Toward a Diagnostic Imaging Algorithm for Undifferentiated Pulsatile Tinnitus

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Objective: Decisions around the diagnostic evaluation for pulsatile tinnitus (PT) remain challenging. We describe the usage patterns and diagnostic accuracy of imaging modalities and propose an evidence-based diagnostic approach for undifferentiated PT.
Study Design: Retrospective.
Setting: Single otology/neurotology clinic.
Subjects: Patients with PT presenting between 2009 and 2020.
Main Outcome Measures: Sensitivity, specificity, diagnostic yield, and diagnostic accuracy.
Results: A total of 315 subjects met inclusion criteria (74% female, mean ± SD age = 52 ± 17 years). Subjects were divided into four cohorts based on exam findings: normal (n = 229), venous cohort (n = 34), arterial cohort (n = 16), and outer/middle ear pathology cohort (n = 40). In total, 53% of patients received a nonidiopathic diagnosis for PT. The most common identifiable cause was sigmoid sinus dehiscence (78%) in the venous cohort, carotid stenosis (36%) in the arterial cohort, and glomus tumor (56%) in the outer/middle ear pathology cohort. There was a higher diagnostic rate among patients with positive exam findings compared to those with unrevealing exams ($p = 0.04$). Imaging studies with the highest diagnostic yield were computed tomography (CT) venography (44%), formal angiography (42%), and magnetic resonance venography (40%); studies with the highest specificity were formal angiography (0.82), CT angiography (0.67), and CT venography (0.67). A diagnostic algorithm is proposed.
Conclusions: Reaching a diagnosis in patients with PT requires a systematic approach, taking into account both clinical and radiographic information. Physical examination is a key first step for differentiating patients into venous, arterial, and other cohorts to narrow down the likely pathology and determine which radiographic studies have the highest yield and accuracy.
Key Words: Carotid stenosis—Diagnostic algorithm—Imaging—Pulsatile tinnitus—Sigmoid sinus dehiscence.

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INTRODUCTION

Pulsatile tinnitus (PT) is defined as the perception of rhythmic or pulsating sounds in the ear and is often described as the sensation of hearing one's own heartbeat. Unlike the much more common non-PT, which represents over 90% of tinnitus in general and is often idiopathic (1), many cases of PT can be explained by an underlying pathology, which may have significant health implications, such as cerebrovascular disease, vascular malformations, or tumors that warrant prompt diagnosis (2).

Various imaging studies have been suggested for the workup of patients with undifferentiated PT. Despite this, there is currently no evidence-based consensus on the optimal diagnostic approach, and imaging decisions are largely based on individual and institution-based practice patterns (3). Some authors in the past have suggested computed tomography (CT) angiography or magnetic resonance angiography (MRA) as the initial screening study of choice; others recommend a more selective approach (4,5). Further complicating decision making is the lack of data on the relative accuracy of various imaging modalities. In a systematic review investigating imaging modalities for PT, our group found that the majority of studies were limited by small sample sizes and heterogeneity of reporting standards (3). Most studies only reported diagnostic yield, and few suggested algorithms based on their results. Most larger studies also did not capture more recent advancements in

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both the quality and accessibility of newer imaging modalities (6–8).

The goal of this retrospective study was to provide a comprehensive assessment of the usage patterns, diagnostic yield, and diagnostic accuracy of imaging modalities used in the workup of undifferentiated PT at our institution. Based on results, we also propose a diagnostic algorithm based on the individual strengths and weaknesses of each diagnostic modality to guide clinicians when presented with the undifferentiated PT patient.

METHODS

This study was approved by the Institutional Review Board at the University of Pennsylvania (protocol 833420). A retrospective chart review was conducted of all patients presenting to otology/neurotology clinic with PT between 2009 and 2020. Digital records were queried for patients with the following diagnostic codes for PT: H93.A, H93.A1, and H93.A2. Patients who received an initial workup for PT at an outside institution prior to their first encounter were excluded. Data extracted included patient demographics (age, gender, body mass index), comorbidities, symptoms, physical exam findings, imaging studies ordered, radiographic findings, and final diagnoses. Patients were divided into four cohorts based on exam and audiometric findings: 1) normal (unrevealing), 2) suggestive of venous pathology (decrease in tinnitus with jugular compression), 3) suggestive of arterial pathology (bruit), and 4) suggestive of outer or middle ear pathology.

Imaging techniques are outlined in Supplement A, http://links.lww.com/MAO/B918. Diagnostic yield for a given scan was defined as the number of patients with findings derived from the study report that led to a diagnosis divided by the total number of subjects who underwent the study. The true-positive (TP), true-negative (TN), false-positive (FP), and false-negative (FN) rate for each imaging modality was calculated. TP was defined as the number of scans that correctly identified a nonidiopathic diagnosis, and TN was defined as the number of scans that correctly did not identify any diagnosis, corroborated by an unrevealing exam and negative results from all other testing. FP and FN were defined as the number of scans that incorrectly identified nonidiopathic or idiopathic diagnoses, respectively. The correct diagnosis, including classification as idiopathic, was defined as the final diagnosis reached by the treating neurotologist 3 months after initial presentation. This time period was determined a priori, which was felt to be enough allotted time for the treating physician to have reached a diagnostic determination. Accuracy was calculated by dividing the sum of true positives and true negatives by the total number patients who underwent the scan.

To evaluate the value of additive imaging modalities, patients that received specific initial "screening" studies followed by subsequent "second-line" imaging were reviewed in subgroup analyses, and the rate that subsequent imaging identified initially negative results was recorded.

Descriptive statistics were performed using R (3.6.3) via RStudio (RStudio Inc., Boston, MA). Differences between cohorts were explored using χ^2 test and Fisher exact test for categorical data and independent-samples *t*-test for continuous data. All testing was performed with a two-sided alpha level of 0.05 and 95% confidence interval.

RESULTS

In total, 315 patients met inclusion criteria. Demographics and cohort data are summarized in Table 1. Mean ± SD age was 52 ± 17 years with a female predominance (74%). PT was lateralized to the right in 43%, left in 41%, and bilateral in 16% of patients. In regard to associated symptoms, 25% of patients reported headaches and 3% reported vision changes. By cohort, 229 patients had unrevealing exams, 34 had exams suggestive of venous pathology, 16 had exams suggestive of arterial pathology, and 40 had exams suggestive of outer or middle ear pathology. Between cohorts, there were no significant differences in age, gender, or comorbidities.

Table 2 displays the final diagnosis stratified by cohort. Fifty-three percent (168/315) of patients received a nonidiopathic diagnosis for their tinnitus. There was a significantly greater diagnostic rate among patients with positive exam findings compared to patients with unrevealing exams (63% vs. 50%,

TABLE 1. *Patient characteristics stratified by cohort*

		Cohort by Physical Exam			
	Overall, N = 315	Unrevealing, n = 229	Venous, n = 32	Arterial, n = 14	Outer/Middle Ear, n = 40
Age	52 (17)	52 (16)	49 (18)	54 (21)	54 (14)
Sex					
Female	234 (74%)	167 (73%)	27 (84%)	8 (57%)	32 (80%)
Male	81 (26%)	62 (27%)	5 (16%)	6 (43%)	8 (20%)
BMI	28 (7)	28 (6)	28 (7)	28 (7)	39 (8)
Comorbidities					
HTN	92 (29%)	64 (28%)	11 (34%)	5 (36%)	12 (30%)
DM	26 (8.3%)	20 (8.7%)	3 (9.4%)	2 (14%)	1 (2.5%)
CAD	6 (1.9%)	5 (2.2%)	0 (0%)	1 (7.1%)	0 (0%)
Symptoms					
Headaches	79 (25%)	57 (25%)	8 (26%)	5 (38%)	9 (22%)
Vision changes	10 (3.2%)	9 (3.9%)	0 (0%)	0 (0%)	1 (2.5%)

Data are presented as mean (SD) and n (%).
CAD indicates carotid artery disease; DM, diabetes mellitus; BMI, body mass index; HTN, hypertension.

TABLE 2. *Final diagnoses stratified by cohort*

		Cohort by Physical Exam				
	Overall, N = 315[1]	Unrevealing, n = 229	Venous, n = 32	Arterial, n = 14	Outer/Middle Ear, n = 40	p^a
Idiopathic	146 (47%)	115 (50%)	14 (44%)	3 (21%)	15 (38%)	0.10
Sigmoid sinus dehiscence	48 (15%)	34 (15%)	12 (38%)	2 (14%)	0 (0%)	<0.001
Superior canal dehiscence	29 (9.2%)	24 (10%)	2 (6.2%)	1 (7.1%)	2 (5.0)%	0.8
Intracranial hypertension	9 (2.9%)	7 (3.1%)	0 (0%)	1 (7.1%)	1 (2.5%)	0.5
Glomus Tumor	23 (7.3%)	8 (3.5%)	1 (3.1%)	0 (0%)	14 (35%)	<0.001
Aneurysm	13 (4.1%)	10 (4.4%)	1 (3.1%)	2 (14%)	0 (0%)	0.13
AVM	14 (4.4%)	11 (4.8%)	0 (0%)	3 (21%)	0 (0%)	0.018
Carotid stenosis	8 (2.5%)	4 (1.7%)	0 (0%)	4 (29%)	0 (0%)	<0.001
Otosclerosis	24 (7.6%)	14 (6.1%)	2 (6.2%)	2 (14%)	6 (15%)	0.14
Other	29 (9.2%)	23 (10%)	1 (3.1%)	1 (7.1%)	4 (10%)	0.7
Cholesteatoma	2 (0.6%)	1 (0.4%)	0 (0%)	0 (0%)	1 (2.5%)	0.5
Acoustic neuroma	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	1 (2.5%)	0.3

Data are presented as n (%).
[a]Pearson chi-squared test; Fisher exact test.
AVM indicates arteriovenous malformation.

respectively, $p = 0.04$). In the venous cohort, the most common cause of tinnitus was sigmoid sinus dehiscence (38%, 12/32) followed by superior canal dehiscence (6.2%, 2/32). In the arterial cohort, the most common diagnoses were carotid artery stenosis (29%, 4/14) and arteriovenous malformation (21%, 3/14). In the outer/middle ear pathology cohort, the most common diagnoses were glomus tumor (35%, 14/40) and otosclerosis (15%, 6/40). Patients with unrevealing exams had a variable distribution of diagnoses; the most common diagnosis was sigmoid sinus dehiscence (15%, 34/229) followed by superior canal dehiscence (10%, 24/229).

Selection of Imaging Studies

An average of 2.2 imaging studies were ordered per patient within 3 months of presentation (Table 1). The arterial cohort had the highest average number of imaging studies ordered (2.7), and the outer/middle ear pathology cohort had the fewest average number of imaging studies ordered (1.6). The outer/middle ear cohort required significantly fewer imaging studies compared to the other three cohorts ($p = 0.001$). The most commonly ordered studies for patients with unrevealing exams were CT temporal bone (CTTB) (60%, 138/229) and MRA (53%, 122/229). The most commonly ordered scans in the venous cohort were CTTB (69%, 22/32) and MRA (50%, 16/32), in the arterial cohort were MRA (64%, 9/14) and CTTB (43%, 6/14), and in the outer/middle ear pathology cohort were CTTB (55%, 22/40) and MRI (53%, 21/40). MRA was ordered more frequently than CTA (49% vs 30%). Only 2.8% of patients underwent formal angiography.

Diagnostic Yield, Sensitivity, and Specificity

Table 3 displays the diagnostic yield of imaging studies. The imaging modality with the highest diagnostic yield was CT venography (CTV) (44%, 7/16), followed formal angiography (42%, 8/19) and MRV (40%, 20/50).

We then considered the diagnostic accuracy of each study. Table 4 displays the TP, TN, FP, FN, sensitivity, specificity, and accuracy for each imaging study. Formal angiography had the greatest sensitivity, specificity, and diagnostic accuracy (0.94, 0.82, and 0.87, respectively). The imaging study with the lowest accuracy was CT head (CTH) (0.62); the study with the lowest sensitivity was MRV (0.80), and the study with the lowest specificity was CTH (0.50).

Utility of Second-Line or Additive Imaging Modalities

To evaluate the value of "second-line" modalities, we considered subpopulations of patients that received specific combinations of imaging studies. Eighty-one patients with an initially negative CTTB or CTH subsequently underwent minimally invasive angiography (CTA/V or MRA/V). The diagnostic yield of minimally invasive angiographic studies after a negative CT was 30% (24/81). Among seven patients in the arterial cohort with a negative minimally invasive angiographic study who subsequently underwent formal angiography; 43% (3/7) resulted in a new positive finding leading to a diagnosis (one aneurysm and two arteriovenous

TABLE 3. *Diagnostic yield of individual imaging studies*

	Unrevealing	Venous	Arterial	Outer/Middle Ear	Overall
MRI	26% (26/101)	42% (5/12)	50% (5/10)	67% (14/21)	35% (50/144)
CTH	31% (4/13)	0% (0/1)	0% (0/1)	25% (1/4)	26% (5/19)
CTTB	30% (42/138)	64% (14/22)	67% (4/6)	64% (14/22)	39% (74/188)
CTA	25% (20/79)	25% (2/8)	50% (2/4)	60% (3/5)	28% (27/96)
CTV	42% (5/12)	33% (1/3)	100% (1/1)	0% (0/0)	44% (7/16)
MRA	27% (33/122)	31% (5/16)	56% (5/9)	43% (3/7)	30% (46/154)
MRV	36% (13/36)	38% (3/8)	100% (4/4)	0% (0/2)	40% (20/50)
Formal Angiography	46% (6/13)	0% (0/2)	67% (2/3)	0% (0/1)	42% (8/19)

TABLE 4. *Diagnostic accuracy of individual imaging studies*

	FN	FP	TN	TP	Accuracy	Sensitivity	Specificity
MRI	34	5	60	45	0.73	0.90	0.64
CTH	7	0	7	5	0.62	0.91	0.50
CTTB	48	5	66	69	0.72	0.93	0.58
CTA	23	2	46	25	0.74	0.93	0.67
CTV	3	0	6	7	0.79	0.93	0.67
MRA	38	6	70	40	0.71	0.87	0.65
MRV	11	4	19	16	0.70	0.80	0.63
Formal Angiography	2	0	9	8	0.87	0.94	0.82

malformation). Among 189 patients who received a CTA or MRA, 35% (66/189) also underwent CTV or MRV. The diagnostic yield of additive venography to a negative minimally invasive angiography study was 17% (8/46).

DISCUSSION

Unlike for non-PT, an underlying cause can be identified in the majority patients with PT. There is currently no consensus on the ideal diagnostic approach, and the evaluation may result in any number of possible permutations of radiographic studies. This is the largest study to our knowledge to investigate patterns of radiographic workup and to compare the utility of various imaging modalities in patients with PT. We discuss the diagnostic yield and accuracy of common imaging modalities and propose a diagnostic algorithm to guide future clinicians when encountering patients with undifferentiated PT.

Among patients in this study, the affected demographics, the associated symptoms, and the comorbidity profile of patients with PT are similar to prior reports and have not drastically differed between studies (9,10). Most patients presented in middle age between the ages of 40 and 65 years with a female predominance. About half (53%) of the patients in our series received a nonidiopathic diagnosis, which is comparable to published diagnostic rates between 50% and 70% (2,3).

Efforts have been made in the past to suggest a workup algorithm for PT based on the diagnostic yields for various imaging modalities (2,6,10). A weakness of these analyses is they reported amassed calculations of diagnostic yield, without considering how stratifying patients by likely pathology may help optimize yield. Prior studies also did not evaluate the impact of additive or second-line imaging.

In this study, we divided patients into four cohorts based on initial exam findings: unrevealing, suggestive of venous pathology, suggestive of arterial pathology, and suggestive of outer/middle ear pathology. For venous pathology, the sensation of tinnitus should be compared with digital pressure over the ipsilateral internal jugular vein. PT of venous origin may decrease or subside with this maneuver (6). A bruit on auscultation is suggestive of an arterial etiology. About three quarters of patients in this study presented with unrevealing exams, and no single etiology was found to be explanatory in more than 15% of these cases.

The presence of an abnormal exam was significantly correlated with a nonidiopathic diagnosis. For example, among subjects with tinnitus that decreased with jugular compression, 78% were ultimately diagnosed with sigmoid sinus dehiscence. Among patients with bruits, carotid artery stenosis and arteriovenous malformations together accounted for half of final diagnoses (29% and 21%, respectively). In patients with abnormal outer/middle ear exams, the most common diagnoses were glomus tumor (56%) and otosclerosis (24%). The ability for initial exam findings to stratify patients where the majority could then be explained by one or two possible diagnoses underscores the potential for examination to guide further imaging decisions.

To determine the best initial imaging study, we first calculated diagnostic yield. Consistent with prior reports, the overall diagnostic yield was low across all imaging modalities, ranging from 25% to 46%. As expected, we found that noncontrast CTH and CTTB had high sensitivity but the lowest specificity (3). In patients with a negative CTH or CTTB, the addition of minimally invasive angiography was valuable, leading to a diagnosis 30% of the time. In those with negative minimally invasive angiography, formal angiography provided additional diagnostic information in 43% of cases.

Although diagnostic yield is an important metric, sensitivity, specificity, and diagnostic accuracy provide additional measures and have not been as readily reported in the literature (3). We found that all imaging modalities had relatively high sensitivity, ranging from 0.80 to 0.94; however, specificity was much more variable. Formal angiography had the highest specificity, whereas CTH and CTTB had the lowest. These estimates may vary depending on the prevalence of the various underlying causes of PT within a given patient population.

Altogether, these results suggest that noncontrast CT imaging alone may be insufficient to rule out the potential causes of PT and that both minimally invasive and formal angiography may play a role, particularly when vascular etiologies are suspected.

Diagnostic Algorithm for Patients with Undifferentiated PT

The potential etiologies of PT span a breadth of anatomical regions and pathophysiologies, requiring a systematic approach to diagnosis. Therefore, we sought to propose a diagnostic algorithm for undifferentiated PT based on the findings of this study and a previously conducted systematic review (3). These recommendations are summarized in Figure 1. On initial assessment, patients should undergo a thorough history, physical exam, and audiologic evaluation. Focused clinical evaluation is performed with the purpose of determining if the underlying etiology may be venous, arterial, or nonvascular in origin.

Venous Cohort

If the physical exam is concerning for venous pathology, the most likely diagnosis is sigmoid sinus dehiscence. Consistent with prior studies, we found that CTTB in this context had the highest diagnostic yield out of any imaging modality and is an appropriate screening modality in this group (1,2,11,12). Minimally invasive angiography should

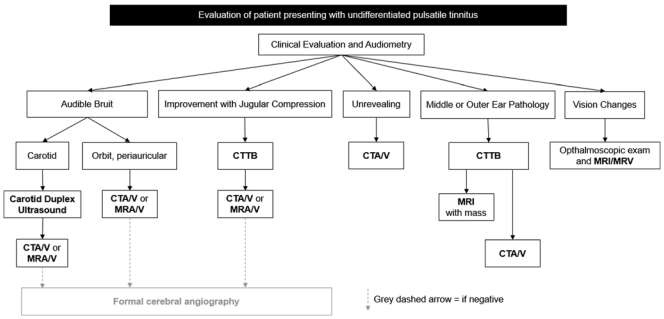

FIG. 1. Diagnostic approach for evaluation of undifferentiated PT. stratified into cohorts based on initial history, examination, and audiometry.

be considered as an adjunct to CTTB regardless if the CTTB is negative or positive. In our study, we found that minimally invasive angiography identified vascular pathology in 30% of patients with negative CTs. To this end, even among those with bony findings on CTTB, there may be up to a third of patients who may still have additional vascular findings that could be missed had the workup concluded with a CTTB.

The choice between CTA/V and MRA/V is less clear; we found MR-based angiography had comparable diagnostic yield and accuracy to CTA/V. MR may be associated with increased costs and decreased accessibility; however, MRA and MRV do not require contrast or radiation. Conversely, the ability to perform bone window reconstructions is an advantage for CTA/V, which may be of particular interest in the venous cohort where common pathologies involve bony dehiscence. Ultimately, the choice between CT and MR-based minimally invasive angiography depends on individual provider, patient, and facility-specific preferences.

Arterial Cohort

Although not included in this study, carotid doppler sonography (CDS) has previously shown a high diagnostic accuracy for cervical carotid pathology, which is the most common etiology of PT in patients with exams concerning for arterial pathology. As reported by Waldvogel et al. (7) and Tsai et al. (13), CDS has a comparable specificity to CT, MRI, and minimally invasive angiography for identifying carotid pathology. After CDS, evaluation with minimally invasive angiography is also recommended. CTH and CTTB may be skipped due to high false-negative rates; for example, in our arterial cohort, a third of patients with negative screening CTs demonstrated findings on subsequent angiographic studies. If an audible bruit is auscultated over the orbit or periauricular area, a minimally invasive angiographic study should be performed.

As in the venous cohort, the diagnostic yield of CT and MR-based minimally invasive angiography is comparable. Given their similarities, the choice between CT and MR-based minimally invasive angiography should also be made on an individual basis. If minimally invasive angiography remains nondiagnostic, we recommend formal angiography, which has significant additive value, and in our series was able to diagnose approximately half of patients with negative initial minimally invasive angiographic studies.

The relationship between vascular loop and PT remains controversial. Vascular compression of the eight cranial nerve theoretically causes axonal demyelination and reorganization, leading to the sensation of tinnitus; however, evidence remains mixed (14,15). In our practice, we generally do not attribute anterior inferior cerebellar artery loops as a cause for PT. For those who do, strongly T2-weighted MRI sequences, including CISS (constructive interference in steady-state imaging), FIESTA (fast imaging employing steady-state acquisition), and FFE (balanced fast-field echo), are ideal for evaluating this finding.

Outer/Middle Ear Pathology

Retrotympanic vascular masses such as a high-riding jugular bulb, aberrant carotid artery, or glomus tumor may all be appreciated. Schwartze's sign may be identified in those with otosclerosis. When examination or audiometry demonstrates an outer or middle ear pathology, CTTB is the optimal screening study and had the highest diagnostic yield for this cohort at 64%. This should be followed with CTA/V or MRI if a middle ear mass is suspected (12).

Unrevealing Exam

The diagnostic approach for an unrevealing head and neck exam is challenging, and other aspects of the patient's history become more important to narrow the differential. Elderly patients with risk factors for arterial disease such as prior cerebrovascular accidents, transient ischemic attacks, hyperlipidemia, hypertension, and smoking history should be evaluated for carotid stenosis. Obese females with headaches and visual disturbances may be suspected for idiopathic intracranial hypertension (IIH). If visual changes are suspected, formal evaluation by a neuro-ophthalmologist is mandatory.

Otosclerosis and superior canal dehiscence were two of the most common pathologies overall; however, both were associated with normal exams (Table 2). The pathophysiology of PT for otosclerosis has not been completely elucidated. One theory is the exchange hypothesis, which postulates that highly vascularized otospongiotic bone leads to sensations of PT (16). Another theory is that PT results from changes in perilymphatic vibratory properties secondary to the deposition of bony metabolites. For superior semicircular canal dehiscence, the sensation of PT is caused by the transmission of dural pulsations through the dehiscence

into the inner ear (17). The prevalence of superior canal dehiscence is 0.5% of the general population (18). However, imaging reports tend to overestimate the diagnosis by several fold so an alternative screening study is recommended to rule out other vascular findings.

In most patients with unrevealing exams, such as those with otosclerosis or evidence of superior canal dehiscence, a screening study with CTA/V is appropriate even if a CTTB was performed prior and balances high diagnostic yield with accuracy. MRI and MRV should also be performed in cases of increased intracranial pressure, which can show distension of the optic nerve sheaths, ventriculomegaly, or stenosis of the venous sinuses. In addition to imaging, blood and urine studies are important, particularly in cases where the exam is unrevealing. An in-depth review of additional laboratory studies is outside the scope of this report.

Limitations

There are important limitations to this study. Similar to other single-institution retrospective studies, heterogeneity exists in the diagnostic approaches used by individual clinicians and reporting patterns of radiologists. The distribution of pathologies and their relative frequencies cannot be generalized to the general population, as they may be influenced by differences in physician referral patterns and local demographics. As part of accuracy analysis, we defined true negative as a correct idiopathic diagnosis if the negative imaging result was corroborated by other testing that also did not identify pathology, and after an a priori workup period of 3 months; however, it is possible we overestimated the number of true negatives if there were some cases that would have been diagnosed after the 3-month period or with further testing. The diagnostic algorithm proposed in this study is based on retrospective observations. Future work should be directed at evaluating diagnostic yield and accuracy in a prospective design. Finally, small sample sizes in some cohorts limit statistical analysis on subgroup analysis. Further studies with larger, multi-institutional cohorts should be considered.

CONCLUSION

We present the results of our institutional experience with the diagnostic imaging workup in patients presenting with undifferentiated PT. Although most patients will have unrevealing exams, positive exam findings are associated with nonidiopathic diagnoses. The initial diagnostic study and subsequent testing should be tailored to the individual patient based on suspected pathology on examination. Our proposed stratification system, which separates patients into normal (unrevealing), venous, arterial, and outer/middle ear categories, allows for a diagnostic approach that optimizes the diagnostic yield and accuracy of subsequent radiographic study selections.

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