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## Original Investigation

# Clinical Predictors of Abnormal Magnetic Resonance Imaging Findings in Patients With Asymmetric Sensorineural Hearing Loss

Syed F. Ahsan, MD; Robert Standing, MD; Daniel A. Osborn, MD; Ed Peterson, PhD; Michael Seidman, MD; Rajan Jain, MD

**IMPORTANCE** Asymmetric sensorineural hearing loss (ASNHL) is commonly encountered in an otolaryngologic clinical practice. Determining what factors are associated with abnormal magnetic resonance imaging (MRI) findings will help with diagnostic workup.

**OBJECTIVE** To evaluate the association between clinical and audiometric factors and abnormal MRI findings in patients with ASNHL.

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective medical record review from an urban, tertiary referral center of 451 patients with ASNHL who underwent MRI testing between January 2005 and December 2011.

**MAIN OUTCOMES AND MEASURES** Medical records were reviewed for audiometric parameters as well as clinical presentation and compared with MRI results, which were categorized as abnormal, normal, or incidental. Data analysis included  $\chi^2$  tests, logistic regression analysis, and multivariate analysis.

**RESULTS** A total of 48 patients (10.6%) had abnormal MRI findings. Only 21 patients (4.7%) had a mass of the cerebellopontine angle/internal auditory canal on MRI, making up 40% of all abnormal MRI findings. The next most common MRI finding was labyrinthitis (n = 13; 25%). Vertigo/dizziness (n = 20; P = .01), tinnitus (n = 18; P = .02), sudden hearing loss (n = 15; P = .054), and 15-dB asymmetry at 3 kHz (n = 39; P = .01) were associated with abnormal MRI findings. Loud noise exposure was associated with normal MRI findings. Logistic regression analysis showed that vertigo/dizziness (odds ratio [OR], 2.14; 95% CI, 1.15-3.96; P = .02), unilateral tinnitus (OR, 2.15; 95% CI, 1.14-4.03; P = .02), and 15-dB asymmetry at 3 kHz (OR, 2.62; 95% CI, 1.24-5.57; P = .01) were significantly associated with abnormal MRI findings. Multivariate analysis showed that only 15-dB asymmetry at 3 kHz (OR, 2.42; 95% CI, 1.07-5.50; P = .03) was significantly associated with an abnormal MRI finding.

**CONCLUSIONS AND RELEVANCE** This study found that asymmetry of 15 dB at 3 kHz on audiometry was associated with higher positive yield on use of MRI in evaluating patients with ASNHL. We recommend that patients who present with ASNHL with this audiometric characteristic undergo MRI as part of their diagnostic workup.

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Patients with asymmetric sensorineural hearing loss (ASNHL) often present a diagnostic quandary. The condition is relatively common, found in 35% to 50% of the population, but occasionally it may be indicative of retrocochlear disease.<sup>1</sup> The cause is frequently multifactorial, with no definitive single etiologic factor.<sup>1,2</sup> Contrast-enhanced magnetic resonance imaging (MRI) is the gold standard in evaluating ASNHL. In a recent study, over 95% of American neurotologists reported ordering MRI for patients with suspected ASNHL.<sup>2</sup> However, MRI is expensive and often has a low diagnostic yield in the evaluation of ASNHL.<sup>2-4</sup>

It is likely that MRI has become routine in evaluation of ASNHL out of concern for missing an intracranial tumor.<sup>2</sup> Vestibular schwannoma (VS) is the most common tumor of the cerebellopontine angle (CPA) and accounts for 5% to 10% of all intracranial tumors in adults.<sup>3,5</sup> However, VS is rare, with an overall prevalence of 1 per 100 000, and found only in 2% to 8% of patients with ASNHL.<sup>1,2</sup> While patients with VS often present with the classic symptoms of unilateral hearing impairment, tinnitus, and/or imbalance, up to 45% are asymptomatic.<sup>2,5</sup> Furthermore, when observed over a period of years, some patients with VS had no changes in their audiograms or size of tumors.<sup>6</sup>

With rising medical costs and limited health care resources, excessive and possibly unnecessary imaging has come under scrutiny. The purpose of the present study was to evaluate the association between clinical and audiometric factors and to determine which criteria can be used to increase the diagnostic yield of the MRI examination in patients presenting with ASNHL.

The electronic medical and radiographic records of these patients was performed. The clinical criteria used to perform the MRI and criteria previously reported to be associated with retrocochlear disease were recorded, including the degree and type of ASNHL, “acute” (<72 hours) onset of symptoms, unilateral tinnitus, bilateral tinnitus, and generalized disequilibrium or vertigo.<sup>1,6,7</sup> This retrospective medical record review was approved by the Henry Ford Hospital institutional review board, which waived participant written informed consent.

The MRI results were categorized as normal, incidental, or abnormal. A normal MRI result was defined as showing no abnormal findings. An incidental MRI result was one in which the abnormal findings could not explain the patient’s hearing loss. An abnormal MRI result was one in which the findings explained the patient’s hearing loss. The radiologists reviewing the MRIs were blinded as to the type or degree of ASNHL.

There were 615 patients initially identified to have had an MRI for ASNHL. The audiograms of these patients were evaluated. The patients were divided into groups based on prior definitions of ASNHL, including 15% difference between ears in word recognition scores (WRS), a 10-dB difference between ears at 3 contiguous frequencies, 15-dB difference at 2 contiguous frequencies, and a 15-dB difference at 3 kHz. Of the 615 patients identified, 451 had audiograms that fulfilled our criteria for ASNHL and had MRI results available for review.<sup>5,8</sup> A patient was included in the study if he or she fulfilled at least 1 of the inclusion criteria. A total of 119 patients did not fit these criteria, while the audiograms could not be located for 45 patients.

## Methods

A total of 615 consecutive patients at our institution who underwent MRI for ASNHL between January 2005 and December 2011 were identified through a search of the radiology information system. A detailed retrospective investi-

### MRI Protocol

All study patients underwent conventional MRI on a 1.5-T or 3.0-T machine using either a conventional or acoustic protocol. The conventional protocol included sagittal T1, axial T2 fast spin-echo (FSE), and axial T2 fluid attenuated inversion recovery (FLAIR), axial T1 precontrast, axial T1 postcontrast, and coronal T1 postcontrast sequences using 5-mm slice thickness. The acoustic protocol included all sequences from the conventional brain protocol plus high-resolution axial T2, axial T1 precontrast, axial T1 postcontrast, and coronal T1 postcontrast sequences of the internal auditory canal and posterior fossa with 3-mm slice thickness. One-millimeter reconstructed axial slices from the 3-dimensional sequences were reviewed. Postcontrast images were acquired after administration of a standard dose, 0.1 mmol/kg, of gadodiamide (Magnevist, Bayer Healthcare). Most patients underwent MRI with acoustic protocol (96.2%, n = 434). Seventeen patients underwent conventional-protocol MRI.

### Statistical Analysis

Comparisons were made between patients with an abnormal MRI and patients with incidental or normal MRI for clinical and audiometric characteristics. We used  $\chi^2$  tests for 2 × 2 tables to compare specific clinical and audiometric variables. In addition, logistic regression analysis was performed and odds ratios (ORs) calculated for some of the audiometric and vestibular variables in determining what predicts an abnormal MRI result. A multivariate analysis was also performed with the 4

Table 1. Distribution of Abnormal MRI Findings

Abnormal Finding	Patients, No. (%)	
	Total (n = 451)	Abnormal MRI Findings (n = 48)
CPA-IAC and/or cochlear mass	21 (4.7)	21 (40)
Labyrinthitis	13 (2.9)	13 (25)
Infarct	3 (0.7)	3 (6)
Vascular abnormality	3 (0.7)	3 (6)
Intracranial hypotension	2 (0.4)	2 (4)
Ramsay Hunt syndrome	1 (0.2)	1 (2)
Arachnoid cyst	1 (0.2)	1 (2)
Midbrain tumor and/or hydrocephalus	1 (0.2)	1 (2)
Glomus tumor	1 (0.2)	1 (2)
Cochlear dysmorphism	1 (0.2)	1 (2)
Multiple sclerosis	1 (0.2)	1 (2)

Abbreviations: CPA, cerebellopontine angle; IAC, internal auditory canal; MRI, magnetic resonance imaging.

Table 2. Association of Audiometric and Clinical Variables With an Abnormal MRI

Variable	Patients, No. (%)		P Value <sup>a</sup>
	Normal/Incidental MRI (n = 403)	Abnormal MRI (n = 48)	
Unilateral tinnitus	88 (21.8)	18 (38)	.02
Bilateral tinnitus	90 (22.1)	3 (6)	.01 <sup>b</sup>
10-dB Difference in 3 contiguous frequencies	380 (94.3)	46 (96)	>.99
15-dB Difference in 2 contiguous frequencies	366 (90.8)	44 (92)	.85
15-dB Difference at 3 kHz	252 (62.3)	39 (81)	.01
15% Difference in WRS	153 (39.2)	24 (50)	.17
Right side	191 (47.4)	17 (35)	.12
Vertigo/dizziness	103 (25.1)	20 (42)	.01
Sudden/acute hearing loss	78 (19.4)	15 (31)	.054
Loud noise exposure	60 (15.1)	1 (2)	.01 <sup>b</sup>
10-dB Difference in 3 contiguous frequencies plus 15% WRS	388 (96.3)	47 (98)	>.99
15-dB Difference in 2 contiguous frequencies plus 15% WRS	378 (93.8)	45 (94)	>.99
15-dB Difference at 3 kHz plus 15% WRS	295 (73.2)	41 (85)	.07

Abbreviations: MRI, magnetic resonance imaging; WRS, word recognition score.

<sup>a</sup> All P values calculated using  $\chi^2$  tests.

<sup>b</sup> Bilateral tinnitus and loud noise exposure were significantly associated with normal MRI findings.

asymmetric audiometric criteria (10-dB difference at 3 contiguous frequencies, 15-dB difference at 2 contiguous frequencies, 15-dB difference at 3 kHz, and 15% asymmetry in WRS). All ORs were calculated and assessed using linear logistic analysis to determine which variable was most likely to predict a CPA/internal auditory canal (IAC) mass.

## Results

Of the 451 study patients, a majority had a 10-dB difference at 3 contiguous frequencies (n = 426) and/or a 15-dB difference at 2 contiguous frequencies (n = 410). Only 290 and 176 patients had a 15-dB difference at 3 kHz and 15% WRS, respectively. All patients with the 15-dB difference at 3 kHz had either a minimum 10-dB difference at 3 contiguous frequencies or a 15-dB difference at 2 contiguous frequencies. Of the 451 included patients, 89.4% had normal (51.0%) or incidental (38.0%) findings on MRI that did not explain their ASNHL. Only 10.6% of patients had abnormal MRI findings (n = 48) that explained their clinical presentation.

A CPA/IAC mass was the most common abnormality noted and accounted for the majority of the abnormal MRI findings (n = 21; 40%). This represented 4.7% of all MRI scans performed. The size of the identified CPA/IAC mass ranged from a 3-mm intracochlear mass to a large 3.6 × 2.7-cm CPA tumor. The next most common abnormality (n = 13; 25%) was labyrinthitis (indicated by enhancement of the labyrinth or fluid-filled space of cochlea and IAC without a mass effect), which represented 2.9% of all MRI results evaluated (Table 1). Common incidental findings included paranasal sinus disease (n = 69), pituitary adenomas (n = 9), arachnoid cysts (n = 8), and meningioma (n = 6) away from the CPA/IAC region. Of the conventional protocol MRIs, there were 3 abnormal MRI results. None of these revealed a CPA/IAC mass. The remainder

of the MRI findings were normal (n = 5) or had incidental findings (n = 9) not related to the hearing loss.

Overall, 13.5% of patients with a 15-dB difference at 3 kHz had an abnormal MRI result, followed by 12.5% of patients with a 15% difference in WRS. Only 10.8% and 10.7% of patients with a 10-dB difference at 3 frequencies and a 15-dB at 2 contiguous frequencies, respectively, had abnormal MRI findings. Further  $\chi^2$  analysis (Table 2) revealed that unilateral tinnitus (P = .02) was more often associated with abnormal MRI findings, whereas bilateral tinnitus (P = .01) and loud noise exposure (P = .01) were associated with normal MRI results. Asymmetry of 15 dB at 3 kHz and vertigo/dizziness were also significantly associated with an abnormal MRI (Table 2). Sudden hearing loss was associated with an abnormal MRI finding, but the association did not reach statistical significance (P = .054). Other audiometric and clinical criteria evaluated did not show a statistically significant association with abnormal MRI findings (Table 2). Because of the low number of CPA/IAC masses, we did not evaluate the relationship between audiometric criteria and tumor size.

Logistic regression analysis used to calculate ORs showed that unilateral tinnitus (OR, 2.15; 95% CI, 1.14-4.03), 15-dB asymmetry at 3 kHz (OR, 2.62; 95% CI, 1.24-5.57), and vertigo/dizziness (OR, 2.16; 95% CI, 1.15-3.96) all were risk factors for predicting an abnormal MRI result. Interestingly, bilateral tinnitus was more likely to predict a normal MRI result (OR, <1.00) (Table 3). Multivariate analysis of the 4 audiometric criteria revealed a significant increase in abnormal MRI results only in patients who had a 15-dB difference between ears at 3 kHz (OR, 2.42; 95% CI, 1.07-5.50; P = .03) (Table 4). In comparing each audiometric and clinical variable to determine which was more likely to predict a CPA/IAC mass, we found that unilateral tinnitus and a 15-dB difference at 3 kHz were both significantly associated with finding of a CPA mass (P = .01 and P = .048, respectively) (Table 5).

**Table 3. Predicting an Abnormal MRI Result Using Logistic Regression Analysis**

Variable	OR (95% CI)	P Value
Unilateral tinnitus	2.15 (1.14-4.03)	.02
Bilateral tinnitus	0.24 (0.07-0.78)	.02 <sup>a</sup>
Difference of 10 dB at 3 contiguous frequencies	1.39 (0.32-6.09)	.66
Difference of 15 dB at 2 contiguous frequencies	1.11 (0.38-3.27)	.85
Difference of 15 dB at 3 kHz	2.62 (1.24-5.57)	.01
15% Asymmetry of WRS	1.55 (0.83-2.90)	.17
Right side	0.61 (0.33-1.14)	.12
Vertigo/dizziness	2.14 (1.15-3.96)	.02
Sudden/acute hearing loss	1.89 (0.98-3.66)	.057

Abbreviations: OR, odds ratio; WRS, word recognition score.

<sup>a</sup> Bilateral tinnitus, with OR less than 1, was not associated with an abnormal MRI result.

## Discussion

Over 28 million Americans have some degree of hearing loss.<sup>9</sup> Sensorineural hearing loss (SNHL) accounts for about 90% of all hearing loss and results from dysfunction at the level of the vestibulocochlear nerve, inner ear, or central processing centers of the brain. In general, imaging of patients with SNHL is often low yield because the abnormality most commonly occurs at the level of the hair cells of the organ of Corti, far beyond the resolution of current imaging technologies.<sup>9,10</sup>

With sudden ASNHL, especially in the presence of unilateral tinnitus, vertigo/disequilibrium, or focal neurological deficits involving the 5th or 7th cranial nerve distributions, there is increased concern for retrocochlear disease.<sup>6</sup> Depending on the setting where patients are evaluated, they may receive additional laboratory tests, auditory brainstem response (ABR) evaluation, and/or MRI. Often patients presenting with ASNHL of more than 10 years' duration do not need further workup in the absence of any significant progression or neurological changes.<sup>11,12</sup>

Standard audiometry cannot directly identify retrocochlear disease. In addition, abnormal acoustic reflex testing may suggest retrocochlear abnormality but cannot identify the cause. It can be used as an indicator for retrocochlear disease along with serial audiometric screening, which may be used to assess progression of ASNHL and as an indicator of higher likelihood of retrocochlear disease.<sup>6,12</sup> It is important to also realize that the hearing loss caused by a VS or non-VS CPA tumor may exhibit a cochlear (abnormal distortion-product otoacoustic emissions [DPOAEs] and SNHL on audiometry) or retrocochlear (normal DPOAEs and SNHL) pattern.<sup>13,14</sup> Therefore, findings on DPOAE testing may not help in determining if a retrocochlear disease may be present.

Patients with ASNHL may be screened by ABR. The ABR test is sensitive for a vestibular schwannoma larger than 1 cm but is limited in the evaluation of smaller tumors or in patients with significant hearing loss.<sup>12</sup> One prospective, multi-institutional study comparing ABR vs MRI for evaluation of ASNHL demonstrated that ABR had a sensitivity of 71%, speci-

**Table 4. Results of Multivariate Analysis**

Variable	OR (95% CI)	P Value
Difference of 10 dB at 3 contiguous frequencies	1.13 (0.22-5.71)	.88
Difference of 15 dB at 2 contiguous frequencies	0.62 (0.18-2.15)	.45
Difference of 15 dB at 3 kHz	2.42 (1.07-5.50)	.03
15% Asymmetry of WRS	1.41 (0.75-2.66)	.29

Abbreviations: OR, odds ratio; WRS, word recognition score.

ficity of 74%, and a false-negative rate of 29%, particularly in smaller tumors.<sup>11</sup> Cost analyses have shown that ABR-MRI screening algorithms may not be cost-effective owing to the high false-negative rate of ABR and should be abandoned.<sup>7,11</sup> However, ABR testing may be useful in certain clinical scenarios, such as in older patients in whom the missed diagnosis of a small tumor may be less consequential or if an MRI is contraindicated owing to the presence of metallic implants (eg, pacemakers, aneurysm clips).<sup>12,15</sup> A recent meta-analysis evaluating the use of ABR testing in diagnosing VS noted high sensitivity and specificity (pooled sensitivity of 95.6% for tumors >1 cm and 85.8% for tumors <1 cm).<sup>16</sup> However, there was significant heterogeneity among the studies used for the analysis, and the overall quality of the studies was not reported.

Saliba et al<sup>5,17</sup> found that the criteria of asymmetric SNHL of 15 dB or more at 3 kHz was more reliable in selecting patients with ASNHL who would have a vestibular schwannoma detected on MRI. Of 212 patients they evaluated with MRIs for ASNHL, 39.6% of patients were noted to have a VS (n = 84). The authors suggested that this high rate was because of their tertiary referral center. They concluded that if ASNHL was discovered by applying their "Rule 3,000," then there was a greater probability of the patient having a retrocochlear disease.<sup>17</sup> Our study confirms their finding in that of the 4 audiometric criteria of ASNHL that we evaluated, a significant increase in abnormal MRI results was noted only in patients with a 15-dB difference between ears at 3 kHz. It is important to understand that these were not isolated loss or asymmetry at 3 kHz, but there was involvement of more than 1 frequency. It is just that an asymmetry at 3 kHz in this setting raises greater suspicion warranting MRI.

An MRI of the brain and internal auditory canals with gadolinium is the most sensitive test for detecting retrocochlear disease.<sup>2-4,12</sup> In our study, 96% of patients underwent acoustic-protocol MRI, while 4% (n = 17) underwent conventional-protocol MRI. There is a definite possibility that, of the 14 of 17 patients noted to have no significant abnormality, a small IAC lesion might have been missed owing to the interslice gap in these "screening" MRI examinations. However, due to the small number of these MRIs, we believe that the effects on the conclusions are limited. Prompt diagnosis of retrocochlear disease offers the best chance at hearing preservation treatment because smaller tumors are more amenable to resection and are associated with better surgical outcomes.<sup>6,12</sup>

However, obtaining an MRI for every patient who presents with ASNHL would be both cost prohibitive and unnecessary. Therefore, screening criteria have been developed to

Table 5. Audiometric and Clinical Variables That Predict CPA/IAC Mass

Variable	Patients, No. %		OR (95% CI)	P Value
	No CPA/IAC Mass (n = 430)	CPA/IAC Mass (n = 21)		
Unilateral tinnitus	96 (22.3)	10 (48)	3.16 (1.30-7.67)	.01
Bilateral tinnitus	91 (21.2)	1 (5)	0.196 (0.03-1.41)	.10
Difference of 10 dB at 3 contiguous frequencies	405 (94.2)	21 (100)	2.71 (0.15-48.60)	.50
Difference of 15 dB at 2 contiguous frequencies	389 (90.5)	21 (100)	4.58 (0.26-79.67)	.30
Difference of 15 dB at 3 kHz	272 (63.3)	18 (86)	3.49 (1.01-12.02)	.048
15% Asymmetry of WRS	172 (40.1)	9 (43)	1.12 (0.46-2.71)	.81
Right side	202 (47.0)	6 (29)	0.45 (0.17-1.19)	.11
Vertigo/dizziness	116 (27.0)	5 (24)	0.85 (0.30-2.36)	.75
Sudden/acute hearing loss	88 (20.5)	5 (24)	1.22 (0.43-3.41)	.71
Loud noise exposure	62 (14.4)	0	0.14 (0.01-2.34)	.17

Abbreviations: CPA/IAC, cerebellopontine angle/internal auditory canal; OR, odds ratio; WRS, word recognition score.

select patients who should undergo MRI testing.<sup>18-23</sup> Unfortunately, there are no prospective randomized clinical trials comparing strategy of investigation vs no investigation for vestibular schwannoma in patients with acute ASNHL.<sup>12</sup> An international multicenter study of MRI findings indicated a very low diagnostic yield of acoustic tumors (5.09%), with a significant proportion of nonpathologic or normal radiologic findings (57%-92.75%),<sup>15</sup> which our study confirms. However, according to Stachler et al,<sup>12</sup> the overall rate of MRI abnormalities directly related to sudden SNHL ranged from 7% to 13.75%, thus supporting the concept that acute onset of unilateral hearing loss may increase the diagnostic yield of MRIs. Our study, however, shows that sudden acute hearing loss was not significantly associated with an abnormal MRI or in predicting a CPA/IAC mass (Tables 3 and 5).

Other clinical symptoms appear to increase the diagnostic yield of MRI, such as the presence of unilateral vs bilateral tinnitus and vertigo/dizziness, which was confirmed in our study. We were not able to differentiate vertigo from dizziness owing to the limitations of reviewing medical records, where the terms were often used interchangeably.

In our medical center during the period covered by this study, there were no standard audiometric criteria used to determine when to obtain an MRI. This is why many of the patients identified through the MRI database could not be used in our analysis. Many had asymmetric hearing loss but the loss did not fit any of our criteria for asymmetry. Although many definitions of ASNHL have been proposed, there is no consensus on a standard audiometric definition of ASNHL or when to pursue further evaluation with MRI. More recently, a cross-sectional study by Cheng and Wareing<sup>15</sup> comparing 15 published audiometric protocols for use in MRI screening of acoustic tumors found that no single protocol achieved 100% sensitivity or 100% specificity and that the specificity and sensitivity rates tended to exhibit an inverse relationship to each other.

The major limitation of our study is its retrospective nature, with the attendant issues of incomplete documentation, unrecorded information, problematic verification of information, and difficulty establishing cause and effect, as well as variability in the quality of information recorded.

The evaluation of the patient with ASNHL is expensive and often results in multiple physician visits, followed by extensive laboratory testing, audiometry, ABR tests, and MRI examinations. Given the high cost and low diagnostic yield of MRI, it may not be indicated as a routine screening tool in all patients presenting with ASNHL. However, specific clinical and audiometric criteria in some patients may increase the diagnostic yield of MRI and should increase suspicion for retrocochlear disease. Patients may be better served by a thorough clinical history, audiometric screening with serial audiometric follow-up, and further evaluation by MRI only if indicated. We propose that patients with ASNHL that includes asymmetry of 15 dB at 3 kHz and patients with ASNHL as defined by the other criteria evaluated (unilateral tinnitus or dizziness/vertigo) undergo evaluation with an MRI to assess for retrocochlear disease.

## Conclusions

In our study, 89.4% of patients undergoing MRI for evaluation of ASNHL had normal or incidental findings. Only 10.6% had an abnormal MRI result. A finding of a CPA/IAC mass was noted in only 4.7% of patients with ASNHL. In patients with ASNHL, asymmetry of 15 dB at 3 kHz was significantly associated with an abnormal finding on MRI. Those patients who present with ASNHL that includes this audiometric characteristic should undergo MRI of the brain. Patients with ASNHL and unilateral tinnitus or ASNHL and dizziness/vertigo are also more likely to have an abnormal MRI finding.

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for the integrity of the data and the accuracy of the data analysis.

*Study concept and design:* Ahsan, Standing, Osborn, Jain.

*Acquisition, analysis, or interpretation of data:*

Ahsan, Standing, Osborn, Peterson, Seidman, Jain. *Drafting of the manuscript*: Ahsan, Osborn, Seidman, Jain.

*Critical revision of the manuscript for important intellectual content*: Ahsan, Standing, Peterson, Seidman, Jain.

*Statistical analysis*: Ahsan, Peterson, Seidman, Jain. *Administrative, technical, or material support*: Ahsan, Seidman.

*Study supervision*: Standing, Seidman, Jain.

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**Additional Information**: Dr Seidman is the founder of a nutritional supplement company and medical director of Visalus. He is also the recipient of National Institutes of Health grant funding for work studying simulation.

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