Development of a Statistical Model for the Prediction of Common Vestibular Diagnoses

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IMPORTANCE Treatment of patients with vestibular disorders can be complex, requires lengthy clinic visit time, and uses greater clinical resources for diagnosis. A pre-encounter intake questionnaire may predict the most common disorders, allowing for more efficient allocation of resources and use of clinicians.

OBJECTIVE To develop a statistical model for predicting vestibular diagnoses, prior to clinical evaluation, from an intake questionnaire.

DESIGN, SETTING, AND PARTICIPANTS Retrospective review of 414 consecutive new vestibular patient intake questionnaires (September 2012 through January 2014) and associated medical records with performance of logistic regression analyses and development of predictive models (July 2013 through May 2015).

INTERVENTIONS Use of a vestibular intake questionnaire for triaging of new patients with complaints of dizziness.

MAIN OUTCOMES AND MEASURES Predictors for the diagnosis of benign paroxysmal positional vertigo (BPPV), Ménière's disease, and vestibular migraine.

RESULTS Of the 414 questionnaires analyzed, 381 (92%) had clinician information necessary to define a final diagnosis. Patients were 34% male and had a mean (range) age of 57 (19-91) years. Of the diagnoses, 183 (48%) were ear related (including 103 BPPV and 49 Meniere’s disease), 141 (37%) neurological (including 109 vestibular migraine), 36 (9%) medical, 8 (2%) of psychological origin, 46 (12%) of unknown etiology, and 33 (9%) other causes. The diagnosis of BPPV could be predicted from 4 variables with a sensitivity of 79% and specificity of 65%. The diagnosis of Ménière’s disease could be predicted from 5 variables with a sensitivity of 81% and specificity of 85%. The diagnosis of vestibular migraine could be predicted from 4 variables with a sensitivity of 76% and specificity of 59%.

CONCLUSIONS AND RELEVANCE A pre-encounter history questionnaire can provide useful diagnostic information for common vestibular disorders. This can help direct appointment scheduling to improve clinical efficiency, time to intervention, and use of resources. Further refinement may enable the use of shorter questionnaires or screening algorithms.
Dizziness is among the most common chief complaints among patients presenting to frontline clinicians.1,2 Whereas dizziness is a symptom with many causes, evaluation by an otolaryngologist is commonly recommended. Treatment of patients with vestibular disorders is complex, requires additional clinic time, and uses greater resources (eg, videonystagmography [VNG], rotary chair). Many patients are found not to have otologic disease, leading to patient and clinician frustration and delays in diagnosis.

Patient history plays a critical role in the evaluation of vestibular complaints.3,4 The nature of the dizziness (ie, vertigo, lightheadedness, imbalance), the temporal pattern of the dizziness (ie, single episode, recurrent), the duration of attacks (ie, seconds, hours), and associated symptoms (ie, hearing loss, headache) can identify otologic vs nonotologic disease, and even a specific diagnosis.5 Physical examination may help establish a vestibular diagnosis but often has normal results. Similarly, vestibular testing may be useful in establishing a diagnosis but requires a narrow differential diagnosis for correct test selection and interpretation of test results.3

A questionnaire focusing on key elements of the history may provide adequate information for development of a narrow differential diagnosis prior to the office visit.4,6 Our program began using a vestibular disorders intake questionnaire in September 2012. This 10-page questionnaire was designed as a quality improvement measure to provide more efficient and timely care to patients. The results of the questionnaire have been used to direct appointments (eg, to physician, vestibular therapist, nurse practitioner, neurologist) and to inform choice of testing (eg, VNG, rotary chair, posturography, vestibular evoked myogenic potentials [VEMPs]). Many sources (eg, video-nystagmography [VNG], rotary chair). Many patients are found not to have otologic disease, leading to patient and clinician frustration and delays in diagnosis.

We performed data analyses of the triage questionnaire. This study used 414 consecutive patient questionnaires for descriptive analyses and predictive model building. Results of this study may be generalized to practice management for allocating resources and improving efficiency of patient evaluation.

Methods
Approval was obtained from the Medical College of Wisconsin institutional review board. Informed consent was waived due to the retrospective nature of this study. This project analyzes a clinically used intake questionnaire specifically designed to triage new patients with vestibular disorders.

Questionnaire
The questionnaire was developed at Mayo Clinic and was modified slightly before being implemented in our institution. A total of 162 data variables were captured from each questionnaire. The questionnaire captures demographic information including medical, family, and social history, and current medication use. There are sections that focus on:

1. The nature of the dizziness perception. This includes a series of check boxes to describe the dizziness, and questions as to the onset, duration, and frequency of spells (episodes), triggers for spells, and the relationship of spells to motion.
2. Headache, migraine, and migraine-associated symptoms.
3. Otologic problems including hearing loss, tinnitus, aural pressure, otalgia, and otorrhea.
4. Prior tests and results including audiograms, imaging, VEMPs, VNG, rotary chair, cardiac Holter monitors, tilt table testing, and so forth.

Predictive Model Development
The development of predictive models for the diagnosis of benign paroxysmal positional vertigo (BPPV), Ménière’s disease, and vestibular migraine incorporated an initial data set for identifying key variables for further data collection and a large data set for predictive model building. The initial group consisted of 212 consecutive new patient intake questionnaires. All variables and fields were collected from these questionnaires for analysis. We initially tried to develop models using all available variables, but this resulted in complex algorithms with unsatisfactory sensitivity and specificity. By repetitively narrowing the data set, and checking for improvements in sensitivity and specificity, we identified a set of factors with strong correlation with specific diseases. A subsequent 202 consecutive questionnaire were then interrogated for this narrow set of variables. These variables from the combined 414 questionnaires were then analyzed to build the statistical models for diagnosis predictions.

Statistical Analysis
The initial data set was screened to identify variables using 3 criteria: (1) significant (P < .05) association with the 3 diagnoses, (2) sufficient number of observations (≥5 per cell after cross-tabulation with the outcome), and (3) clinical importance and relevance. All variables were converted into dichotomous form (ie, 0 = absent; 1 = present).

The final data set had information on 414 individuals, of which 381 were ultimately fully evaluable (see Results). Logistic regression analyses were performed to build parsimonious predictive models with model variables significant at P < .05. All 2-way interactions between significant model variables were investigated for statistical significance. A forward stepwise variable selection procedure was used. The 3 final parsimonious models included only variables significant at the P < .02 level, more stringent than the initially planned significance cutoff of .05. The receiver operating characteristic (ROC) curve, area under ROC curve, sensitivity, and specificity at selected cutoffs (ie, linear predictor [LP] values) were assessed using 10-fold cross-validation.

The statistical analysis was performed using the open-source software R, version 3.1.1 (http://www.r-project.org). Two-tailed Wald tests were used for statistical significance testing.

Results
Of the 414 questionnaires analyzed, 381 had clinical information necessary to define a final diagnosis (Figure). Of these, 183
(48%) were ear related, 141 (37%) neurological, 36 (9%) considered medical, 8 (2%) believed to be of psychological origin, 46 (12%) of unknown etiology, and 33 (9%) of other causes. Of those deemed ear related, the majority were BPPV (57%), followed by Ménière's disease (27%), vestibular neuronitis (8%), bilateral hypofunction (8%), labyrinthitis (6%), and labyrinthine fistula (perilymph fistula or superior semicircular canal dehiscence) (2%).

Of the 141 patients with conditions judged to be neurological, 118 had a specific diagnosis. These consisted of migraine (92%) and traumatic brain injury/postconcussive syndrome (9%). Thirty-three patients with migraine were further classified as having visual vertigo (23 [70%]), severe motion sensitivity (7 [21%]), and mal de debarquement syndrome (3 [9%]). Nonneurological medical diagnoses (9% of total) included orthostasis and cardiogenic causes, and represented 28% and 44% of this category, respectively.

**BPPV**

A total of 103 patients had BPPV. All were seen and evaluated by a clinician to confirm the BPPV diagnosis. In some patients, symptoms had resolved by the time of evaluation, but a clinically obtained history, rather than just the questionnaire, suggested BPPV as the definitive diagnosis.

As expected, 78% of those with BPPV indicated that lying down and/or rolling in bed was a trigger compared with 32% of those without BPPV ($P < .001$). Similarly, 78% of those with BPPV described their dizziness as vertigo compared with 57% of those with other diagnoses ($P < .001$). Reported duration of attacks was also significantly different, with 48% of patients with BPPV indicating a duration of seconds whereas only 15% of those without BPPV indicated a duration of seconds ($P < .001$).

Those with BPPV were more likely to say that the dizziness was not continuous ($P = .01$) and that it occurred when they moved ($P = .04$). Those without BPPV were more likely to indicate that automobile rides or loud sounds were triggers than those with BPPV ($P = .002$ and $P < .001$, respectively). Stress as a trigger was also significantly more prevalent in those without BPPV ($P = .003$). Those with BPPV were less likely to exhibit hearing loss than those with other diagnoses, 42% to 61% ($P = .005$).

**Ménière's Disease**

There were 49 patients evaluated in the clinic with confirmed Ménière's disease meeting probable or definite criteria.$^{24}$ Those with Ménière's disease, compared with those without, were more likely to describe their dizziness as vertigo, 86% to 59% ($P < .001$). They also were most likely to indicate duration of attacks as minutes to hours, with 75% choosing this option.

Hearing loss is a hallmark of Ménière's disease, and 96% of the patients with Ménière's disease indicated that they had documented hearing loss compared with only 49% of those without Ménière's disease ($P < .001$). Fluctuating hearing also strongly favored patients with Ménière's disease, with 46% noting changes in hearing as opposed to only 6% of patients with other disorders ($P < .001$).

**Vestibular Migraine**

A total of 109 patients were ultimately believed to have vestibular migraine. Diagnosis was based on clinical impression, which generally follows defined diagnostic criteria for vestibular migraine.$^{9,10}$ As expected, those with vestibular migraine had a higher likelihood of self-reporting migraine than those with other vestibular conditions, 42% to 22% ($P < .001$). Photophobia with a headache was reported in 80% of those with a diagnosis of vestibular migraine compared with 37% of those with other conditions ($P < .001$). Similarly, other migraine symptoms also showed increased prevalence in those with vestibular migraine such as history of headache with nausea and vomiting ($P = .007$), unilateral headache ($P = .02$), and throbbing headache ($P = .008$).
There was a significantly higher response that visual and motion stimuli could trigger dizziness in patients with vestibular migraine. Automobile rides (P < .001), reading (P = .001), going through aisles and/or tunnels (P = .003), and turning when walking (P = .002) were all more commonly noted as triggers. In addition, stress (P = .03) and association with menstrual cycle (P = .01) were slightly more common in those believed to have vestibular migraine.

**Predictive Model Building**

**BPPV**

The variables predicting BPPV related to triggers for dizziness, the nature of the dizziness, and the timing of spells. In particular, having dizziness described as vertigo and indicating lying down and/or rolling over as the main trigger were the strongest positive predictors. The other main predictors were related to duration of spells (Table).

The questionnaire had 4 check boxes for duration of spells: (1) seconds to minutes, (2) minutes to hours but less than 24 hours, (3) days but less than a week, and (4) days, and can be continuously for weeks. A patient with BPPV would be expected to choose category 1, and indeed this was selected by 48% of patients with BPPV. However, 33% chose minutes to hours and approximately 10% chose each of the longer durations. As such, duration of seconds to minutes was not a positive predictor on its own. Therefore, the model uses longer-duration spells to negatively affect the predictive formula, thus strengthening the relationship between short spells and BPPV. The formula identified for the linear predictor (LP) of BPPV is thus, $LP = -2.19 + 1.87 \times (\text{Lying Down or Rolling Over}) + 0.92 \times (\text{Vertigo}) - 0.98 \times (\text{LOS: Minutes to Hours}) - 1.11 \times (\text{LOS: Days}) - 1.84 \times (\text{Vertigo}) \times (\text{LOS: Days to Weeks})$.

In this formula, if the variable is present it is replaced by “1” and if not present replaced by “0.” For example, if the patient indicates dizziness with rolling over, vertigo, and spells lasting days, the formula computes as $LP = -2.19 + 1.87 + 0.92 - 1.11$, which equals –0.51. The LP is then transformed into an estimated probability of BPPV with the following formula: $\text{Pr}(\text{BPPV}) = \exp(\text{LP})/(1 + \exp(\text{LP}))$.

For example, $\text{LP} = -0.51$ translates into a probability estimate of BPPV equal to 0.375. Cross-validation of this model confirmed good predictive properties with an area under the curve (AUC) of 0.76. At LP greater than or equal to 0.2, the cross-validated sensitivity for BPPV is 0.79 and specificity for BPPV is 0.65.

**Ménière’s Disease**

Positive predictors for Ménière’s disease included classification of the dizziness as vertigo and indicating a length of spell lasting minutes to hours. A strong predictor relating to hearing loss was having a documented history of hearing loss, in contrast to a perception of hearing loss. Furthermore, having unilateral tinnitus, in contrast to bilateral tinnitus or no tinnitus, was a strong predictive variable. Tinnitus in the right ear only was a slightly stronger predictor than tinnitus in the left ear. The resultant formula for the linear predictor of Ménière’s disease is thus,
Cross-validation of this model confirmed an ROC curve with AUC of 0.86. At LP greater than or equal to 0.15, the cross-validated sensitivity for Ménière’s disease is 0.81 and cross-validated specificity for Ménière’s disease is 0.85.

**Vestibular Migraine**

The nature of the dizziness was not a predictive variable for vestibular migraine. Patients with vestibular migraine noted many forms of dizziness including vertigo (69%), wooziness (60%), imbalance (70%), faint (57%), swimming sensation (34%), pulsion (23%), and other (9%).

The positive predictors for vestibular migraine related to a history of migraine, migraine aura symptoms, and motion sensitivity, which is frequently found in patients with migraine. Thus, the variables “Diagnosis of Migraine” and “Photophobia With Headaches” were both significantly related to vestibular migraine in contrast to other conditions. Also, selecting automobile rides as a trigger for attacks of dizziness was a strong positive predictor.

The effect of having a diagnosis of migraine and dizziness with automobile rides together skewed the balance between specificity and sensitivity in the model and required a negative correction factor if both were present. A negative predictor was also the indication that attacks last seconds. The final linear predictor for vestibular migraine is thus,

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LP = -7.08 + 1.78 \times (\text{Vertigo}) + 3.22 \times (\text{Documented Hearing Loss}) + 1.40 \times (\text{LOS: Minutes to Hours}) + 2.04 \times (\text{Tinnitus: Right Ear Only}) + 1.52 \times (\text{Tinnitus: Left Ear Only}).
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Cross-validation of this model confirmed good predictive properties with AUC of 0.65. At LP greater than or equal to 0.25, cross-validated sensitivity for vestibular migraine is 0.76 and cross-validated specificity for vestibular migraine is 0.59. Given the often vague or varied complaints of dizziness in vestibular migraine, it is expected that the specificity would be lower compared with other disorders.

**Discussion**

The efficacy of any questionnaire relies on accuracy in completing the form. The majority of patients were comprehensive in addressing all fields, but some were cursory. In these cases, an advanced practice nurse prescriber with training in vestibular disorders called the patient for further detail. Some of these cases seem to reflect patient attitude that the questionnaire is a formality to obtaining a physician appointment rather than a useful diagnostic tool.

Effectiveness of the questionnaire is also dependent on patient interpretation of the questions. For example, a number of patients with BPPV chose the prompt that dizziness lasts for days to weeks. We interpret this as a failure to distinguish between individual episodes and the period of time during which they have episodes. This confusion has been previously noted. This suggests that questionnaires may need follow-up questions to clarify answers or rigorous study to validate each field. Reliability may be improved with an electronic questionnaire using branching logic to ask additional questions if needed to clarify answers.

It is not clear whether the high association of some variables in this study is specific to the form in which they are presented to the patient. For example, the variable “lying down/rolling in bed” was a strong positive predictor of BPPV but was presented as a check box within a list of 17 potential triggers. Zhao and colleagues, using a questionnaire that primarily asked yes/no questions, also found that dizziness with lying down was a strong predictor of BPPV. Similarly, they found BPPV negatively associated with long attacks, vestibular migraine positively associated with light sensitivity, and Ménière’s disease positively associated with unilateral hearing loss or tinnitus. Whereas this may suggest good concordance with the present study, they also identified many variables that differed from those in this report. Therefore, the manner of presentation of the question may play a role in the utility of the questionnaire to predict specific conditions.

The strongest model was that predicting the diagnosis of Ménière’s disease. Similar high sensitivity and specificity have been found with other questionnaires for Ménière’s disease. This may reflect the strong association of hearing loss and tinnitus with Ménière’s disease. These conditions are easily recognized by patients and thus the data collection for these variables may be more accurate. Furthermore, the diagnostic criteria for Ménière’s disease include these conditions, thus increasing the probability of Ménière’s disease when present.

In contrast to Ménière’s disease, the model for predicting vestibular migraine had comparable sensitivity but low specificity. This may reflect the varied clinical nature of vestibular migraine and the weaker diagnostic criteria. For example, patients with vestibular migraine often describe dizziness as an “off” sensation that may be poorly interrogated by the questionnaire. Migraine is also significantly underdiagnosed, and therefore a key diagnostic criterion for vestibular migraine may be absent from many questionnaires. Furthermore, by means of written history, subtle distinctions that would enable vestibular migraine to be distinguished from persistent postural and perceptual dizziness can be missed. In fact, this study categorized visual vertigo and motion sensitivity as forms of vestibular migraine, which has been our traditional clinical practice, but which may be better considered to be persistent postural and perceptual dizziness (aka chronic subjective dizziness).

Limitations of this study include the use of a single center with the reliance on clinical impression, rather than strict diagnostic criteria, to obtain final vestibular diagnoses. A multicenter study with additional clinicians can better reflect the general clinical experience as regards these disorders. Statistically, we performed validation on the same data set as the model building. The internal cross-validation (10-fold cross-validation) partially addressed the validation issue but is not as robust as validation of the predictive models on external, or separately collected, data.
The goal of initiating a quality improvement project was to alter the clinical practice paradigm for vestibular disorders away from a physician-centric model. Barriers to this are patient and clinician acceptance of a potential nonphysician-based assessment and treatment encounter, limited evidence demonstrating efficacy and efficiency of such a program, and uncertainty in key areas of the clinical pathway used for guiding decision making. The results of this study can provide evidence for patients and referring clinicians as to the diagnostic accuracy of pre-encounter questionnaires and the potential improvement in clinical efficiency. Clinical efficiency is becoming an important metric used to evaluate clinician quality. Time to next appointment, enough time spent with the patient, and clinic on-time performance are all metrics being used by health care systems to measure the quality of services. Structured systems for triaging patients into those requiring a physician evaluation vs ancillary clinicians have been effective. In a primary care setting, access to the practice increased by almost 30% and more than 80% of patients triaged to a nonphysician clinician did not need to follow-up with a physician.20 Similarly, using a structured questionnaire as support for medical decision making for viral respiratory infection showed that military medics could reduce the need for physician referrals by 37%.21

Conclusions
The outcomes in this study have been used in our institution to improve access by using ancillary clinicians. For example, patients with BPPV can be seen within 1 week for vestibular therapy without waiting for a physician appointment. A similar triage model involving vestibular disorders has shown high patient satisfaction, likely due to simultaneous evaluation and treatment.22 In our practice, patients with substantial headache component and prediction of vestibular migraine are offered neurological consultation as a best first assessment. Freeing the otolaryngologist’s schedule from nonotologic patients with vestibular disorders may allow faster access for those predicted to have Ménière’s disease or other otologic conditions.

ARTICLE INFORMATION

Author Contributions: Drs Friedland and Tarima had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Friedland. Acquisition, analysis, or interpretation of data: Friedland, Tarima, Erbe, Miles. Drafting of the manuscript: Friedland, Tarima. Critical revision of the manuscript for important intellectual content: Friedland, Tarima, Erbe, Miles. Statistical analysis: Friedland, Tarima. Obtained funding: Friedland, Tarima. Administrative, technical, or material support: Friedland, Erbe, Miles. Study supervision: Friedland.

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