Patterns of Migraine Disease in Otolaryngology: A CHEER Network Study

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Abstract

Objective. To evaluate the prevalence of migraine disease in an otolaryngologic cohort and migraine-related otologic and sinonasal symptoms in this population.

Study Design. Cross-sectional study utilizing the CHEER (Creating Healthcare Excellence through Education and Research) network for recruitment.

Setting. Patients were recruited in a cross-sectional and pragmatic manner in 14 CHEER sites between June 2015 and March 2017 (9 academic, 5 community based).

Subjects and Methods. Patients were included if they were aged ≥ 18 years and seen for any concern that was not head and neck cancer. Patients with any history of brain abnormality or headaches that began within 2 weeks of a medical illness, trauma, or head injury were excluded. Patients were screened for migraine with a validated instrument. If they screened positive on the Migraine Assessment Tool (MAT), the subjects also filled out validated and custom questionnaires for sinonasal, otologic, and migraine-specific symptoms.

Results. Of 1458 patients screened, 235 (16.1%) screened positive for migraine (MAT+), which is higher than general population (13%, \( P < .001 \)). The MAT+ group was significantly younger (47.2 vs 55.6 years of age, \( P < .001 \)) and predominately women (80.0% vs 55.9%, \( P < .001 \)). The MAT+ cohort commonly reported ear- and sinus-related symptoms, such as tinnitus (70.5%), ear pressure (61.9%), balance problems (82%), facial pressure (85%), and rhinorrhea (49.9%). There were significantly higher levels of sinus burden with higher levels of dizziness handicap, Jonckheere-Terpstra test \( = 11,573.00, z = 7.471, P < .001 \).

Conclusion. Migraine disease has a higher prevalence in an otolaryngologic cohort than in the general population, presenting with a high rate of sinonasal and otologic symptoms that may be due to or exacerbated by migraines.

Keywords
migraine, headache, Ménière’s disease, sinusitis, dizziness, rhinosinusitis, vestibular migraine, benign paroxysmal positional vertigo, sinus headache, CHEER

Migraine is an inherited syndrome of abnormal neurologic activity in the central nervous system. Through a variety of mechanisms, migraine can cause or modify symptoms anywhere in the body but predominantly in the head and neck. Migraine is classically defined by the quality of head pain and the presence of associated neurologic symptoms, but it has become increasingly apparent that the cardinal symptom of head pain need not be present during a migraine episode. In fact, transformation of migraine symptoms can occur over the course of a patient’s life, with classic symptoms predominating in youth but later evolving into atypical symptoms with markedly reduced headache or no headache at all.

Over the past 30 years, clinicians have become increasingly aware of the various manifestations of migraine disease. A comparison of the first American Migraine Study (AMS)5 and the second (AMS II)6 established that the prevalence of migraine, affecting 18% of women and 6% of men, had not changed significantly, even as the disease gained more attention. While there was a modest increase in

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the diagnosis of migraine, approximately half of all migraine sufferers remained undiagnosed.\(^7\) Underdiagnosis of migraine is likely related to vague and indistinct clinical presentation of this disorder. In 2001 results from the AMS II indicated the leading migraine symptoms as pulsatile pain (85%), light sensitivity (80%), sound sensitivity (76%), nausea (73%), and unilateral pain (59%). In otolaryngology, the diagnosis of “headache” is 1 of the top 20 diagnoses made during the office visit,\(^8\) but when screening for a wider range of symptoms via retrospective chart review, Sabra et al\(^9\) found that 10.8% of 1002 consecutive patients presenting to an otolaryngology clinic had a chief complaint that could be related to migraine.

Atypical migraine may mimic other common disorders, making diagnosis challenging. Only recently have we been become aware that there is significant overlap among symptoms of vestibular migraine (VM), Ménière’s disease (MD), and benign paroxysmal positional vertigo.\(^10,11\) Not until the most recent version of International Classification of Headache Disorders, third edition beta (ICHD-3 beta) has VM been classified as an episodic syndrome that may be associated with migraines.\(^12\) Additionally, it has been argued that the current ICHD-3 beta criteria still do not account for the heterogeneity and natural history of the disorder.\(^13\)

Similarly, we do not have good diagnostic methodologies to distinguish the sinonasal symptoms of migraine from those of infection or inflammation. Recent studies indicated that the majority of patients who complain of sinus headache satisfy the diagnostic criteria for migraine.\(^14,15\) The findings from a study of 2991 patients presenting with “sinus” headache similarly questioned the accuracy of the current diagnostic criteria to predict rhinosinusitis.\(^16\) Eighty-eight percent of these patients fulfilled the International Headache Society’s migraine criteria (80%) or migrainous criteria (8%). The most common symptoms reported by patients were sinus pressure (84%), sinus pain (82%), and nasal congestion (63%). The only clearly distinct condition was nasal polyposis, presenting with the unique symptom of anosmia/hyposmia.\(^17\) In 2013, a study of 130 patients with migraine reported that 106 (81.5%) were misdiagnosed as having sinusitis, particularly the patients with chronic migraine. The mean ± SD delay in diagnosis was 7.75 ± 6 years.\(^17\)

This cross-sectional study, which uses validated screening tools, evaluates the prevalence of otologic and sinonasal complaints that might be related to migraine disease. Our hypothesis is that the prevalence of migraine in otolaryngology patients is significantly higher than that in the general population. The study aims are to (1) describe the demographics and prevalence of migraine sufferers seen in an otolaryngologist’s office in association with their primary ear, nose, or throat complaint and clinical diagnosis; (2) determine the otologic and sinonasal symptoms among the patients who screen positive for migraine through previously validated questionnaires; and (3) further analyze clinical characteristics of sinus and otologic disease in this population with custom patient and clinician questionnaires.

Given the potential large number of people with undiagnosed migraine, there is a significant opportunity to lessen patient suffering and reduce unnecessary and costly treatments and interventions.\(^18,19\)

**Methods**

**Setting and Subjects**

This cross-sectional study utilized the Creating Healthcare Excellence through Education and Research (CHEER; cheerapplied.org) network for recruitment.\(^20\) Patients were recruited in a pragmatic manner in 14 CHEER sites between June 2015 and March 2017: 9 sites were academic, and 5 were community based. The study sample included patients aged ≥18 years seen for any concern that was not head and neck cancer. Patients were also excluded if they had any history of brain abnormality, such as tumors or hydrocephalus, or if their headaches began within 2 weeks of a medical illness, trauma, or head injury. An on-site research coordinator obtained informed consent from eligible adults.

**Institutional Review Board Approval**

This study was approved by the Institutional Review Board of the Duke University School of Medicine.

**Materials**

The study coordinator administered a validated migraine screening questionnaire called the Migraine Assessment Tool (MAT)\(^21\) to consented patients. The MAT has a specificity of 0.79, a sensitivity of 0.89, a positive predictive value of 0.85, and a negative predictive value of 0.84, as compared with the International Headache Society’s diagnostic criteria.\(^21\) The MAT contains 8 questions that are scored, and it takes approximately 2 minutes to administer. All patients received a demographics questionnaire. Patients who screened positive for migraine using the MAT (MAT+) received 3 additional validated patient-reported instruments: AMS American Migraine Prevalence and Prevention (AMPP) diagnostic questionnaire,\(^22,23\) Sino-Nasal Outcome Test (SNOT-20),\(^24\) and Dizziness Handicap Inventory (DHI).\(^25\) A custom patient questionnaire (CPQ) and a custom clinician questionnaire (CCQ) were collected to further characterize the MAT+ population.

**Recruitment**

Consecutive interval-based pragmatic recruitment occurred at each site for 5 to 10 days per quarter. Site staff determined the best model for recruitment for their clinic flow.

**Power Analysis**

Prevalence data from the literature for migraine in the general and otolaryngology populations were used to perform a power analysis. Adjustments were made for typical consent rates (20%-30%) and to enrich for a subset analysis of patients. The target sample size determined via these assumptions was 2000 evaluable subjects to be screened with the MAT. Our enrollment of patients in the MAT+ group supports power (90%) in this study.
Database
Patient and clinician questionnaires were entered by site research coordinators into a secure REDCap database.

Statistical Plan
Descriptive statistics were utilized to describe the patients in this study. Chi-square and analysis of variance were used to explore differences between groups of interest. Rank-based nonparametric tests were used to compare DHI and SNOT-20 categories.

Results

Aim 1

Demographics and prevalence of migraineurs seen in an otolaryngologist’s office

Of the 1458 patients screened, 235 (16.1%) screened MAT+. The MAT+ cohort was significantly younger than the MAT− group (47.2 vs 55.6 years, \( P < .001 \)). The MAT+ group had a much higher proportion of women versus MAT− (80.0% vs 55.9%, \( P < .001 \)). While there was no significant difference in the racial composition of the 2 groups, patients with Hispanic ethnicity had a higher percentage of MAT+ versus MAT− results (7.3% vs 3.3%, \( P = .004 \)). There was no statistically significant difference (\( P = .28 \)) in the prevalence of MAT+ across the 9 academic sites (15.2%, \( n = 118 \)) and the 5 community sites (17%, \( n = 117 \)).

The scores on the AMPP are collapsed into categories based on a modified ICHD-3 beta definition. Our MAT+ population is categorized as follows: 81.3%, migraine; 8.5%, episodic tension headache; 8.5%, other headache not otherwise specified; and 1.7%, probable migraine.

Aim 2

Otologic and sinus-related symptoms in the MAT+ population per validated questionnaires

The mean SNOT-20 score for the MAT+ cohort was 37.8 (95% CI, 35.0-40.6) out of a possible 100, which falls in the “moderate problem” category (Figure 1). The SNOT-20 was also evaluated by 4 clinically relevant domains. When weighted to the base scale of 0 to 100 (lowest to highest disease burden), the mean scores were as follows: sleep function, 48.7; psychological function, 39.7; ear and/or facial symptoms, 38.5; and rhinologic symptoms, 28.0.

The mean DHI score for the MAT+ cohort was 28.1 out of 100 (lowest to highest problem), which falls in the “mild” category. However, 33.3% of these patients noted that their dizziness was a “moderate” or “severe” problem (Figure 2).

To analyze what percentage of patients in the MAT+ group had both sinus and dizziness symptoms, we cross-tabulated the results from the SNOT-20 and DHI (Table 1, Figure 2).
The top 3 cross-tabulations by volume are as follows: no handicap (DHI) and moderate (SNOT-20) (n = 38), mild (DHI) and moderate (SNOT-20) (n = 33), and mild (DHI) and moderate to severe (SNOT-20) (n = 30).

A Jonckheere-Terpstra test for ordered alternatives showed that there were significantly higher levels of sinus burden (mild, moderate, moderate to severe, severe) with higher levels of dizziness handicap (no handicap, mild, moderate, severe), $T_{JT} = 11,573.00$, $z = 7.471$, $P < .001$.

**Aim 3**

- Clinical characteristics of, and chief complaint diagnosis given to, patients who screen positive for migraine with the custom patient and clinician questionnaires

We evaluated the presence of the specific diagnoses presented in Tables 2 and 3 (primary and secondary) for patients in the MAT+ population collected via the CCQ. For the primary diagnosis, only 16 (6.8%) patients had diagnoses related to migraine (n = 10, migraine; n = 6, VM). For the secondary diagnosis, 51 (21.8%) patients had diagnoses related to migraine (n = 36, migraine; n = 15, VM).

The results of the CPQ for the MAT+ population are provided in Tables 4 and 5. A large portion of the patients had ear-related symptoms, such as tinnitus (70.5%) and ear pressure (61.9%). Similarly, many were affected by what they expressed as dizziness, and only 18% did not have any balance-related symptoms. Of these symptoms, lightheadedness (68.5%) and unsteadiness (48.6%) were the most common.

Sensory sensitivities commonly associated with migraine disorders were present in 64.5% of the MAT+ population, and half the patients had motion sensitivity and ear sickness. Nearly half the patients had exacerbation of their symptoms by weather changes and 69.4% by stress. Less than a third of the MAT+ cohort had headaches occurring ≥15 days a month; 89.1% of patients had sinus symptoms, such as facial pressure, most commonly behind the eyes.

**Discussion**

This study begins to assess national patterns of migraine disease in daily practice within an otolaryngologist’s office. Although study participants were seen for any concern that was not head and neck cancer, we found that an otolaryngologist may see a higher prevalence of migraine in this patient population than in the general population (16.1% vs 13%, $P < .001$).

**Otologic Symptoms**

In 1979, Slater first emphasized an association between forms of vertigo and migraine. Twenty years later, Neuhauser et al and Furman et al first established clinical criteria for diagnosing vertigo related to migraine and proposed that the vertigo can occur without a concomitant headache. It is now more widely recognized that VM is the most common cause for recurrent spontaneous vertigo, with a lifetime-prevalence in the general population of about 1%.2

In our study, the prevalence of vestibular symptoms was significant. Only 18% of the MAT+ group did not report some form of vestibular sensitivity (spinning, light-headedness, rocking or swaying, unsteadiness, or feeling of being displaced in space). In contrast to the spinning sensation characteristic of
benign paroxysmal positional vertigo or MD, the MAT+ cohort suffered most commonly from light-headedness (68.5%), unsteadiness (48.6%), the sensation of feeling displaced in space (30.2%), and rocking or swaying (24.3%).

As a large portion of the MAT+ population in our study complained of aural pressure (61.9%) and/or tinnitus (70.5%), it is quite possible that the symptoms of patients diagnosed with MD may in part be due to migraines. In a recent study that evaluated the effect of barometric pressure on patients with MD, Gurkov et al found that the symptoms most commonly exacerbated by barometric pressure were vertigo and aural pressure rather than hearing and tinnitus fluctuation.33 Additionally, while epidemiologic data on the prevalence of tinnitus among migraine sufferers are scarce, 1 large study revealed that the incidence of tinnitus among young adults with headaches was 8.9%,34 and another study showed a 44% prevalence of migraine among patients with tinnitus and a correlation between tinnitus and headache laterality.35 These findings suggest that migraine disease affects many parts of the sensory nervous system beyond the trigeminal.

Note that half (49.8%) of all patients in the MAT+ group reported a history of carsickness (motion intolerance). Previous studies revealed a history of childhood motion sickness in 40% to 50% of pediatric and adult migraine sufferers, in contrast to 10% of controls.36-38 Motion intolerance and migraine share similar interactions within the trigeminal system and vestibular nuclei.37 Hyperexcitability of brainstem circuits produces symptoms of motion sickness and migraine, as well as heightened susceptibility to visual illusions of movement. Significant increased sensitivity to tilt has been demonstrated in patients with migraine.39,40 Finally, vasomotor and chemical changes may occur in the labyrinth during a migraine attack and may cause vestibular dysfunction.41 Drummond concluded that multiple mechanisms increase susceptibility to motion sickness in migraine sufferers. It has been argued that motion sickness is a reliable minor criterion in the diagnosis of migraine for children and adults.44

**Sinonasal Signs and Symptoms**

Sinonasal symptoms are also extremely common in the migraine population. In our study, 85% of patients in the MAT+ cohort experienced facial pressure, with the majority citing the sensation behind their eyes (71.9%) and forehead (55.7%) but also across both cheeks (33.9%) and within a unilateral cheek (15.8%). The CPQ also revealed that 21.9% reported an eyelid droop and 20.0% had eyelid swelling associated with a headache. From the results of the SNOT-20 questionnaire, 49.9% of the patients who screened MAT+ reported rhinorrhea.

<table>
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<tr>
<th>Table 2. Clinician Primary Diagnosis for Patients Screening Positive on the Migraine Assessment Tool.</th>
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<tr>
<td>Custom Clinician Questionnaire Options</td>
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<tr>
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<tr>
<td>Ménière’s disease</td>
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<tr>
<td>Migraine</td>
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<tr>
<td>Sinusitis: recurring</td>
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<tr>
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<tr>
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<tr>
<td>Headache</td>
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<tr>
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<tr>
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Abbreviation: NOS, not otherwise specified. \(^a\)n = 234.

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congestion, and localized edema that mimic an allergic condition or sinus infection.\textsuperscript{47,48} These symptoms are cardinal signs of rhinosinusitis.\textsuperscript{49} Our findings raise the question of whether patients with migraine who have a combination of facial pressure, periorbital symptoms, and rhinorrhea are being misdiagnosed with acute, recurring, or chronic sinusitis. The fact that multiple studies demonstrated no direct correlation between patients' symptoms and objective findings on computed tomography scans for chronic sinusitis should prompt practitioners to consider secondary causes, such as migraine disorder,\textsuperscript{50} while treating these patients.

In our study, the CCQ revealed that 22.6% of the MAT cohort was labeled with primary or secondary diagnoses of recurring or chronic sinusitis. Given the high rate of otolaryngology patients with migraine who complain of facial pain and rhinorrhea, this neurologic condition may explain the high failure rate (80%-84%) of antibiotics to relieve rhinosinusitis\textsuperscript{51,52} and the poor correlation between a patient's sinonasal symptoms and objective computed tomography findings.\textsuperscript{53,54} Practitioners should routinely consider exploring possible symptoms for migraine, as presented in Tables 4 and 5, before treating with antibiotic, steroid, and surgical interventions. Unfortunately, this approach is hampered by the ICHD-3 beta classification system, which does not recognize migraine-related rhinosinusitis as a diagnostic entity unless it is associated with underlying acute rhinosinusitis.

**Overlap of Otologic and Sinonasal Symptoms**

A comparison of SNOT-20 and DHI scores highlights the strong association of vestibular and rhinosinus symptoms, particularly as the symptoms increase in intensity (Table 1). This raises questions about the common neurobiological factors that link the intensity of the ear and rhinosinus symptoms, such as shared genetic variants and hormonal effects. Migraine-related conditions that often occur without a concomitant headache may share a similar pathophysiology—a chronic dysesthesia trigeminovascular system.\textsuperscript{55} This study reinforces the common but distinctive presentations of

\begin{table}[h]
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\begin{tabular}{l|ccc|ccc|ccc}
\hline
Question & \multicolumn{3}{c|}{No} & \multicolumn{3}{c|}{Yes} & \multicolumn{3}{c}{Not Sure} \\
 & n & n & % & n & n & % & n & n & % \\
\hline
Do you ever have eyelid droop with your headache? & 219 & 105 & 47.9 & 48 & 21.9 & 66 & 30.1 \\
Do you ever have eyelid swelling with your headache? & 220 & 136 & 61.8 & 44 & 20.0 & 40 & 18.2 \\
Do you experience burning tongue or mouth soreness? & 217 & 187 & 86.2 & 30 & 13.8 & 0 & 0.0 \\
Do you experience ear pressure? & 218 & 83 & 38.1 & 55 & 25.2 & \ & \ & \ \\
\quad One ear & & & & & & & & & \ \\
\quad Both ears & & & & & & & & & \ \\
Do you have foreign body sensation in the ear? & 218 & 150 & 68.8 & 68 & 31.2 & \ & \ & \ \\
Do you experience ringing or noise in the ear? & 220 & 65 & 29.5 & 155 & 70.5 & \ & \ & \ \\
Do your headaches ever occur $\geq15$ d/mo for $\geq3$ mo? & 217 & 155 & 71.4 & 62 & 28.6 & \ & \ & \ \\
When you have symptoms of dizziness, do they improve with medication? & 86 & 42 & 48.8 & 44 & 51.2 & \ & \ & \ \\
Is it a problem to read or ride in the back seat of a car? & 231 & 116 & 50.2 & 115 & 49.8 & \ & \ & \ \\
\hline
\end{tabular}
\caption{Custom Patient Questionnaire.\textsuperscript{a}}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{l|c}
\hline
Question & n \\
\hline
Do you have episodes of . . . & 222 \\
\quad Spinning? & 74 \\
\quad Light headedness? & 152 \\
\quad Rocking or swaying? & 54 \\
\quad Unsteadiness? & 108 \\
\quad Feeling “displaced in space”? & 67 \\
\quad None & 40 \\
Do you have unusual sensitivity in any of the following areas? & 220 \\
\quad Ear? & 62 \\
\quad Scalp? & 56 \\
\quad Skin? & 32 \\
\quad Smells? & 71 \\
\quad None & 78 \\
Do you experience face pressure . . . & 221 \\
\quad Across the forehead? & 123 \\
\quad In one cheek? & 35 \\
\quad In both cheeks? & 75 \\
\quad Behind the eyes? & 159 \\
\quad None & 24 \\
Do you have unusual ear sensitivity to . . . & 221 \\
\quad Cold? & 56 \\
\quad Wind? & 67 \\
\quad Touch? & 21 \\
\quad None & 127 \\
Are your symptoms modified or affected by . . . & 216 \\
\quad Weather? & 103 \\
\quad Stress? & 150 \\
\quad None & 41 \\
\hline
\end{tabular}
\caption{Custom Patient Questionnaire.\textsuperscript{a}}
\end{table}

\textsuperscript{a}Patients were allowed to skip questions.

\textsuperscript{a}“All answers that apply” are checked.
migraine disease to otolaryngologists. It is likely that these forms of migraine have not been characterized in the literature or classification system as well as other forms, because those who suffer from them do not often seek the opinions of neurologists.

In our study, many of the commonly found complaints among patients in the MAT+ group reflected diminished quality of life. In the SNOT-20—which is more a quality-of-life questionnaire than an objective diagnostic tool for sinus disease—the MAT+ cohort scored an average of 37.8. This score is on the border of the “moderate” and “moderate to severe” categories. It is possible that many of the sinus symptoms are exaggerated in this population due to underlying migraine disorder. This could explain why there was a significantly higher sinus burden among patients with migraine who scored higher on the dizziness questionnaire. However, one needs to consider that at least part of this may be due to similar quality-of-life questions in both questionnaires.

Additionally, while the SNOT-20 questionnaire does ask about runny nose, ear fullness, dizziness, ear pain, or facial pain/pressure, it does not effectively separate the different causes of these symptoms. The SNOT-20 did not prove to be useful as a screening tool for identifying migraine among patients who have rhinosinus complaints.

Limitations

This study utilized a pragmatic approach intended to evaluate research questions in routine clinical practice in a timely fashion. Inherent in this approach are several limitations. The small sample size of the MAT+ population prevents more rigorous subset analyses other than descriptive. Additionally, we do not have the full questionnaire packet on the MAT− group; it would have been untenable to collect in busy daily practice, yet it limits having a comparison group.

Conclusion

Our study demonstrates that two-thirds of those patients who screened positive for migraine disease were previously undiagnosed. This high rate of missed diagnosis among otolaryngologists highlights the flawed ICHD-3 beta diagnostic system and inadequate training of otolaryngologists in the understanding and recognition of migraine disease. This observation suggests a significant opportunity for otolaryngologists to improve their understanding of a relatively common yet uncommonly diagnosed condition. A better understanding of the possible presentations of migraine, which can mimic many head and neck complaints, may hasten the identification of patients with migraine disease, improve treatment planning, add the study of migraine to otolaryngology residency programs, and stimulate more clinical and basic science migraine research within our specialty.

This study sets the foundation for a subsequent study, which is to develop and validate an evidence-based screening tool and treatment guideline for otolaryngologic patients with migraine disease.

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Author Contributions

Kristine A. Schulz, methodology, protocol development lead, analytic lead, preparation of manuscript, first author; Elnaz Esmati, study implementation, analytic review, review of manuscript; Frederick A. Godley, advisor, analytic review/input, preparation of manuscript; Claude L. Hill, methodology review, statistics lead, review of manuscript; Ashkan Monfared, advisor, analytic review/input, preparation of manuscript; Michael Teixido, advisor, analytic review/input, review of manuscript; Debara L. Tucci, advisor, analytic review/input, review of manuscript; David L. Witsell, methodology advisor, analyses review and interpretation, preparation of manuscript/last author.

Disclosures

Competing interests: Frederick A. Godley, Amgen—speaker’s bureau. Debara L. Tucci, Otonomy, Inc—consultant. David L. Witsell, Association of Migraine Disorders—principal investigator and recipient of grant for this study.

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