1. Introduction

Vertigo is one of the most common complaints in neurology and otology. Its prevalence increases with age but is often underestimated in elderly adults (1). Although most cases of vertigo are self-limiting, some cases of vertigo may be life-threatening such as brain stem or cerebellar infarction. Vertigo can also affect quality of life (2,3). Patients with isolated vertigo are commonly encountered in clinical practice, but little is known about the underlying cause of their symptoms. The diagnosis and management of the patients complaining of acute isolated vertigo are challenging endeavors for both neurologists and otologists. A thorough understanding of the anatomy and physiology in peripheral and central vestibular system, neuro-otological physical examination, and appropriate laboratory tests can sometimes help to produce an exact diagnosis.

MRI is the first-choice examination in central vertigo, allowing the evaluation of the whole central vestibular pathway. Some patients with isolated vertigo undergo a series of neurological and otological examinations including cranial CT examination, and the causes of vertigo remain unclear. The diagnostic value of cranial MRI in these patients is yet to be determined

In recent years there were several large clinical studies to survey the cause of vertigo: Most showed that benign paroxysmal positioning vertigo (BPPV) was the most common cause of vertigo, and vertigo of unknown cause (VUC) was reported in 4.2-47.1% (4,5,6,7). Until now, more detailed studies are still rare in patients with VUC, and a better understanding of the underlying diseases in these cases is needed.

1.1 Definition and epidemiology of vertigo

There are several definitions of vertigo used in the literature. Definitions taken from well known medical dictionaries are as follows:

Dorland's Illustrated Dictionary defines vertigo as "An illusory sense that either the environment or one's own body is revolving; it may result from diseases of the inner ear or may be due to disturbances of the vestibular centers or pathways in the central nervous system. The term is sometimes used erroneously to mean any form

of dizziness” (8). Mosby’s Medical Dictionary defines vertigo as “a sensation of instability, giddiness, loss of equilibrium, or rotation, caused by a disturbance in the semicircular canal of the inner ear or the vestibular nuclei of the brainstem. The sensation that one’s body is rotating in space is called subjective vertigo, whereas the sensation that objects are spinning around the body is termed objective vertigo.” (9). Steadman’s Medical Dictionary defines vertigo as “a sensation of spinning or whirling motion. Vertigo implies a definite sensation of rotation of the subject or of objects about the subject in any plane” (10). The Random House Dictionary defines vertigo as “a disorder situation in which one feels oneself or one’s surrounding whirling about” (11).

Although there are many definitions of vertigo, at least we can generally conclude that vertigo is an incorrect sensation of motion either of the body or the surrounding environment. Vertigo can be caused by a vestibular system malfunction or even a psychiatric problem. Strictly speaking, vertigo is not the same as dizziness, but the term is sometimes used erroneously to mean any form of dizziness.

Drachman and Hart first described dizziness by categorizing "dizzy" into 4 symptoms: presyncope, disequilibrium, lightheadedness, and vertigo. Presyncope is the sensation of impending loss of consciousness (12). It is generally caused by transient brain blood flow decrease such as cardiovascular disease, hypotension, or hypersensitive vasovagal reaction. Disequilibrium is a sense of imbalance, it often can be accompanied by subjective vertigo. Lightheadedness is also described as “giddiness” or “wooziness” by the patients. When patients complain of symptoms like lightheadedness, giddiness, or presyncope, the clinician must keep an open mind to consider cardiovascular, metabolic or other system problems but not just vestibular system problems. This description of vertigo is now widely accepted (13,14,15,16). From a large statistical survey, vertigo is diagnosed in 68.9% of 1300 dizziness patients (17).

Vertigo is one of the most common symptoms which neurologists and otologists are confronted with. After headaches, vertigo is the most commonly occurring leading symptom in neurology (18). J.M.Gulilemany et al. found that in an ENT outpatient

clinic, there were a total of 3283 patients, of whom 591(18%) were suffering from vertigo (19). Crespi found that dizziness and vertigo were frequent causes of presentation at the emergency room, with an annual incidence close to 3.5%(20). A large survey showed that the overall prevalence of balance problems at age 70 was 36% in women and 29% in men, and that it increases with age (21).

1.2 The anatomy and physiology of vestibular system

The vestibular system can be divided into the central and the peripheral vestibular system by anatomical and functional classification. According to the lesion within the vestibular system, we can classify vertigo as peripheral vertigo or central vertigo. Knowledge of anatomy and physiology of vestibular system is very important in understanding the mechanism of vertigo.

1.2.1 The peripheral vestibular system

The peripheral vestibular system consists of the bony and membranous labyrinth. The bony labyrinth is filled with perilymphatic fluid whose chemistry is similar to that of cerebrospinal fluid (high Na^+/K^+ ratio). The membranous labyrinth is suspended within the bony labyrinth and surrounded by perilymph fluid. The membranous labyrinth is filled with endolymphatic fluid, which resembles intracellular fluid (high K^+/Na^+ ratio). Perilymph and endolymph systems are separated by a membranous portion and have no communication under normal circumstances (22).

The labyrinth contains 5 sensory organs, 3 semicircular canals (SCCs) and the two otolith organs, the utricle and saccule.The 3 SCCs are called horizontal (lateral), anterior (superior) and posterior canal. The horizontal canal lies orthogonal to the sagittal plane at a 30-degree angle with the true horizontal plane, tilting inferoposteriorly. The other 2 canals are in vertical positions almost orthogonal to each other, each at a 45-degree angle with the sagittal plane. Semicircular canals are paired, allowing redundant reception of movement, which can explain compensation after unilateral vestibular loss (23). The utricle is oval-shaped, and the saccule is of spherical shape. The macula of the saccule is located on the medial

wall of the saccule. The macula of the utricle lies mainly in the horizontal plane. The anterior part of it tilts to 70-110 degrees, so the two otolith organs can also sense 3-dimensional head movements.

The SCCs sense angular acceleration and the otolith organ senses linear acceleration. The hair cells, which are biological sensors of the vestibular system, have similar structure and function. Each hair cell has only one kinocilium and 50-100 stereocilia, and the position of kinocilium and stereocilia are relatively fixed. "Ampullofugal" refers to movement "away" from the ampulla, whereas "ampullopetal" refers to movement "toward" the ampulla. In the superior and posterior semicircular canals, when the ampullofugal endolymph flow induces the utriculofugal displacement of the cupula, the stereocilia bend towards the kinocillium, then cause the hair cells' increased neural firing. There is a stimulated neural firing. When the ampullopetal endolymph flow induces the utriculopetal displacement of the cupula, the stereocilia bend away from the kinocilium, causing the hair cells' decreased neural firing. There is an inhibitor neural firing. The converse is true for the lateral semicircular canal .

Unlike the semicircular canals, the saccule and utricle sense the head movement not through endolymph flow but otoconia displacement. Otoconia lie in the superfical region of the maculae and are inorganic crystalline deposits composed of calcium carbonate or calcite. Otoconia have a higher density than endolymph, so they have more inertia. When the head moves with linear accelerating, otoconia displace in the oppositing direction. This causes the cilium of the hair cells to bend, which in turn causes the hair cells to change the neural firing. The macula can be divided into 2 areas by a narrow curved zone named striola that extends through its middle. In the utricular macula, the hair cells are found to be polarized with the kinocilium facing the striola, whereas in the saccular macula, the kinocilium of each cell face away from the striola. Each hair cell in the macula is positioned differently between the stereocilia and the kinocilium, so otolithic organs can sense linear motion in multiple trajectories. For example, in a linear accelerating movement at any angel of the horizonal plane, the inertia of the otoconia and the different position relation between

the stereocilia and the kinocilium in each hair cell will cause the stereocilia in some hair cells in the utricle to bend toward the kinocilium, which causes an increase in the neural firing and thereby the sensation of movement. The mechanism is similar in the saccule.

1.2.2 The central vestibluar system:

The exact anatomy of the central vestibular system is not fully clear. The vestibular nerve fibers are the afferent projections from the bipolar neurons of Scarpa's ganglion. The vestibular nerve is interposed between the labyrinth and the brain stem. It synapses on cells in the vestibular nuclear complex and other central nervous system structures such as the cerebellum, and no primary vestibular afferents cross the midline. The vestibular nuclear complex and the cerebellum are the two main targets for vestibular input from primary afferents.

The vestibular nuclear complex consists of four major nuclei (superior, medial, lateral, descending). This large structure is located primarily within the pons, but also extends into the medulla, into the floor of the fourth ventricle. Some vestibular nuclei receive only primary vestibular afferents, but most receive afferents from the cerebellum, reticular formation, spinal cord, and contralateral vestibular nuclei, and also project to the extraocular nuclei, spinal cord, cerebellum, contralateral vestibular nuclei, and the vestibular cortex. The superior vestibular nucleus projects in an ascending direction to the nuclei of the extraocular muscles by way of the medial longitudinal fasciculus. This pathway can stabilize images on the retina by causing the eyes to rotate to compensate for head movements. It is called vestibuloocular reflex (VOR). The lateral vestibular nucleus has been shown to be the sole source of fibers to the vestibulospinal tract. These fibers terminate near the anterior horn cells of all the spinal cord levels and mediate trunk and limb muscle reflexes. This circuit is helpful for postural balance. It is called vestibulospinal reflex (VSR). The descending vestibular nucleus appears to be the nucleus most clearly related to the cerebellum. The medial vestibular nucleus receives afferents from the semicircular canals and the utricle; its projections are both ascending and descending in the medial

longitudinal fasciculus. The caudal medial vestibular nucleus and the superior vestibular nucleus can influence parasympathetic and sympathetic outflow, either directly via projections to the brain stem or indirectly via relays in the parabrachial nucleus (24). In humans, the cortical representation of the vestibular system is commonly assumed to be located in distinct parietal and temporal regions of the brain. In fact, PET has even provided results indicating a frontal area involvement in vestibular function (25).

1.2.3 Blood supply of the vestibular system

The vertebrobasilar arterial system provides the vascular supply for both the central and the peripheral vestibular system. The peripheral vestibular organs are supplied by the labyrinth artery. The labyrinth artery has a variable origin: In 45% from the anterior-inferior cerebellar artery, in 24% from the cerebellar artery and in 16% from the basilar artery. The blood supply for the central vestibular system is more extensive and generally described as the vertebrobasilar arterial system.

1.3 Special physical examination in patients with isolated vertigo

The physical examination is very important in the diagnosis of vertigo. The cause of vertigo sometimes can be diagnosed only by medical history and physical examination. The manifestations of a neurological deficit often indicate a central cause of vertigo, and the manifestations of an otological defect often indicate a peripheral cause of vertigo. But if patients with isolated vertigo can show no deficit in either routine otological or neurological tests, it is very important for them to undergo a neuro-otological examination. Unfortunately, the special neuro-otological examination is not widely used by either neurologists or otologists (26,27,28,29,30).

The neuro-otological examination is very important and sometimes difficult in patients with isolated vertigo. It provides information on the functioning of the vestiblulo-ocular and vestibulospinal systems. The results of these examinations can give us more cues about the classification of the vertigo into peripheral or central. But even so, in some cases the cause of vertigo still remains unknown.

1.3.1 Spontaneous nystagmus and gaze nystagmus

Spontaneous nystagmus can manifest itself as rotatory, horizontal, vertical, and combined forms. When the spontaneous nystagmus is not very pronounced, it can be suppressed by visual fixation. Frenzel glasses have 20+diopter lenses that prevent visual fixation, allowing mild vestibular nystagmus to be seen. The nystagmus with rotatory-horizontal beating clockwise-left or counterclockwise-right may favor vertigo of periphersal origin. Pure vertical or linear nystagmus often implies a central etiology (28). Gaze nystagmus is performed by asking the patient to gaze at a target placed 20 to 30 degrees to the left and right of center for 20 seconds. The ability to maintain steady fixation in each direction of eccentric gaze is tested, noticing any centripetal drift and eccentric corrections. Gaze evoked nystagmus can be associated with the lesion of the central origin, such as the cerebellar flocculus or brainstem (27,.28).

1.3.2 Smooth pursuit and saccade

The patient is asked to follow the examiner’s finger or a pen as it is slowly moved in all directions making sure the patient can see the target clearly and examiner doesn’t exceed 60 degrees in total arc or 40 degrees per second. Physiologically, the patient’s eye movement is smooth following the movement of the target. Although cerebellar or brain stem disease can cause saccadic eye tracking in which the patient repeatedly loses the target and then catches up with a small saccade, in many cases abnormal pursuit is not only associated with the central origin (30). Saccades are rapid eye refixating movements that are examined by asking the patient to look back and forth between two outstretched fingers held about 12 inches apart in the horizontal or vertical plane. The observer should pay attention to the latency, accuracy, speed, and conjugacy of the saccades. Saccades are associated with lesions of the frontal lobes, brain stem reticular formation and oculomotor nuclei. Delayed saccades can be seen in cortical and brain stem lesions, inaccurate saccades (especially overshoots) are associated with lesions of the cerebellar vermis

and fastigial nuclei. Disconjugate eye movements with slowing of the adducting eye and overshoots of the abducting eye imply medial longitudinal fasciculus lesions, often seen in multiple sclerosis (30,31).

1.3.3 Skew deviation

A concomitant vertical misalignment suggests a skew deviation of central origin if the misalignment is not explained by a palsy of a peripheral nerve or an ocular muscle. Ocular misalignment can be examined by cover testing. Patients often develop a static contralateral head tilt to improve their alignment. Skew deviation, head tilt, and ocular torsion are also referred to as ocular tilt reaction. The ocular tilt reaction often goes unrecognized because severely ill bedridden patients may have an unnoticed head tilt, especially while supine, and skew deviation and ocular torsion are subtle eye movement abnormalities that require a high index of suspicion for the diagnosis. The ocular tilt reaction is commonly associated with the central origin lesion (31).

1.3.4 Vestibulo-ocular reflex (VOR) testing.

Vestibulo-ocular reflex (VOR) testing includes the head thrust test, post-headshake nystagmus, and dynamic visual acuity. A perfectly compensating VOR would produce a rotation of the eyes in the orbit of equal amplitude and exactly opposite to that of the head, resulting in a gain of –1, gain being the ratio of eye velocity to head velocity. The head thrust test can be performed by asking the patient to view a fixed target while the head is moved rapidly to one side. When a unilateral reduced vestibular function exists, a refixation saccade can be observed while the head is thrust in the ipsilateral direction. Bilateral vestiblular loss leads to a refixation saccade following head thrusts to both the right and the left. Bilateral refixation movements are seen frequently in cases of ototoxicity (27,32).

The test for post-headshake nystagmus is performed by asking the patient to tilt the head forward 30 degrees and shake the head in the horizontal plane at 2 Hz for 20 seconds. Frenzel glass is used to observe the post-headshake nystagmus. Thus, head-shaking nystagmus is a physical sign that can be easily evoked and gives

useful information about the presence of vestibulo-ocular reflex asymmetry. Central lesions may produce vertical nystagums after horizonal head shaking, referred to as “cross-coupling”. A peripheral cause is identified with a horizonal nystagmus in most cases. Initially the nystagmus' slow phase is directed towards the side of lesions, and often there is a late reversal phase with slow phases away from the lesion side (28,29,33).

1.3.5 Positional and postioning tests.

Positional testing is performed by observing the patient’s eye with Frenzel glasses while the patient assumes the supine, head left, left lateral, head right, right lateral positions. When a persistent nystagmus exists in all positions, a direction-fixed positional nystagmus (a nystagmus beats in the same direction in all positions) suggests a peripheral lesion, while the direction-changing nystagmus can be caused by either peripheral or central vestibular disease.

The positioning test is very important for the diagnosis of benign paroxysmal positional vertigo, such as the DixHallpik test (27,30). The patient's head is turned 45 degrees either to the left or to the right and then the patient is rapidly brought from the seated to the supine position. The patient's eyes are observed for nystagmus. If present, latency, direction, fatigue (decrease on repeated maneuver), duration, and reversal upon sitting up are noted. The typical BPPV positional nystagmus is of geotropic torsional direction, brief latency (5-20 seconds), 30 seconds or less duration, it declines with repeated maneuvers and is reversed upon arising. BPPV can be diagnosed through the typical symptom history and the typical positioning maneuver test.

1.4 The most common causes of vertigo

A large survey has revealed the relative frequency of various causes of vertigo (4). Vertigo attributed to BPPV was dianosed in 18.8% of patients, PPV in 16.0%, central vertigo in 13.2%, basilar/vestibular migraine in 9.1%, vestibular neuronitis in 7.9%, Menier’s disease in 7.4%, and vertigo with unknown cause in 4.2%. Some

researchers reported vertigo of unknown cause (VUC) in 4.2- 47.1% of all vertiginous patients (4,6,7,34).

1.4.1 The peripheral forms of vertigo

1.4.1.1 Benign paroxysmal positional vertigo (BPPV)

BPPV is the most common form of vertigo. In a large survey, BPPV was the cause of vertigo in 18.8% of patients (4). Particles in the posterior semicircular canal underlie most cases of BPPV, although the other two canals can also be affected. These particles are otoconia displaced from the otolithic membrane in the utricle, and free-floating within a semicircular canal. Another theory of BPPV is particles adherent to the cupula of a semicircular canal (35)

Patients with BPPV complain of episodic vertigo provoked by head movements and many of them can specify the exact movement that causes vertigo (36). Vertigo usually lasts seconds but can be very intense. Typical nystagmus in DixHallpik test is of geotropic torsional direction, brief latency (5-20 seconds), 40 seconds or less duration, it declines with repeated maneuvers and is reversed upon arising. In horizontal canal BPPV, a purely horizontal geotropic or apogeotropic nystagmus may occur when the examiner turns the patient's head in supine position laterally towards the side being tested. Overall, the history and ocular symptoms during positional testing are the gold standard for diagnosing BPPV (37).

The treatment of BPPV includes maneuver management and rarely surgical therapy. There are several maneuvers for management of BPPV, which are considered safe and efficacious (37,38). Few patients with posterior canal BPPV who don’t respond to maneuver management can receive posterior canal occlusion surgery (39).

1.4.1.2 Vestibular neuritis (VN)

VN is thought to result from a selective inflammation of the vestibular nerve, presumably of viral origin. It is also called “vestibular neuronitis”, “labyrinthitis” or “neurolabyrinthitis”. The fact that it often has a viral prodrome, and that it may affect several members of the same family, and that it occurs in epidemics supports a viral

cause (40). It is a clinical syndrome characterized by the acute onset of prolonged severe vertigo, which is associated with nystagmus of peripheral origin, postural imbalance, and nausea without auditory or neurological symptoms. Signs of vestibular neuritis include spontaneous nystagmus and unsteadiness, rarely skew deviation.

VN has a benign course. It usually takes 3 weeks to recover due to peripheral restoration of labyrinthine function and central vestibular compensation. A vestibular exercise program is a widely accepted treatment. Vestibular exercises should be started when the acute stage of nausea and vomiting has ended, and exercises should be done for several minutes at least twice daily but may be repeated as often as the patient can tolerate (41)

1.4.1.3. Meniere's disease (MD)

MD is characterized by episodic attacks of vertigo, tinnitus, fluctuating hearing loss, and aural pressure or fullness in the affected ear, which may last 20 minutes or longer. The directon of nystagmus can be observed toward the unaffected ear. The American Academy of otolaryngology has published criteria for the diagnosis of MD in 1995 (42). The theory that endolymph hydrops is the causal mechanism in MD is widely accepted. The pressure from this excess fluid interferes with the functioning of the delicate cells that are responsible for balance and hearing. Hearing loss and tinnitus are the result. As the disease progresses, the cells become irreparably damaged. Many people with Meniere's disease can actually feel the fluid building up and the feeling of fullness this produces. Sudden movement of this excess fluid is the most likely cause of the vertiginous attacks that are typical of MD.

1.4.1.4 Perilymph fistula

Perilymph fistula may lead to episodic vertigo and sensorineural hearing loss. The symptoms worsen with coughing, sneezing, loud sounds or hard physical activity. It is caused by a pathologic elasticity of the otic capsule usually at the round or oval window, which permits abnormal transfer of pressure changes to the maculae or

cupulae receptors. The diagnosis can be clincally suspected with reproduction of symptoms after Valsalva's maneuver and confirmed by exploratory tympanotmy with inspection of the round and oval windows. A new variant of perilymph fistula is “superior canal dehiscence syndrom”(43), which is caused by a dehiscence of bone overlying the superior SCC. The changes in pressure are pathologically transducted through the dehiscence to the superior SCC. Most perilymph fistula can heal spontaneously and conservative therapy is advised in the acute phase. When symptoms last more than one month or hearing loss exacerbates, surgery can be considered.

1.4.2 Central cause of vertigo

Any lesion of the central vestibular pathway can cause central vertigo, such as infarct, bleeding, tumor, multiple sclerosis, etc. These diseases are often accompanied by neurological symptoms, and MRI can often show the abnormality. Here, only 2 forms of central vertigo are described which are sometimes difficult to diagnose, vertebrobasilar TIA and basilar migraine.

1.4.2.1 Vertebrobasilar transient ischemic attacks (TIA)

Vertebrobasilar TIA is characterized by brief episodes (<24 hours) of neurological disturbance caused by reduced blood supply in the vertebrobasilar arterial system. Vertebrobasilar artery TIAs account for about 7% of all TIAs - clinical features are more diverse than those that may occur in carotid artery TIA. Besides vertigo, other symptoms of vertebrobasilar TIA include visual disturbance, drop attacks, unsteadiness or incoordination, weakness, confusion, headache, hearing loss, numbness, speech disturbance, abnormal noise in the ears, and numbness around the mouth. Cranial CT or MRI often shows no abnormality corresponding to these symptoms. Recent studies show that isolated vertigo can be caused by vertebrobasilar ischemia (44,45), so isolated vertigo may be the only symptoms of the vertebrobasilar TIA. But when patients only have isolated vertiginous symptoms, it is very difficult to diagnose it as vertebrobasilar TIA.

1.4.2.2 Basilar migraine (BM)

Basilar migraine is a less common form of migraine headache. Vertigo has been attributed to BM in 9.1% (4). BM is often regarded as a central form of vertigo, but some authors regard it as a special subtype of vertigo (4,46,47). The aura symptoms of BM originate from the brain stem or from both occipital lobes. The symptoms of an aura most often arise before the onset of headache, but can also start while a headache occurs. Besides vertigo, other neurological symptoms include visual disturbances, hearing loss, diplopia, tinnitus, ataxic gait, bilateral numbness/tingling in extremities that often spread up the limbs, tingling around mouth, confusion and disorientation, rarely unconsciousness. In some cases, the aura syndrome remains monosymptomatic—presenting only with rotational vertigo. In such cases the diagnosis may be difficult and only be made after exclusion of other diseases.

1.4.3 Phobic postural vertigo (PPV)

Some patients with psychogenic conditions can suffer subjective postural imbalance and gait unsteadiness. Psychogenic vertigo can only be considered if it (a) is part of a recognized psychiatric symptom complex (such as vertigo during panic attack) and (b) cannot be explained by a vestibular disorder (48,49). The most common form of psychogenic verigo is phobic postural vertigo. Patients with PPV complain of vertigo and subjective imbalance while standing or walking and of momentary perceptions of illusory body perturbations. The unsteadiness can be continuous or occur in attacks with or without anxiety. Symptoms occur spontaneously but often are also elicited by certain perceptual stimuli (e.g. crossing bridges) or social situations (department stores, restaurants, etc). There is a tendency for rapid conditioning and development of avoidance behaviour. Otoneurological and balance tests such as spontaneous and gaze-evoked nystagmus, pursuit, caloric test, vestibulo-ocular reflex test, and Romberg’s test do not show any pathology.

1.5 MRI in vertigo patients

1.5.1 MRI as a diagnostic tool for vertigo

Although some cases of vertigo can be diagnosed on the basis of the medical history and a targeted physical examination, other diagnostic tools include blood tests, electrocardiogram, Doppler sonography, electronystagmography, computer tomograhy (CT), magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), angiography, etc.

MRI is the first-choice examination in central vertigo, allowing the evaluation of the whole central vestibular pathway. Cerebrovascular ischemia, multipe sclerosis, CNS tumor, CNS infection, etc., are clearly distinguished by MRI. Diffusion-weighted MRI can detect acute ischemia at very early stages. MRI can very sensitively detect lesions in the brain stem and other posterior fossa structures, which are an important part of the vestibular pathway (50). CT can diagnose most cerebellar hemorrhages, tumors and some cerebellar and brainstem acute ischemia, while it is not sensitive in detecting posterior fossa tissue structures. Early cerebral infarction sometimes can show normal findings on CT.

The use of cranial MRI in peripheral vertigo is controversial. Some forms of peripheral vertigo such as BPPV can be diagnosed only on the basis of the medical history and a typical positional nystagmus examination, requiring no MRI. On the other hand, defects of the internal auditory meatus or intralabyrinthine abnormalities such as inflammatory changes, hemorrhages, and malformations can be detected with thin-slice of brain MRI (51). Meniere's disease is characterized on MRI by decreased evidence of the endolymphatic duct and sac on the affected side and the reduction of bone thickness between the posterior semicircular canal and the posterior fossa (50). Many diseases of peripheral vertigo are only diagnosed when other causes of vertigo are excluded. MRI is performed to rule out other pathologies and to confirm the diagnosis.

1.5.2 MRI in patients with isolated vertigo

Most studies of isolated vertigo in MRI are case reports. Brain MRI can show infarct, tumor or MS in these patients (71,72,73). Lee H et al. (66) reported a patient with purely isolated vertigo, ipsilesional spontaneous nystagmus, and contralesional axial lateropulsion without neurological symptoms or signs. MRI showed a small left cerebellar infarct selectively involving the nodulus. He also reported a patient with sudden deafness and vertigo as the sole manifestation. The patient had a tiny infarct in the right lower pontine tegmentum on MRI with diffusion imaging (67,68). Gomez CR et al. (69) reported 2 patients with isolated vertigo in whom vertebrobasilar ischemia was confirmed with MRI. Kim JS (70) reported 3 patients with isolated vertigo and gait ataxia without other neurological or otological symptoms/signs. Cranial MRI showed small infarcts selectively involving the most dorsolateral portion of the rostral medulla. Bencsik K (72) et al. reported a patient with isolated vertigo and paraesthesias, MRI results supported the diagnosis of MS. Haegelen C (73) et al. reported a patient with vertigo, headache and ataxia, MRI showed a tumor located in the fourth ventricle. Norrving B (74) studied 22 isolated vertigo patients with MRI, and found 4 patients with a cerebellar infarct and 18 patients with normal posterior fossa imaging.

Although cranial MRI is the best way to rule out the central vertigo, its high costs argue against routine use in isolated vertigo. MRI investigations are costly and time-consuming, and abnormal findings are not always detected with MRI in patients with isolated vertigo. Therefore, the appropriate use of MRI examination in patients with isolated vertigo should be further studied.

1.6 The clinical characteristics of VUC

In the present study, all patients with isolated vertigo underwent extensive neurological and otological examination including cranial CT and MRI examination, but the causes of vertigo often remained unknown, leading to the diagnosis of vertigo of unknown cause (VUC). Studies of patients with VUC are rare, and most of the

prior research reports only focussed on single characteristics of these patients, such as MRA, migraine or blood sugar.

Some researchers studied patients with VUC using MRA and showed that these patients had more abnormalities in vertebral and basilar artery, and suggested that these patients might have suffered from vertebrobasilar ischemia (52,53). But the anatomy of vertebrobasilar artery has many normal variations, and abnormalities such as kinking or tortuosity may be of no significance. MRA can also overestimate the degree of stenosis of the blood vessel (54). So the results are still controversial.

Hyung Lee et al. (55) studied 72 consecutive patients who suffered isolated recurrent vertigo of unknown cause. All these patients underwent extensive neuro-otological evaluation to exclude identifiable causes of vertigo. These patients had a higher prevalence of migraine than the control group. But high prevalence of migraine is not only found in patients who suffer from VUC, but also in many other forms of vertigo, such as BPPV, Meniere's disease (MD) (56,57,58). Radtke A et al.. (56) studied the prevalence of migraine in patients with MD compared to sex- and age-matched controls. The lifetime prevalence of migraine was higher in the MD group (56%) compared to controls (25%; $p < 0.001$). Forty-five percent of the patients with MD always experienced at least one migrainous symptom (migrainous headache, photophobia, aura symptoms) with Meniere attacks. So the relationship between migraine and VUC should be further studied.

Kazmierczak H and Doroszewska G (59) have studied 48 patients suffering from vertigo, and/or tinnitus and/or hearing loss of unknown origin. All subjects had undergone a complete neurootologic examination and appropriate audiometric and vestibular tests. Patients were overweight significantly more often compared to the control group. Systolic and diastolic hypertension was found significantly more often in the male group than in the control group. The authors also reported (61) that the occurrence of hyperinsulinemia was significantly more common in the patient group (43.8%), than in the control group (22.6%). Also the insulin levels in the second hour of OGTT (oral glucose tolerance test), were significantly higher in patients than in the controls, and Diabetes mellitus was not present in any controls but was identified in

four patients. Only the occurrence of hyperlipoproteinemia seemed not to differ between patients and control subjects, but there were some differences in lipid phenotype and severity of hyperlipidemia between the two groups (61,62). The study showed that the patients with VUC had more prevalence of hypertension, overweight, Diabetes mellitus, which were also identified to be risk factors of cerebrovacular disease.