

## Review Article

# Clinical and otopathologic findings on age-related vestibular loss: state of the art review

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## ABSTRACT

Age-related vestibular loss is a complex and multifactorial condition, involving several anatomic and functional changes in vision, proprioception and more importantly the inner ear. Vestibular testing and histopathologic reviews have revealed relevant information about those changes; however, little is known about its clinical and otopathologic correlation over the last two decades. We aim to extend the understanding of this process and provide a comprehensive picture of it. Currently available literature was analyzed for understanding the clinical and histopathological correlation of age-related vestibular loss. Age-related vestibular loss articles were reviewed; 467 articles were found on different databases and 33 (9 retrospective chart reviews, 7 cross-sectional, 4 prospective cohorts, 13 histopathology studies) were included in the state of art review. The overall prevalence of age-related vestibular loss is 35.4% in patients older than 40 years. There are other studies that have reported prevalence ranging from 18% to 53% for patients older than 50 years. The most evident is at 75 years of age and vestibular loss is related to people with a lower educational level, less physical activity, smokers and with diabetes or cardiovascular disease. We provide the latest evidence in clinical and histopathologic findings, their relationship, and upcoming challenges in this review. The deepest understanding of these changes would provide better comprehension of this process for primary care physicians, otolaryngologists, neurologists, and neuro-otologists. It will allow better and targeted healthcare attention in elderly patients with balance problems.

**Keywords:** Vestibular system/pathology, Aging, age-related, Vestibular loss

## INTRODUCTION

Imbalance and unsteadiness in elderly population may result from impairment of the peripheral and central processing systems.<sup>1</sup> These are usually associated with functional progressive loss in targeted cells in the utricle, saccule, or semicircular canals.<sup>2</sup> The vestibular system is a critical contributor of balance and gait function. Therefore, during aging the vestibular damage may result in falls and other health problems, constituting a major public health

issue as among the most common and morbid conditions affecting older persons are balance impairments and falls.<sup>1,2</sup> According to earlier studies, approximately 30% of seniors 65 and older experience a fall each year, and the death rate associated with it has drastically climbed in recent years, rising from 51.6 per 100,000 people in 2000 to 122.2 per 100,000 people in 2016.<sup>3</sup> According to reports, there were 80 million falls among Americans in 2008, and 10 million people were hurt as a result.<sup>4</sup> Due to

this, balance and gait issues are regarded as the major contributing factors to falls in older adults.<sup>5</sup>

In the elderly, several causes of vertigo may manifest differently, as patients tend to report less rotatory vertigo, and more nonspecific dizziness and instability than younger patients, making diagnosis more challenging and complex.<sup>1,2</sup> Patients over 60-years-old have an estimated prevalence for balance disorders ranging from 30% to 50% in patients beyond 85-years-old.<sup>6</sup> Although, elderly patients present benign balance disorders, there is a multifactorial impairment of their central and peripheral vestibular system. Mainly, there is a loss of vestibular and proprioceptive functions with impairment of central integration and other sensory inputs associated with aging.<sup>1</sup> In addition, the skeletal muscle strength and mass are reduced with aging, increasing the risk of fall-related injuries in elderly individuals, reducing gait speed and decreasing overall life quality.<sup>7</sup>

Only in the United States, up to 49% of older adults may experience falls each year and these are one of the most common causes of accidental death in elderly patients.<sup>8</sup> Although a fall may result from a variety of complex factors, including environmental and physiological causes, the vestibular decline is one of the main contributors to falls and physical impairment.<sup>8</sup> But the various interconnected physiological and pathophysiologic mechanisms that cause balance deterioration in older people and can guide treatment therapy are not fully understood.<sup>9,10</sup> The vestibular system is still a key factor in balance and gait function, and strong epidemiologic data indicate that vestibular impairment is a major factor in imbalance and falls in older U.S people.<sup>9,10</sup> As reported, a vestibular impairment significantly raises the risk of falling.<sup>9</sup> However, despite the fact that vestibular impairment's clinical significance has received widespread recognition in the pertinent literature, older people who experience balance issues and falls are rarely checked for or treated for this illness. For that reason, the aim of this literature review is to examine the available literature in age-related vestibular loss, regarding histopathology, clinical and testing findings over the last 20 years.

## METHODS

### *Search strategy and selection criteria*

This review was conducted between January and March 2022. The search strategy included the following MeSH terms: “vertigo,” “vestibular system,” “vestibular labyrinth” and “aging” to search PubMed, Embase, Scopus, and Google Scholar databases for relevant articles. The search was limited to articles published between 2001 and 2022, where most of the research publications were released.

Papers were initially screened by their titles only. However, to better define their status according to the inclusion criteria, the abstract and/or manuscript was read

to clarify ambiguities. We included English-language manuscripts and meeting the aims of the review to include patients with age-related vestibular loss. Studies outside the field of neurotology, neurology, and otolaryngology were excluded.

Duplicates were removed manually by the authors. Review articles, letters of opinion, comments to the editor and case reports were excluded. Articles in languages other than English were also excluded. Further, for the purpose of the review, relevant papers were read and mined for relevant content (Figure 1). Results were cross-checked among all the authors. All articles were evaluated for quality and fit the research aims for titles that seemed worthy of inclusion. If the article was applicable, qualitative, and quantitative data was extracted, and then the content was analyzed and categorized. Information and content from the selected publications were categorized and grouped into histopathologic and clinical findings.

In total, 467 indexed papers were identified in the initial search. From these, only 33 indexed articles were selected because they met the inclusion criteria, which reported vestibular related aging conditions. Data were manually extracted as profiles of manuscripts with major findings relevant to the review were added to an excel spreadsheet. The quality of evidence in the published articles was reviewed according to the 2009 levels of evidence of the Oxford Center for Evidence-Based Medicine.<sup>11</sup>

## RESULTS

33 articles were found (9 retrospective chart reviews, 7 cross-sectional, 4 prospective cohorts, 13 histopathology studies). Patients with age-related vestibular loss were selected (Figure 1).<sup>12,13</sup> The overall prevalence of age-related vestibular loss is 35.4% in patients over 40-years-old. Other prospective studies have reported higher prevalence for patients over 50-years-old ranging from 18 to 56%.<sup>13</sup> According to previous studies, the mean age for vestibular decline is 40 years old, when at least one-third of patients present with this condition.<sup>14</sup> However, the most evident clinical findings are present in patients over 75-years of age.<sup>12,13</sup> Age-related vestibular loss is expected to increase from 12.9% to 23.7% over the upcoming 30 years.<sup>14</sup> Usually, age-related vestibular loss was higher and sooner in individuals with lower educational status, lower physical activity, smoking and with diabetes or cardiovascular disease.<sup>14-16</sup>

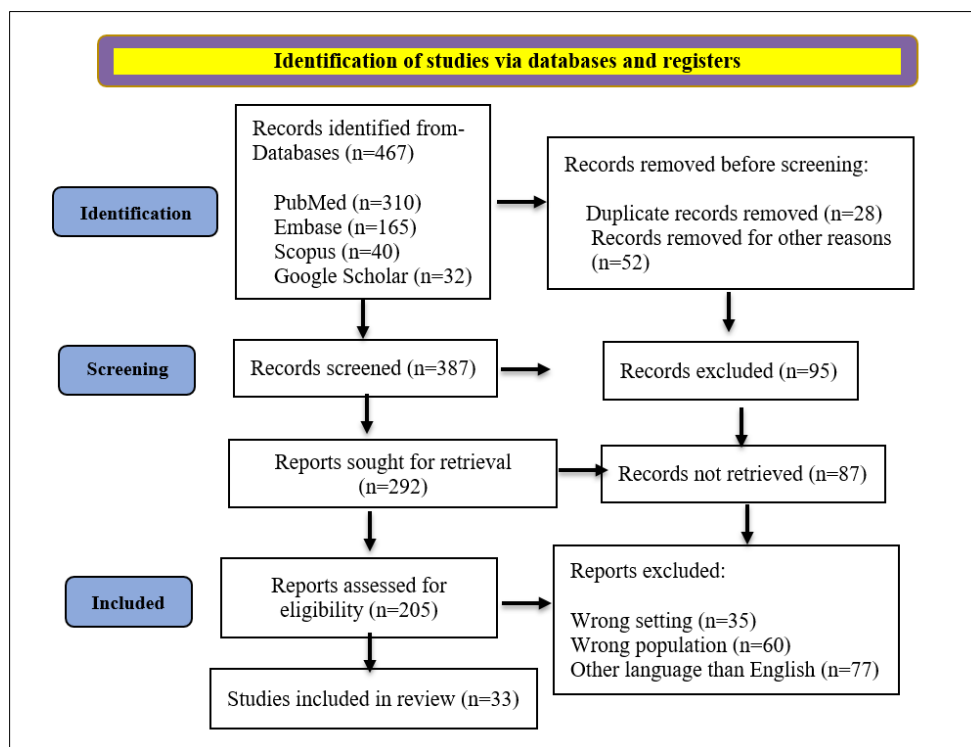
## DISCUSSION

### *Clinical setting and pathology correlation*

A decline in postural and balance was related to specific anatomic and physiological changes within sensory and motor centers involved in vestibular function.<sup>16</sup> Age-related vestibular loss is associated with degeneration of different neuronal structures including vestibular receptors, central vestibular neurons, cerebellum, and

proprioceptive and visual pathways as seen in Table 1.<sup>17-24</sup> Part of these structures are involved in one of the most critical structures of balance, the inner ear, which plays a role in functions such as acceleration, rotation, vertical and horizontal movements generation.<sup>1</sup> Functionally the greatest deficit appears to be on the semicircular canals, whereas the utriculus and sacculus function remains less involved. However, this is a multifactorial condition,

including microvascular changes, demineralization in bone structures, and degeneration on sensory receptors associated with mass reduction and destruction of ciliary and neural elements.<sup>24-27</sup> These are the most relevant histopathologic findings according to 13 histopathological studies in several areas involved in balance (Table 1).<sup>25,26,28-31</sup>



**Figure 1: Flowchart of review process of clinical and otopathologic findings on age-related vestibular loss.**

### Clinical manifestations

Clinical manifestations of age-related vestibular loss include a variety of symptoms that may vary from individual to individual, some of them usually rise after an acute episode of intense rotatory vertigo known as a unilateral vestibulopathy, some others are more obvious after some recidivate episodes of benign paroxysmal positional vertigo. In other cases, the onset of age-related vestibular loss remains unknown.<sup>32</sup>

Patients after these episodes usually present impairment of dynamic visual acuity, inability to compensate head and eye movements, altered perception of clearances and impaired proprioception when walking or swaying.<sup>32</sup> These symptoms are mostly common in the first phase of age-related vestibular loss. Furthermore, with the development of a chronic phase, comes intolerance and insecurity with movement, and gait instability which correlates with the development of vestibulo-ocular reflex (VOR) asymmetry and may be an important predictor of falling.<sup>32</sup> Compensation mechanisms become less functional and even weaker throughout time due to the degeneration of multiple non-vestibular systems, which

include somatosensory pathways, limbic pathways, loss of Purkinje cells from the cerebellum, decrease on vibration and sensation thresholds, proprioception disturbances, muscle strength, and visual accuracy.<sup>6</sup>

The onset of age-related vestibular loss in humans is usually based on audiometric and clinical findings, but findings in histopathology studies usually report changes in older patients.<sup>17-26,28-30</sup> The loss of cochlear function is described in pure tone audiometry at around 40 years old. While the saccular function decline is usually revealed by altered cervical vestibular evoked myogenic potentials (cVEMP) on the superior semicircular canal in patients above 55-years-old. Similarly, the decline of the horizontal canal function is based on diminished gain and asymmetries on the video head impulse test (VHIT).<sup>33,34</sup> Usually, functional changes are seen in the utricular function around 70 years of age, according to some studies based on ocular vestibular evoked myogenic potentials (oVEMP) testing.<sup>33</sup> Other structural changes such as striaal atrophy in the apical turns of the cochlea and loss of vestibular ganglion neurons related to loss of vestibular hair cells are usually seen after 30 years of age, being the first structures to be involved in the vestibular system aging (Table 2).<sup>33</sup>

Besides hearing and vision loss in elderly patients, vestibular impairment is considered a progressive, bilateral, and partial loss of vestibular function.<sup>32</sup> Age-related vestibular loss could present as unilateral, asymmetric or bilateral loss.<sup>32</sup> This is usually attributed to degenerative changes and more frequently presented in patients with cardiovascular, neurologic, sensory, psychological, and medication-related problems.<sup>32,35</sup> Other conditions can contribute to age-related vestibular loss including changes in the visual system, proprioceptive sensors, and cognitive impairment. The visual system can present changes in patients with age-related vestibular loss. In addition to visual acuity, functions such as depth perception, accommodation, contrast, sensitivity, and dark adaptation could decline with age.<sup>36</sup> Depth perception and contrast sensitivity have been described as the most important visual impairments that may contribute to falls.<sup>36</sup> These impairments may affect the ability of elderly patients to accurately avoid obstacles and keep straight in short and long distances.<sup>36</sup> Besides this, other findings in elderly patients are associated with deterioration of the dynamic visual acuity and the complaint of blurred vision during head movements, which increases with age and may be related to vestibular-ocular reflex degeneration.<sup>36</sup>

The proprioceptive sensors in muscles, tendons and joints are also associated with age-related vestibular loss.<sup>37</sup> Vibration and touch thresholds decline, and the inability to detect position and direction of joint movements are some of the irreversible changes on the proprioceptive system related to age.<sup>37,38</sup> Other studies have demonstrated a decrease in postural stability when proprioception input is altered providing inaccurate information regarding orientation.<sup>39</sup> Functional magnetic resonance imaging studies have shown that older adults exhibited less strength in the vestibular cortex activation, deactivation at motor centers in gray matter instead of activation patterns, and less activation and progressive deactivation at somatosensory and visual cortex. Older adults rely more strongly on vision for balance and in proprioception, however age-related changes on proprioception may lead to changes in postural instability, which are associated with a decline in muscle mass starting from the sixth decade, also a decline in compensatory muscle response, including co-contraction of muscles to maintain balance are diminished since sixth to seventh decade.<sup>40</sup> These changes can affect power, strength, force, and speed in lower limbs increasing the risk of falling.<sup>39</sup>

Another factor related to aging involved in age-related vestibular loss is the degeneration of the cervical spine as well as reduced hip motion, reduced angular velocity of the lower trunk, increased anterior pelvic tilt and hip extension that disturbs postural control and may contribute to falls.<sup>27</sup>

Cognitive impairment has also been implicated in age-related vestibular loss.<sup>38</sup> The cerebellum which plays a critical role on vestibular nuclei inputs and adaptation of the vestibular pathways suffers multiple changes associated with aging including volume decrease and decline on the density of the Purkinje cells and the floccular nodule lobe white matter.<sup>41</sup> Studies have found that elderly patients performed poorer on dynamic spatial navigation tasks and had a lower performance on neurocognitive tests of spatial and navigational condition.<sup>38</sup> Impaired spatial memory was associated with hippocampal atrophy in patients suffering from vestibular conditions such as Meniere’s disease.<sup>42</sup> Greater errors in angle rotation on a path integration task have been also described in these patients as other impairments in daily tasks related to short-term memory, difficulties with word retrieval, attention, inability to prioritize tasks and executive functioning.<sup>38</sup> Studies have also found that poorer scores on neurocognitive tests were associated with reduced saccular function, vestibular alterations such as vertigo were also associated with memory loss and confusion in cross-sectional analyses.<sup>42</sup>

**Diagnosis**

Diagnosis can be complex in elderly patients, as a systemic decline starts with aging.<sup>43</sup> A clinical history should be taken from the patient supporting their history with the experiences of caregivers, family or allied healthcare professionals; this should include demographic information, time of onset, intensity, duration of symptoms, clinical signs, cognitive and vestibular testing.<sup>44</sup> Different testing to evaluate balance and compensatory mechanism are suggested such as comprehensive evaluation, low complexity and quick screening alternatives.<sup>43,45</sup> Evaluating the integrity of multiple systems which play a key role on vestibular function or may lead to a differential diagnosis are also recommended and may vary according to each patient, some of the additional assessments that may be done are vision integrity, proprioception, musculoskeletal system, ocular motor pathways, cardiovascular assessment, and psychogenic evaluation (Table 3).<sup>32,46</sup>

**Table 1: Age-related vestibular loss reported histopathologic changes.**

Anatomical region	Structure	Anatomical changes
<b>Bony labyrinth Semicircular canals</b> <sup>78</sup>	Bone	Demineralization
	Hair cells	Decreased
	Type I and type II	Decreased
<b>Sacculle</b> <sup>17</sup>	Hair cells	Decreased
	Type I and type II	Decreased
	Ampulla hair cells	Decreased and degenerated

Continued.

Anatomical region	Structure	Anatomical changes
		Destruction of ciliary elements
	Otoconia	Degenerated – reduction in mass and fracture and fragment formation
<b>Utricle</b> <sup>17,18</sup>	Hair cells	Decreased
	Type I and type II	Decreased Afferent fibers loss in the calyceal innervations in the utricular extrastrisolar region
	Otoconia	Degenerated – reduction in mass and fracture and fragment formation
	Ampulla hair cells	Decreased and degenerated Destruction of ciliary elements
<b>Vestibular ganglion cells</b> <sup>20</sup>	Superior vestibular ganglion cells	Decreased compared with inferior ganglion cells counts
<b>Vestibular nucleus</b> <sup>21,22</sup>		Decreased
<b>Medial</b> <sup>23</sup>	Neurons Commissural fibers	Decreased + Lower neuron density
<b>Inferior a</b> <sup>23</sup>	Neurons	Decreased ++
<b>Lateral</b> <sup>24</sup>	Neurons	Decreased +++
<b>Superior</b> <sup>79</sup>	Neurons	Decreased ++++
<b>Vestibular nerve</b> <sup>79</sup>	Hair cells	Decreased
<b>Cerebellum</b> <sup>28,29</sup>	Purkinje cells (cerebellar vermis and flocculonodular lobe)	Decreased 2.5% per decade Decreased
	Cerebellar volume	Loss of myelination
<b>Other central nervous system structures</b> <sup>30,31</sup>	Brainstem vestibular nuclei neurons	Neurons reduced

+ = Mild, ++ = moderate, +++ = severe, ++++ = profound change

**Table 2: Clinical testing findings of patients with age-related vestibular loss and their clinical correlation.**

Testing	Findings
<b>Rotatory chair</b> <sup>62,80</sup>	Reduced vestibulo-ocular reflex gain to higher stimulus velocities, vestibulo-ocular reflex asymmetry, decreasing time constant, longer time constant asymmetry
<b>Videonystagmography</b> <sup>25,62,64-68</sup>	Decreased slow phase velocity, increasing preponderance, increasing slow-phase velocity to maximum age and posterior slight decline, lower nystagmus frequency and higher nystagmus amplitude, significant declines in vestibulo-ocular reflex fixation suppression with advancing age, increased in slow-phase velocity of the induced nystagmus (particularly in response to warm irrigations), poorer fixation index, smooth pursuit significantly reduced in elderly mainly between 66-87 years, saccadic tracking with peak eye velocities reduced, reduced optokinetic gain for elderly over 70 years with increased latency to circular vection, increased asymmetry and decreased torsional nystagmus
<b>vHIT</b> <sup>69-71,81</sup>	Diminished visual accommodation and depth perception and ability to suppress nystagmus by visual fixation; increased saccade latency, reduced tracking velocity, steady asymmetrical decreased of sensing angular rotation
<b>cVEMP</b> <sup>60,72,82</sup>	Decreasing absolute amplitude by 0.14 μV per decade, increasing threshold, significant decline in absolute P1g-N1 amplitudes, decreasing N1 latencies
<b>oVEMP</b> <sup>55,56</sup>	Decreased amplitude in patients over 70, reduction in amplitude by 2.9 μV per decade of life and increased in latency of 0.12 ms per decade of life
<b>Subjective visual vertical (SVV)</b> <sup>57</sup>	Deviated
<b>Posturography</b> <sup>83</sup>	Decreased capacity for compensation by other inputs to maintain postural stability

vHIT: The video head impulse test; cVEMP: cervical vestibular evoked myogenic potentials; oVEMP: ocular vestibular evoked myogenic potentials; SVV: subjective visual vertical



**Table 3: Diagnostic test for age-related vestibular impairment.**

Test	Description
<b>Electronystagmography or videonystagmography</b>	Which record eye movements in different settings and may include target following, rapid eye movement, light and dark setting responses. <sup>43</sup>
<b>Rotatory chair test</b>	Where eye movements are recorded measuring the head and eye coordination to different speed movements. <sup>43,45</sup>
<b>Computerized dynamic visual activity</b>	Which helps evaluate the compensatory mechanism developed during vestibular alterations. <sup>44</sup>
<b>Computerized dynamic posturography</b>	Evaluates the integrity of visual, somatosensory, and vestibular systems for balance. Allows the assessment of the non-vestibular proprioceptive components and central integration. <sup>45</sup>
<b>Vestibular evoked myogenic potential</b>	Evaluated the functional integrity of the inner ear organs (utricle and saccule function independently) and the vestibular nerve. <sup>84</sup>
<b>Video head impulse test (vHIT)</b>	Widely used to evaluate the function of each of semicircular canals individually, through the eye rotation response measure to sudden head rotation in the canal plane. Adequacy is measured with the ratio of eye movement response to head movement stimulus or vestibulo-ocular reflex (VOR). As mentioned, before vestibular receptors decrease with age, which suggest a decline in VOR with age, however compensatory mechanisms on the cerebellum may be related with the integrity of the system despite the VOR decline. <sup>6,44,45</sup>
<b>Dynamic visual acuity (DVA)</b>	Even though visual acuity is an indirect measure of vestibular function, it is the threshold for recognizing alterations of optotype during head movement and can be evaluated with VOR as an indicator of decreased balance performance. <sup>44</sup>
<b>Low complexity and quick screening alternatives</b>	
<b>Bucket method</b>	Evaluate tilt of the subjective visual vertical (SVV) which is one of the most sensitive signs of vestibular tone imbalance and can imply lesions of the vestibular pathway centrally or peripherally. <sup>43</sup>
<b>Romberg test</b>	Which evaluates balance and sensory interaction and can be done with the patient standing on a medium density compliant foam with arms and eyes closed. <sup>84</sup>
<b>Fukuda stepping test</b>	Screening test of path integration, where the patient walks with his eyes closed measuring the amount of rotation or translation. <sup>44</sup>
<b>Additional assessment</b>	
<b>Vision integrity</b>	Evaluating static and dynamic visual acuity checking for both monocular and binocular vision
<b>Proprioception</b>	Temperature, pain, and vibration thresholds where lower extremity weakness may be present, evaluating for neuropathies
<b>Musculoskeletal system</b>	Evaluate tone, strength, posture, coordination, tandem and walking patterns.
<b>Ocular-motor pathways</b>	Evaluate gaze, nystagmus, saccade, tracking assessing both accuracy and velocity
<b>Cardiovascular assessment</b>	Look for sudden or postural blood pressure changes, changes in heart rhythm and heart sounds
<b>Psychogenic evaluation</b>	Mini-mental state examination, cognition, affective state, and handicap questionnaire

**Differential diagnosis**

When evaluating age-related vestibular loss, differential diagnosis should be evaluated. Cardiologic and neurologic evaluation have been suggested to be a confounding diagnosis in some cases and are in need to differentiate in several patients. Some conditions may mimic age-related vestibular loss and some of their symptoms are quite similar to those usually seen in elderly patients such as: immune diseases such as Cogan syndrome, which is a rare primary vessel vasculitis with systemic involvement in most cases, which manifest with vestibulo auditory and ocular symptoms, which can be differentiated to age-related changes due to its acute onset.<sup>46,47</sup> Vestibular neuronitis, which may be own acute viral inflammatory conditions or previous viral infections.<sup>46</sup> Transient

ischemic attack or stroke of the vertebrobasilar artery which involves the vestibular nerve tracts, brainstem, or cerebellum.<sup>46</sup> Neurodegenerative disorders, which increase on prevalence with aging and may include a variety of diseases such as: Alzheimer’s disease, where spatial disorientation and balance alteration is common.<sup>8,37,42</sup> Parkinson’s disease that courses with postural unsteadiness and increased postural sway. Demyelinating diseases such multiple sclerosis, which can affect vestibular pathways, downbeat and upbeat Nystagmus syndromes which present with unsteadiness of gait and vertigo.<sup>46</sup> Other conditions may present with similar features as vestibular impairment such as cardiovascular conditions such as arrhythmias, postural hypotension, congestive heart failure, and heart valves pathologies, multimodal balance disorder, primary or

secondary neoplasia, somatoform vertigo and psychiatric dizziness, late onset Meniere's disease, labyrinthitis, temporal bone fracture, vestibulotoxic medications like gentamicin, and streptomycin.<sup>46</sup> In addition, some medications that can mimic vestibular symptoms such as: antihypertensives, benzodiazepines, hypnotics, anxiolytics, antiplatelets.<sup>46</sup>

### **Management of age-related vestibular decline**

Different modalities of interventions are available for improving and rehabilitating vestibular decline on elderly.<sup>47,48</sup> All systems involved in gait, balance, and movement must be assessed which include vestibular and non-vestibular pathways. Some of the interventions that have been proven effective on balance are vitamin D supplementation, Tai Chi and exercise.<sup>49</sup> As one of the main risks is falling, innovative interventions such as virtual-reality systems, like balance rehabilitation unit (BRU) have been evaluated to improve balance performance.<sup>50</sup> BRU is a recently valeted method which combines variable conditions (somatosensory, visual, and vestibular) to train and assess balance. The assessment component, through posturography, determines postural control under varying visual stimulation with the patient standing on different firmness surfaces, the test hopes to stress balance, visual and vestibular pathways in a supervised environment with less physical effort than exercise balance programs. Duque et al found that patients that complete BRU-training protocols showed significant reduction in the incidence of falls, and increased limits of stability.<sup>50</sup>

On the other hand, classical vestibular exercises developed by Cawthorne and Cookey can also be useful, and included a series of standardized exercises with eye and head movements, bending, tossing a ball and walking.<sup>49,51,52</sup> Current vestibular rehabilitation is an exercise-bases approach, which includes four different components: exercises to promote gaze stability based on vestibulo-ocular reflex adaptation and substitution, which main objective is to decrease symptoms and promote vestibular adaptation by maintaining focus on a steady or moving target.<sup>51</sup> Exercises to habituate to symptoms: which aim for a decrease in response (like dizziness) with repeated exposure to a provocative stimulus. Training balance and gait, done under challenging conditions both sensory and dynamic, indented to facilitate the use of sensory/visual cues to compensate for missing vestibular function and walking for endurance, and aerobic exercises to improve musculoskeletal strength and to avoid physical limitations often due to symptoms of vestibular origin.<sup>49,51</sup>

### **Implications for practice**

Age-related vestibular loss comprises several functional and histopathologic changes (Tables 1 and 2).<sup>53</sup> A decline in functioning on structures such as semicircular canals, utricle and saccule are supported by otopathologic findings. Demonstrating a severe decline and degeneration

of vestibular hair cells (type I and II) and otoconial mass decline with fracture and fragment formation, which may explain rotational and acceleration disturbances on elderly patients and more frequent presentation of vestibular disorders such as benign paroxysmal positional vertigo (BPPV) over 50 years of age.<sup>41,54</sup> These findings are objectively represented in oVEMPS, cVEMPS and subjective visual vertical supporting a decreased amplitude, thresholds, and latencies over decades.<sup>55-57</sup> Further studies using new diagnostic and less invasive diagnostic tools such as the ocular counter roll test, will benefit the in-patient and out-patient evaluation and would provide information about the otolithic function in elderly patients.<sup>58</sup>

The otolith organs (which comprises the utricle and saccule) are responsible for linear acceleration and enable the two-dimensional spatial orientation in stationary subjects and the three-dimensional spatial orientation in mobile subjects. On the other side, semicircular canals are involved in sensing angular acceleration.<sup>37</sup> Both during rotational and linear acceleration, the cupula or the otolith mass displace the hair cells, causing the needed depolarization and hyperpolarization for the vestibulocochlear nerve to conduce the input to the vestibular nuclei and the integration centers for vertical and torsional eye-head coordination in the midbrain and the thalamus.<sup>37,40</sup> The most common cause of hearing and balance dysfunction is precisely the loss of the hair cells from the sensory epithelia, as mentioned before. Fusion and thinning of stereocilia associated with defects on spine and myosin VI can lead to autophagy of hair cells and hair cell loss due to detachment of the apical membrane of the hair cell from the cuticular plane, which may be owned to the lack of maintenance of stereocilia and have been observed in elderly associated with aging, as expected the fused stereocilia is also unable to work properly and may precede the hair loss.<sup>53</sup>

Moreover, the semicircular canals decline has been found to be even greater than the decline on the otolith function, evaluated through the angular vestibulo-ocular reflex (VOR) which can be evaluated with the rotating chairs or by caloric ear stimulation (Tables 1 and 2). Carol et al found that VOR remained stable until age 79, however it declined significantly at a rate of 0.012/year in later stages of life.<sup>59</sup> Agrawal et al study described a significant decline in dynamic visual acuity with testing of the semicircular canals, which correlated with decline in the utricular function in individuals aged 70 years or more.<sup>60</sup> There is also evidence regarding vestibular cell receptor loss, with primary afferents increase, which would also suggest a decline in VOR with aging.<sup>61,62</sup>

Even though, a decline in critical structures such as neurons, commissural fibers and purkinje cells in vestibular nuclei, evidence indicates that aging does not affect the volume or length of the vestibular nuclear complex. A neuronal loss is seen in the descending, medial, and lateral vestibular nuclei, but not in the superior

nuclei, which could be related with the problems that elderly people have to compensate unilateral vestibular lesions and the alterations of the vestibulospinal reflexes.<sup>63</sup> Many clinical vestibular testing studies on age-related vestibular loss have failed to identify any significant physiologic evidence linked to otopathologic changes.<sup>17,18,20-22,24</sup> In fact, some clinical measures have paradoxically reported an increase in VOR response rate at a time when histologic reports are the opposite.<sup>25,62,64-68</sup> Decrease on vestibular nerve conduction velocity was also found, with initial microscopic changes found as early as age 40, which can also lead as it was mentioned above to VOR impairment.<sup>41</sup>

The preservation of superior vestibular nuclei neurons can explain why vestibulo-ocular reflexes are compensated after unilateral vestibular injuries.<sup>63</sup> Functioning of structures in the central nervous system such as the pons, vestibular nuclei and oculo-motor centers are critically involved in balance.<sup>25,62,64-68</sup> Results given in videonystagmography are also useful to understand how aging alters basic ocular functions such as fixation, saccades generation, pursuit and tracking.<sup>62</sup> Besides the decline in the ocular neurons, studies focusing on eye muscles have demonstrated fewer fibers and less strength when aging processes start around 40 years.<sup>25,62,64-68</sup> This could be the result of the combination of the central nervous system degeneration and eye muscle atrophy that contribute to the decline in the vestibulo-ocular reflex.<sup>50,62,64-67</sup> Future challenges for diagnosing age-related vestibular loss, include a better understanding of caloric responses and VBIT combined with posturography and functional magnetic resonance (fMRI).<sup>69-72</sup>

Age-related vestibular loss still is a challenging condition.<sup>73</sup> As older adults experience vestibular decline differently from younger patients, atypical signs and symptoms may develop which include chronic disequilibrium instead of brief episodes of rotatory vertigo.<sup>51,52,74,75</sup> Furthermore, complex life changes may be encountered with vestibular decline, which may elicit some beneficial and pathological compensations regarding somatosensory pathways.<sup>75,76</sup>

However, due its major impact not only on mobility but on mortality as instability changes may lead to over 50% of accidental deaths own to falls, its management must be conducted using a multidisciplinary approach including medical and physical therapy experts.<sup>48,77</sup>

In the future, having a targeted treatment focused on VOR adaptation exercises could help to control the central system response. It could also include habituation exercises to reduce pathologic responses to a provoking stimulus and substitution exercises to promote the use of the active and remaining sensory system.<sup>49,51</sup> This management could help to decrease the progression of the clinical and pathologic findings described in this scope review.

## CONCLUSION

Age-related vestibular loss involves several anatomical, functional and histopathologic changes starting over 40 years of age. Clinical and histologic findings reveal degeneration, decreased cell population to the ear, and anatomic changes involving vision, proprioception and cognitive decline. Vestibular testing is consistent with clinical and histologic findings. Further studies are needed to correlate results with newer diagnostic tools in elderly population.

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