Association of Headache and Migraine in Patients With Patulous Eustachian Tube

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Introduction

- Patulous Eustachian tube (PET) is characterized by persistent abnormal patency of the Eustachian tube with a reported prevalence of 0.3-7.0% and occurs more commonly in females and young to middle-aged adults.
- Patients typically present with autophony of voice and breathing, aural fullness, tinnitus, and crackling sounds; these symptoms are often debilitating and substantially impair a patient's quality of life.
- Management of PET remains challenging, ranging from conservative measures to Eustachian tube augmentation and surgery, with no universally effective treatment and high rates of recurrence.
- Migraine produces otologic and vestibular symptoms, including dizziness, tinnitus, and aural fullness, that overlap with PET, yet no large-scale study has examined whether PET confers an elevated risk of incident migraine or headache.

Methods

- A retrospective case-control study was conducted using the TriNetX US Collaborative Network, a database of over 75 U.S. healthcare organizations comprising approximately 135 million patients.
- 5,820 patients diagnosed with patulous Eustachian tube (ICD-10-CM H69.0) were identified and matched 1:1 to healthy controls, yielding 11,640 participants in the primary analysis.
- Patients with pre-existing headache (ICD-10-CM R51) or migraine (ICD-10-CM G43), malignancy, rapid weight loss, GLP-1 receptor agonist use, bariatric surgery, or prior Eustachian tube procedure prior to PET diagnosis were excluded.
- Cohorts were balanced using 1:1 propensity score matching on age, sex, and race, with additional matching on relevant comorbidities including gastro-esophageal reflux disease, anxiety, rhinitis, depression, insomnia, and thyroid disease.
- The primary endpoints assessed in this study were the new diagnosis of headache, migraine, and "headache or migraine", evaluated at two follow-up intervals: 0–5 years and >5 years following PET diagnosis (Figure 1A, Table 1).
  - Secondary endpoints included new diagnosis of migraine without aura (ICD-10-CM G43.0) and migraine with aura (ICD-10-CM G43.1), evaluated over the same two intervals (Figure 1B, Table 1).
- A subgroup analysis compared patients with patulous Eustachian tube who developed a new diagnosis of migraine (n = 373) against those who did not (n = 5,619) across comorbidities (Table 2).
- Statistical analyses used the TriNetX Measures of Association tool; relative risk (RR) and risk difference with 95% confidence intervals were calculated, with significance set at $p < 0.05$.

Figure 1A. Relative Risk (RR) for New-Onset Headache and Migraine, 0-5 years and >5 years after Patulous Eustachian Tube Diagnosis

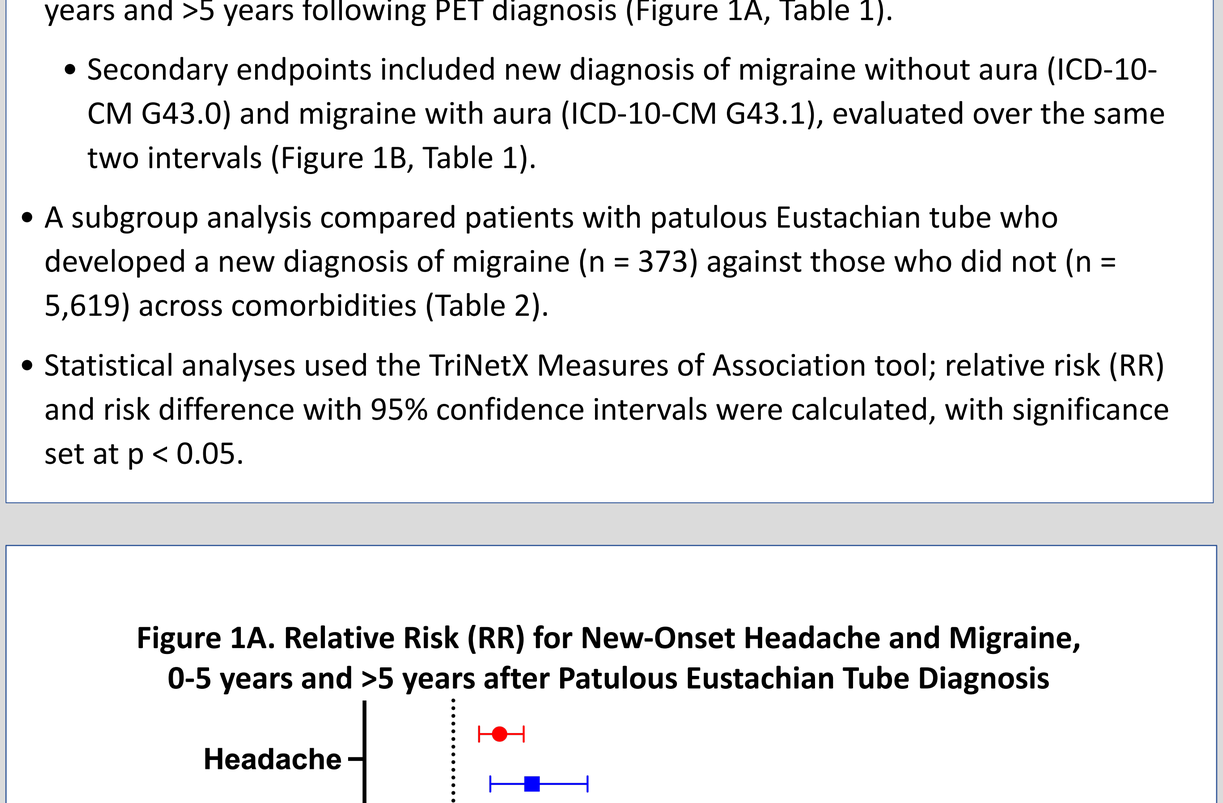


Figure 1B. Relative Risk (RR) for New-Onset Migraine with Aura and Migraine without Aura, 0-5 years and >5 years after Patulous Eustachian Tube Diagnosis

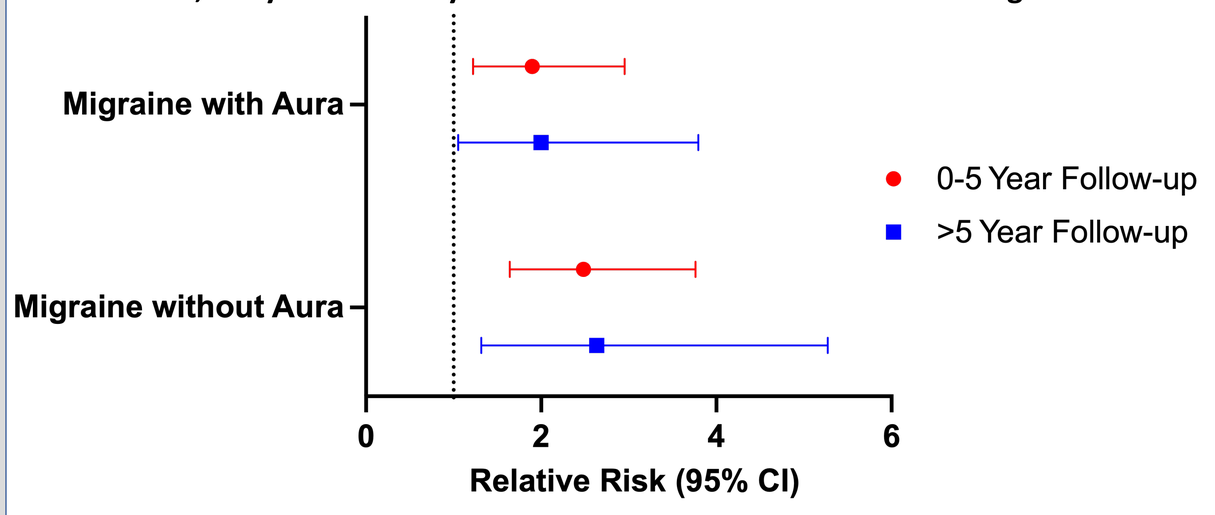


Figure 1. Risk of new-onset headache and migraine diagnosis following patulous Eustachian tube (PET) diagnosis, stratified by follow-up duration. Forest plots display relative risk (RR) with 95% confidence intervals for patients with PET compared to controls without PET, at 0-to-5-year (red circles) and greater than 5-year (blue squares) follow-up. **(A)** Primary endpoints: headache, migraine, and "headache or migraine". **(B)** Secondary endpoints: migraine with aura and migraine without aura. The dotted vertical line at RR = 1 indicates no difference in risk between groups.

Table 1. Relative Risk (RR) of New-Onset Headache or Migraine After Patulous Eustachian Tube Diagnosis, Stratified by 0-5 and Greater Than 5 Years Follow-up, Compared to Controls

	0–5-Year Follow-up		>5-Year Follow-up	
	RR (95% CI)	P-value	RR (95% CI)	P-value
New-Onset Headache and Migraine				
Headache	1.522 (1.291, 1.795)	< 0.001*	1.887 (1.419, 2.511)	< 0.001*
Migraine	2.149 (1.737, 2.658)	< 0.001*	2.044 (1.434, 2.915)	< 0.001*
Headache or migraine	1.688 (1.474, 1.933)	< 0.001*	1.901 (1.498, 2.412)	< 0.001*
New-Onset Migraine With vs. Without Aura				
Migraine without aura	2.484 (1.640, 3.763)	< 0.001*	2.636 (1.318, 5.272)	0.004*
Migraine with aura	1.900 (1.223, 2.952)	0.004*	2.000 (1.054, 3.795)	0.030*

*Statistically significant p-value

Table 2. Comorbidity Profile of Patulous Eustachian Tube Patients with New- Onset Migraine (PET MG) versus without Migraine (PET Non-MG)

Characteristic	PET MG (n = 373)	PET Non-MG (n = 5,619)	P-value
Sex			
Female	306 (82%)	3,333 (59%)	< 0.001*
Male	67 (18%)	2,286 (41%)	< 0.001*
Vestibular & otologic (ICD-10-CM)			
Dizziness and giddiness (R42)	162 (43%)	1,052 (19%)	< 0.001*
Tinnitus (H93.1)	125 (34%)	1,325 (24%)	< 0.001*
Otalgia (H92.0)	113 (30%)	994 (18%)	< 0.001*
Sensorineural hearing loss, bilateral (H90.3)	86 (23%)	1,570 (28%)	0.041*
Benign paroxysmal vertigo (H81.1)	16 (4%)	183 (3%)	0.281
Other ENT & structural (ICD-10-CM)			
Vasomotor and allergic rhinitis (J30)	126 (34%)	1,353 (24%)	< 0.001*
Temporomandibular joint disorders (M26.6)	50 (13%)	438 (8%)	< 0.001*

*Statistically significant p-value

Results

- PET was associated with a significantly elevated risk of headache, migraine, and "headache or migraine" at both 0-5 years and beyond 5 years of follow-up (Figure 1A, Table 1).
- Both migraine with and without aura remained significantly associated with PET at each follow-up interval, with migraine without aura showing the strongest association (Figure 1B, Table 1).
- Migraine relative risks were higher than headache relative risks at both follow-up intervals (Figure 1A, Table 1).
- PET MG had a higher proportion of female patients (Table 2).
- Dizziness, tinnitus, and otalgia were more common in PET MG (Table 2).

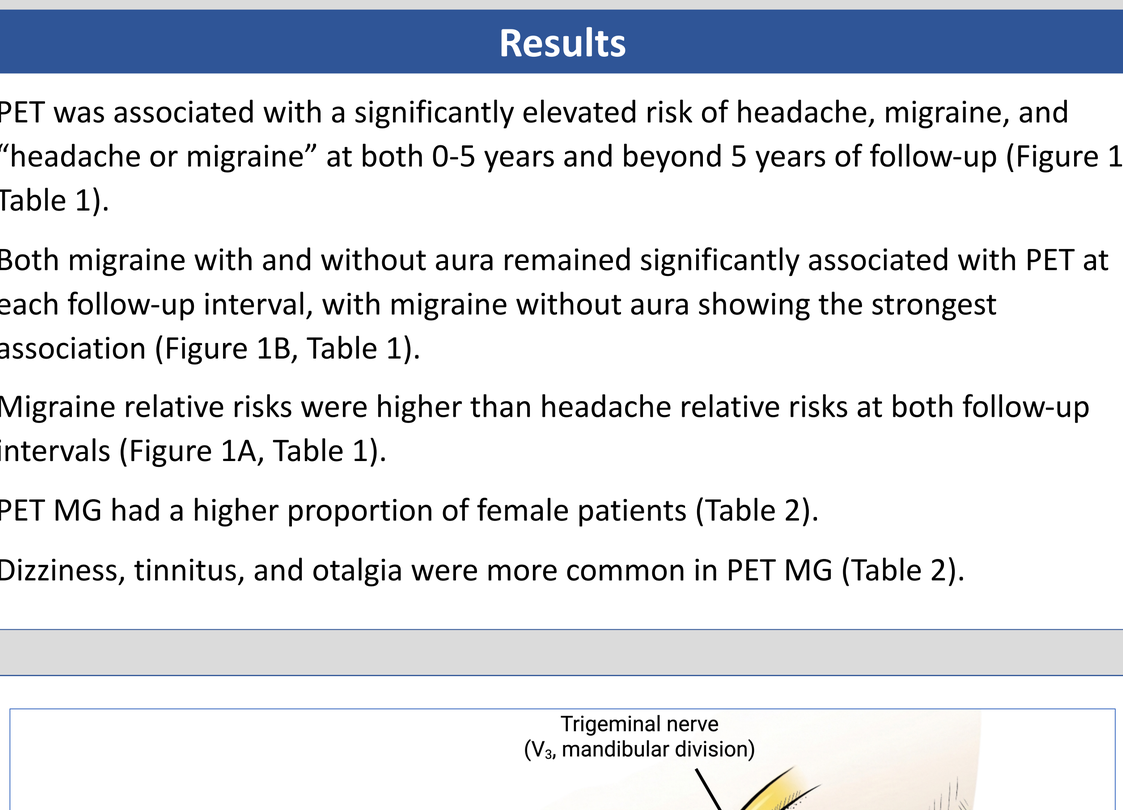


Figure 2. Relationship between the trigeminal nerve, tensor veli palatini muscle (TVP), and Eustachian tube. The trigeminal nerve gives a motor branch to the tensor veli palatini, which inserts on the cartilaginous Eustachian tube and dilates the Eustachian tube when contracted. Sustained trigeminal output can lead to persistent contraction of TVP and lead to patulous Eustachian tube.

Conclusions

- Patients diagnosed with patulous Eustachian tube have a significantly increased likelihood of being newly diagnosed with headache or migraine after their PET diagnosis.
- The risk of new headache or migraine diagnosis persisted in the first 5 years and even 5 years after their PET diagnosis.
- The link between PET and migraine may be mechanistically explained by increased trigeminal nerve activation in migraine patients .
- Tonic trigeminal action increases tone in the tensor veli palatini muscle and potentially leads to persistent Eustachian tube patency (Figure 2).

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