of the patient group, 27 (54%) were women, 23 (46%) were men; mean age was 62.1±7.5 years. Both eyes were evaluated in both the groups. BCVA of all patients was 0 (10/10-Snellen) according to logMAR. IOP was evaluated using an applanation tonometer. IOP was 13.3±6.4 mmHg in the control group and 15.2±3.8 mmHg in the patient group. In the control group, the central corneal thickness (CCT) was 543±31 µm, and it was 546±95 in the patient group. There was no statistically significant difference in terms of the changes of best corrected visual acuity, IOP, and CCT between the control and the patient groups ($p>0.05$).

Right Eye

In the patient group, the RNFL thickness values for the right eye were: average, 96.7±3.5 µm; superior quadrant, 96.76±12.33 µm; inferior quadrant, 103.02±33.44 µm; nasal quadrant, 81.78±74.45 µm; and temporal quadrant, 67.78±37.91 µm.

In the control group, the RNFL thickness values for the right eye were: average, 107.2±9.1 µm; superior quadrant, 122.34±15.46 µm; inferior quadrant, 132.10±79.40 µm; nasal quadrant, 85.64±25.09 µm; and temporal quadrant, 85.82±52.14 µm.

Left Eye

The RNFL thickness values of the left eye in the patient group were: average, 95.8±6.4 µm; superior quadrant, 88.85±98.70 µm; inferior quadrant, 99.64±49.79 µm; nasal quadrant, 80.00±85.16 µm; and temporal quadrant, 69.98±32.33 µm.

In the control group, the RNFL thickness values for the left eye were: average, 108.1±3.6 µm; superior quadrant, 126.22±31.67 µm; inferior quadrant, 124.03±34.42 µm; nasal quadrant, 82.34±29.38 µm; and temporal quadrant, 81.03±89.23 µm.

When the RNFL thicknesses were compared for average and the superior, inferior, and temporal quadrants, a statistically significant difference between the control and patient groups ($p<0.001$) was seen.

Discussion

In the pathophysiological classification of strokes, ischemic strokes are divided into atherothrombotic, embolic, and hypoperfusional. Diabetes, hypertension, hyperlipidemia, and vasculitis are the important etiological risk factors in atherothrombotic strokes. In embolic strokes, atrial fibrillation, myocardial infarction, prosthetic heart valve, and microemboli originating from carotid plaques are the important etiological risk factors. The most common cause of hypoperfusional strokes for anterior circulation is severe carotid stenosis and dilated cardiomyopathy. The cause of hypoperfusional ischemia in the posterior circulation is vertebrobasilar insufficiency [9].

Transient ischemic attacks are defined as neurological dysfunctions that resolve within 1 hour. The most important of transient ischemic attack for anterior circulation is amaurosis fugax. It includes emerging vision loss in 1 eye. It is the occlusion of the central retinal artery with a microembolism and subsequent recovery without retinal infarction.

Hypoperfusional ischemia of posterior circulation is mostly because of vertebrobasilar insufficiency. Transient ischemic attacks in the posterior circulation may be caused by microembolism of the labyrinth artery, which may present with transient vertigo as a symptom of the transient ischemic attack [8].

Diagnosis of ischemic vertigo is increasingly determined by neuroimaging methods, such as diffusion-perfusion MRI. With imaging methods, such as MRI, it is not always possible to demonstrate the occlusion of the central retinal and labyrinth arteries with microemboli. When cranial arterial collateral circulation is considered for investigating the pathologies associated with the posterior system and ischemia in the anterior circulation, new techniques should be used. In our study, we aimed to use the vertebrobasilar Doppler method, which is the best indicator of posterior circulation ischemic vertigo and OCT, which is used in anterior circulation disorders like central retinal artery, together.

With advances in modern neuroimaging, inferior cerebellar and small infarcts in the brain stem are increasingly being identified as a cause of isolated vertigo. Furthermore, the most common cause of transient isolated vertigo is vertebrobasilar insufficiency.

Because the therapeutic diagnosis and prognosis are different and cause morbidity and mortality, it is important to differentiate isolated vertigos of vascular origin from benign diseases of the inner ear. Early recognition of the vascular-induced isolated vertigo may lead to a specific treatment.

Because the perfusion of the inner ear results from the vertebrobasilar system, vertebrobasilar ischemic stroke causes inner ear labyrinth infarction and can present with vertigo and hearing loss [10].

The internal auditory artery (IAA) is a branch of anterior inferior cerebellar artery (AICA). IAA is the artery of the cochlea and vestibular

labyrinth, and occlusion of the IAA causes loss of auditory and vestibular functions. Because the IAA is an end artery with minimal collaterals from the otic capsule, the labyrinth is particularly vulnerable to ischemia. IAA infarction is usually caused by thrombotic narrowing of the AICA or basilar artery at the entrance of the AICA [11].

Because observation of the inner ear is difficult on routine MRI, it is not possible to make a definite diagnosis of the labyrinthine infarction unless a pathological study is performed. The apical region of the cochlea is particularly vulnerable to vascular injuries; therefore, low-frequency hearing loss is common in inner ear ischemia. However, labyrinthine infarction is usually associated with the brain stem and cerebellum infarction fed by AICA. Labyrinthine infarction should be considered in elderly patients with acute unilateral hearing loss and dizziness, especially when there is a history of stroke or known vascular risk factors. Owing to the lack of available labyrinthine infarction diagnostic tools and neuroimaging (including MRIs) [3], leads to delay in definitive diagnosis. Clinical diagnosis considering all the clinical evidence is essential.

RNFL thickness in ophthalmology is a sensitive indicator of the optic nerve health and nerve damage. OCT, a non-invasive technique for cross-sectional tomography imaging of the retina and optic nerve, is used to measure the RNFL thickness.

In conclusion, the retina may be affected in patients with ischemic vertigo caused by atherosclerotic lesions in the carotid and vertebral arteries. In our study, we evaluated the differences in mean RNFL thickness using OCT in patients with early stage vertigo with and without vertebrobasilar Doppler stenosis. In addition, neuroimaging methods and OCT were evaluated together to develop a new diagnostic approach. With OCT, which is a non-invasive method, early and more objective differential diagnosis will be possible.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Trials Ethics Committee of Ataturk University School of Medicine (B.30.2.ATA.0.01.00).

Informed Consent: Informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.N.K., O.A., O.O., Z.K.; Design - M.N.K., O.A., O.O., Z.K.; Supervision - M.N.K., O.A., O.O., Z.K.; Resources - M.N.K., O.A., O.O., Z.K.; Materials M.N.K., O.A., O.O., Z.K.; Data Collection and/or Processing - M.N.K., O.A., O.O., Z.K.; Analysis and/or Interpretation - M.N.K, O.A., O.O., Z.K., ; Literature Search - M.N.K., O.A., O.O., Z.K.; Writing Manuscript - M.N.K., O.A., O.O., Z.K.; Critical Review - M.N.K., O.A., O.O., Z.K.

Acknowledgment: We would like to express our gratitude to Clinical Research, Development and Design Application and Research Center for their support.

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: Authors have no conflicts of interest to declare.

References

1. Kerber KA, Brown DL, Lisabeth LD, Smith MA, Morgenstern LB. Stroke among patients with dizziness, vertigo, and imbalance in the emergency department: a population-based study. Stroke 2006; 37: 2484-7. [Crossref]
2. Roger P, Simon MJA, David A. LANGE Clinical Neurology. 10th ed: McGraw-Hill Education; 2018.
3. Lee H. Isolated vascular vertigo. J Stroke 2014; 16: 124-30. [Crossref]
4. Arch AE, Weisman DC, Coca S, Nystrom KV, Wira CR 3rd, Schindler JL. Missed Ischemic Stroke Diagnosis in the Emergency Department by Emergency Medicine and Neurology Services. Stroke 2016; 47: 668-73. [Crossref]
5. Tarnutzer AA, Lee SH, Robinson KA, Wang Z, Edlow JA, Newman-Toker DE. ED misdiagnosis of cerebrovascular events in the era of modern neuroimaging: A meta-analysis. Neurology 2017; 88: 1468-77. [Crossref]
6. Saber Tehrani AS, Kattah JC, Mantokoudis G, et al. Small strokes causing severe vertigo: frequency of false-negative MRIs and nonlacunar mechanisms. Neurology 2014; 83: 169-73. [Crossref]
7. Choi JH, Kim HW, Choi KD, et al. Isolated vestibular syndrome in posterior circulation stroke: Frequency and involved structures. Neurol Clin Pract 2014; 4: 410-8. [Crossref]
8. Love BB, Biller J. Neurovascular System. In: Goetz CG, editor. Textbook of clinical neurology. 355. Third Edition ed. Philadelphia: Elsevier Health Sciences; 2007. p. 405-34. [Crossref]
9. ElSadek A, Gaber A, Afifi H, Farag S, Salaheldien N. Microemboli versus hypoperfusion as an etiology of acute ischemic stroke in Egyptian patients with watershed zone infarction. Egypt J Neurol Psychiatr Neurosurg 2019; 55: 2. [Crossref]
10. Lima Neto AC, Bittar R, Gattas GS, et al. Pathophysiology and Diagnosis of Vertebrobasilar Insufficiency: A Review of the Literature. Int Arch Otorhinolaryngol 2017; 21: 302-7. [Crossref]
11. Kim HA, Lee H. Recent Advances in Understanding Audiovestibular Loss of a Vascular Cause. J Stroke 2017; 19: 61-6. [Crossref]