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# Clinical characteristics of patients with pulsatile tinnitus accompanied by ethmoid sinus lesions and high jugular bulb

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## Abstract

**Objective** Exploring the temporal bone Computed Tomography (CT) features and clinical characteristics of patients with ethmoid sinus lesions (ESL) combined with high jugular bulb (HJB) and pulsatile tinnitus symptoms.

**Methods** A retrospective analysis was conducted on the clinical data of pulsatile tinnitus (PT) patients. Patients with both ESL and HJB were classified into the combined group, while others were assigned to the non-combined group. The severity of tinnitus was assessed using the Tinnitus Evaluation Questionnaire (TEQ), along with the comparison of the clinical characteristics and treatment outcomes. Meanwhile, univariate analysis and multivariate regression analysis were performed to identify factors affecting the prognosis of patients.

**Results** Among patients with hearing loss in the combined group, the severity of hearing impairment was primarily moderate (65.85%), while that in the non-combined group was mainly mild (49.61%), with differences between the two groups ($P < 0.05$). In the hearing threshold curve classification, meanwhile, the combined group predominantly showed high-frequency hearing loss (64.63%), with the non-combined group mainly exhibiting low-frequency hearing loss (58.10%), and the differences between the two groups were significant ($P < 0.05$). The overall response rate of treatment in the combined group was lower than that in the non-combined group ($P < 0.05$). Moreover, prognostic regression analysis suggested the severity of hearing loss and the presence of ESL + HJB as independent risk factors affecting the prognosis of PT patients ($P < 0.05$).

**Conclusion** PT patients are predominantly affected on the right side, primarily manifested as intermittent tinnitus. The severity of hearing loss and the presence of ESL + HJB are independent factors affecting the prognosis of PT patients.

**Keywords** Ethmoid sinus lesions, High jugular bulb, Pulsatile tinnitus, Temporal bone CT

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## Introduction

Tinnitus has a prevalence of 10-25% in the population, with pulsatile tinnitus (PT) as a rarer type, accounting for about 4% of the overall tinnitus population [1]. Long-term PT can significantly affect the quality of life for patients and may lead to depression or even suicide in severe cases [2]. PT can be classified into arteriogenic and venogenic ones based on different etiologies, with venogenic PT accounting for up to 84% of cases [3], mostly due to abnormalities or variations in the veins [4].

Ethmoid sinus lesion (ESL), identified as one of the critical causes of PT in recent years [5], includes conditions such as stenosis in the junction of the transverse-sigmoid sinus and dysplasia of sigmoid sinus bone walls, such as sigmoid diverticulum and thin or defective bone walls. However, the complex etiology of vascular pulsatile tinnitus poses challenges for diagnosis and treatment. High jugular bulb (HJB) has been considered a source for some PT patients, accounting for about 30% of cases [6]. It has been shown that reduced jugular flow on the same side as PT can alleviate tinnitus symptoms, while increased flow under high-flow conditions is associated with heightened intensity of pulsatile tinnitus [7]. A study by Podoshin L et al. [8] has revealed a strong correlation between the anatomical morphology of the jugular bulb and the resulting blood flow patterns, with elevated transverse sinus stenosis combined with HJB showing significant vortex effects in numerical simulations of jugular bulb hemodynamics.

In clinical practice, it has been found that some PT patients are accompanied by both ESL and HJB, with diverse clinical characteristics, yet there are currently no related reports. Imaging examinations are the most critical diagnostic tool for PT. In this study, a retrospective analysis was conducted on the clinical data of patients with PT caused by venous vascular-related diseases in our hospital, aiming to explore the clinical characteristics of PT patients combined with ESL and HJB, thereby providing references for otolaryngologists to develop appropriate therapies based on the etiologies. The findings are reported as follows.

## Materials and methods

### Study subjects

A retrospective analysis was conducted on the clinical data of patients with PT caused by venous vascular-related diseases who visited the No.2 Hospital of Baoding from January 2018 to June 2024. Patients combined with both ESL and HJB were divided into the combined group, while those with either condition but not both were assigned to the non-combined group. Inclusion criteria: (1) Patients with PT caused by venous vascular-related disease; (2) Imaging examination suggested ESL (including sigmoid diverticulum and exposed, sigmoid sinus wall bone defects, etc.), HJB (the upper edge of the jugular bulb exceeded the lowest edge of the cochlear base); (3) Patients with no history of head/neck/ear/nose/throat surgery and trauma; (4) Age > 18 years; (5) Patient with normal mental development. Exclusion criteria: (1) Patients with chronic otitis media and mastoiditis, tumor, artery-related diseases, trauma, and other lesions involving the skull base; (2) Patients who were unable to complete the scale due to low education levels; (3) Patients with a history of mental illness and family history.

### Study methods

#### *Data collection*

The clinical data of the two groups were collected, including the general data, site of disease, duration of disease, PT characteristics, characteristics of the disease, and accompanying symptoms (headache or dizziness, ocular symptoms, hearing loss, etc.).

#### *Otology-related examinations*

Imaging examination: Temporal bone CT scan was performed with Siemens dual-source CT (SOMATOM Definition); scanning scope: from C4 vertebral body to cranial vault; scanning parameters: tube voltage 120 kV, tube current 120–150 mAs, Layer 0.67 mm, layer spacing 0.67 mm; WC700, WW window level 3600; The scanning range is horizontal from the bottom of the mastoid process to the upper edge of the semicircular canal. Post processing: MPR, MIP.

Criteria for HJB diagnosis: the upper edge of the jugular bulb exceeded the lowest edge around the cochlear base. Criteria for ESL diagnosis: stenosis in the junction of the transverse-sigmoid sinus and dysplasia of the sigmoid sinus bone wall (sigmoid diverticulum and thin and defective bone wall).

Hearing tests: Pure-tone audiometry and acoustic immittance were performed for both groups to determine the presence of hearing loss and the severity and type of hearing loss. Following the WHO criteria formulated in 1997 [8], mean values of 26–40 dB, 41–60 dB, 61–80 dB, and ≥ 81 dB at hearing thresholds of 0.5, 1, 2, and 4 kHz indicate mild, moderate, severe, and very severe hearing loss, respectively.

Hearing threshold curve classification was performed following the 2015 edition of guidelines [9]. Low-frequency hearing loss: hearing loss at 1,000 Hz and below, with hearing loss ≥ 20 dBHL at least at 250 and 500 Hz. High-frequency hearing loss: hearing loss at 4,000 Hz and above, with hearing loss ≥ 20 dBHL at least 4,000 and 8,000 Hz. Flat hearing loss: hearing loss at all frequencies, with hearing loss ≤ 80 dBHL at a mean hearing threshold of 250-8,000 Hz. Total deafness:

hearing loss at all frequencies, with hearing loss ≥ 95 dBHL at a mean hearing threshold of 250-8,000 Hz.

#### *Questionnaires*

All patients were asked and filled in the Tinnitus Evaluation Scale (TEQ) by the same physician during their initial and follow-up visits [10], including 6 items assessing the loudness and duration of perceived tinnitus, the impact on sleep, concentration, and mood, and the overall severity score. The scores for each item are summed to obtain the total score, with a maximum of 21 points, and higher scores indicate more severe tinnitus symptoms, with 1–6 points for grade I, 7–10 points for grade II, 11–14 points for grade III, 15–18 points for grade IV, and 19–21 points for grade V. The higher grade indicates more severe tinnitus.

### Therapy and evaluation criteria

Patients in both groups were given mecobalamin tablets (Jiangxi Qingfeng Pharmaceutical Group, 0.5 mg/tablet, 1 tablet/time, 3 times/d, orally), ginkgo tablets (Hubei Wushi Pharmaceutical Co., Ltd., flavonol glycosides 19.2 mg and betalactone 4.8 mg/tablet, 1 tablet/time, 3 times/d, orally, for 1 month). Mecobalamin is known to support nerve function and enhance neural recovery, making it particularly effective for addressing tinnitus resulting from organic factors [11]. Ginkgo tablets, rich in flavonoids, improve blood circulation and reduce oxidative stress, which can further alleviate tinnitus symptoms [12]. Treatment was continued until patients reported that their tinnitus had disappeared or significantly decreased.

Criteria for determining the efficacy in tinnitus: TEQ was assessed by the same physician again 1 month after drug treatment, with the efficacy determined according to the changes in TEQ grades at initial and follow-up visits. Criteria: (1) Recovered: tinnitus disappeared; (2) Markedly effective; the severity of tinnitus reduced by 2 grades or above; (3) Effective; the severity of tinnitus reduced by 1 grade; (4) Ineffective: the severity of tinnitus did not change. Afterward, the patients were divided into the effective group (recovered + markedly effective + effective) and the ineffective group (ineffective) according to the efficacy.

### Statistical methods

SPSS 26.0 software was used for statistical analysis. The distribution pattern of measurement data was determined using K-S tests, with data following normal distribution expressed as $\bar{x} \pm s$, and t-tests were used for inter-group comparisons. The data not following normal distribution were expressed as M (P25, P75), with the Mann-Whitney U test utilized. Inter-group comparisons of count data were performed using the $\chi^2$ test. Binary logistic regression was adopted to analyze the independent risk factors affecting the prognosis of PT prognostic factors. $P < 0.05$ was considered significantly different.

## Results

### Clinical data

A total of 485 PT patients were included in the study (M = 101, F = 384), aged 14–80 years, with a mean age of 44.10 ± 13.23 years. A total of 186 patients were included in the combined group, including 26 males and 160 females, with a mean age of 41.15 ± 12.54 years, of whom 65 had sigmoid sinus fenestrations and 121 had sigmoid sinus defects (defect width 3.71 ± 2.01 mm). The non-combined group included 299 patients (M = 75, F = 224), with a mean age of 45.94 ± 13.33 years, with the right ear as the predominant site of disease in both groups. The proportion of patients without accompanying symptoms in the combined group was lower than that in the non-combined group (17.20% VS 24.08%), and the proportion of patients with accompanying symptoms of hearing loss was higher than that in the non-combined group (44.09% VS 35.12%), with statistically significant differences between the two groups ($P < 0.05$). Additionally, no significant differences were observed between the two groups in gender, age, site of disease, TEQ grade, PT characteristics, duration of disease, and manifestations of accompanying symptoms (headache or dizziness, ocular symptoms, etc.) ($P > 0.05$). See Table 1.

### The thinning and defect of bone in the sigmoid sinus wall

82 (44.09%) and 105 (35.12%) patients in the combined and non-combined groups experienced hearing loss, respectively, with a higher proportion of patients with hearing loss in the former than in the latter. Among patients with hearing loss in the combined group, the severity of hearing impairment was mainly moderate (65.85%), while that in the non-combined group was mainly mild (47.61%), and the differences between the two groups were statistically significant ($P < 0.05$). In hearing threshold curve classification, the combined group predominantly exhibited high-frequency hearing loss (64.63%), and the non-combined group mainly showed low-frequency hearing loss (58.10%), with statistically significant differences between the two groups ($P < 0.05$). See Fig. 1; Table 2.

### The degree of hearing loss

The combined group: recovered ($n = 26$), markedly effective ($n = 32$), effective ($n = 47$), and ineffective ($n = 81$), with an overall response rate of 54.46%. The non-combined group: recovered ($n = 52$), markedly effective ($n = 73$), effective ($n = 105$), and ineffective ($n = 69$), with an overall response rate of 76.92%. The overall response

**Table 1** Comparison of clinical data between the 2 groups

| Factor | Characteristics | Combined group(186) | Non-combined group(299) | $\chi^2$/t/Z | *P* |
|---|---|---|---|---|---|
| Gender | M | 26(13.98) | 75(25.08) | 0.739 | 0.604 |
| | F | 160(86.02 | 224(74.92) | | |
| Age (Years) | | 41.15 ± 12.54 | 45.94 ± 13.33 | 1.904 | 0.077 |
| Site of disease | Left year | 49(29.07) | 85(28.43) | 7.306 | 0.136 |
| | Right year | 112(60.22) | 175(58.53) | | |
| | Both years | 25(13.44) | 39(13.04) | | |
| TEQ grade | I | 24(12.90) | 37(12.37) | 0.804 | 0.394 |
| | II | 48(25.81) | 74(24.75) | | |
| | III | 53(28.49) | 96(32.11) | | |
| | IV | 41(22.04) | 63(21.07) | | |
| | V | 20(10.75) | 29(9.70) | | |
| PT characteristics | Persistent PT | 47(25.27) | 82(27.42) | 0.523 | 0.085 |
| | Intermittent PT | 139(74.73) | 217(72.58) | | |
| Duration of disease(Month) | | 11.00(3.00,34.00) | 9.00(1.00,20.00) | -1.903 | 0.063 |
| Accompanying symptoms | No | 32(17.20) | 72(24.08) | 1.603 | 0.045 |
| | Headache or dizziness | 23(12.37) | 42(14.05) | 0.405 | 0.085 |
| | Ocular symptoms | 37(19.89) | 63(21.07) | 0.325 | 0.791 |
| | Hearing loss | 82(44.09) | 105(35.12) | 0.703 | 0.352 |
| | Others | 12(6.45) | 17(5.69) | 0.631 | 0.319 |

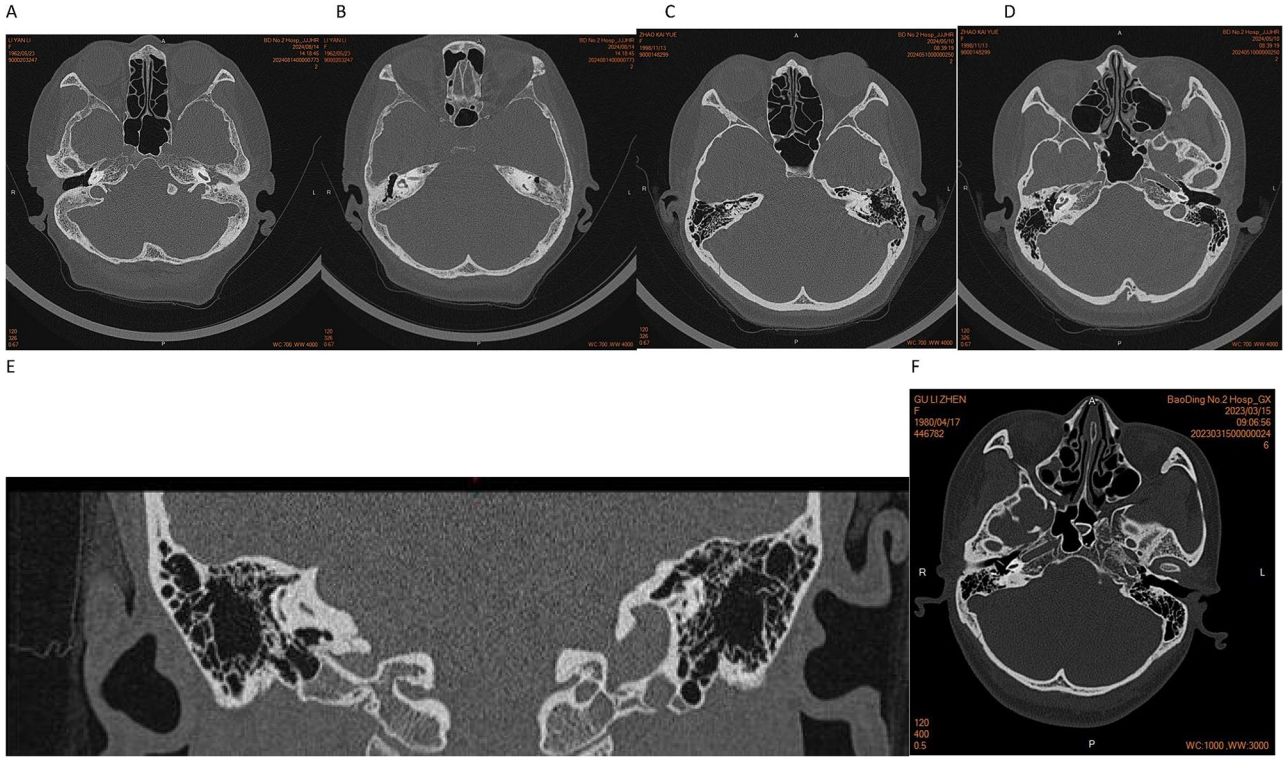


**Fig. 1** **A**: A 62-year-old female presented with a 1-month history of high left ear pain in the jugular fossa and left middle ear mastoiditis. Bilateral without sigmoid sinus disease **B**: A 62-year-old female presented with a 1-month history of left ear pain; left middle ear mastoiditis. High jugular fossa, bilateral, without sigmoid sinus disease **C**: Female 23 years old, normal mastoid process, tinnitus, deep sigmoid sulcus on the left side, diverticulum, thin bone wall, high jugular vein on the left side **D**: Female 23 years old, normal mastoid process, tinnitus, deep sigmoid sulcus on the left side, diverticulum, thin bone wall, high jugular vein on the left side **E**: Female 23 years old, normal mastoid process, tinnitus, deep sigmoid sulcus on the left side, diverticulum, thin bone wall, high jugular vein on the left side **F**: Female 45 years old, tinnitus for half a year, bone wall defect of about 2 mm in superior flexure segment of right sigmoid sinus

**Table 2** Comparison of hearing loss between the 2 groups

| Factor | Characteristics | Combined group(82/186) | Non-combined group(105/299) | $\chi^2$/t/Z | *P* |
|---|---|---|---|---|---|
| Severity of hearing loss | Mild | 14(17.07) | 50(47.61) | 6.903 | 0.022 |
| | Moderate | 54(65.85) | 36(34.29) | | |
| | Severe | 14(17.07) | 19(18.10) | | |
| Hearing threshold curve classification | Low-frequency hearing loss | 17(20.73) | 61(58.10) | 8.704 | 0.010 |
| | High-frequency hearing loss | 53(64.63) | 25(23.81) | | |
| | Flat hearing loss | 12(14.63) | 19(18.10) | | |

**Table 3** Comparison of efficacy between the 2 groups

| Group | Recovered | Markedly effective | Effective | Ineffective | Overall response rate |
|---|---|---|---|---|---|
| Combined group | 26 | 32 | 47 | 81 | 54.46% |
| Non-combined group | 52 | 73 | 105 | 69 | 76.92% |
| $\chi^2$ | | | | | 10.429 |
| *P* | | | | | 0.003 |

**Table 4** Univariate analysis of prognostic factors

| Factor | Characteristics | Ineffective group(150) | Effective group(335) | $\chi^2$/t/Z | *P* |
|---|---|---|---|---|---|
| Gender | M | 27(18.00) | 74(22.09) | 0.802 | 0.784 |
| | F | 123(82.00) | 261(77.91) | | |
| Age (Years) | | 43.61 ± 13.55 | 44.32 ± 13.10 | 1.903 | 0.428 |
| Site of disease | Left year | 39(26.00) | 95(28.36) | 7.495 | 1.205 |
| | Right year | 95(63.33) | 192(57.31) | | |
| | Both years | 16(10.67) | 48(14.33) | | |
| TEQ grade | I | 25(16.67) | 36(10.75) | 1.103 | 0.429 |
| | II | 43(28.67) | 79(25.58) | | |
| | III | 36(24.00) | 113(33.73) | | |
| | IV | 30(20.00) | 74(22.09) | | |
| | V | 16(10.67) | 33(9.85) | | |
| PT characteristics | Persistent PT | 44(29.33) | 85(25.37) | 0.410 | 0.074 |
| | Intermittent PT | 106(70.67) | 250(74.63) | | |
| Duration of disease(Month) | | 10.00(1.00,34.00) | 10.00(1.00,33.00) | -1.503 | 0.293 |
| Accompanying symptoms | No | 36(24.00) | 68(20.30) | 1.803 | 0.136 |
| | Headache or dizziness | 20(13.33) | 45(13.43) | 0.803 | 0.983 |
| | Ocular symptoms | 29(19.33) | 71(21.19) | 0.693 | 0.205 |
| | Hearing loss | 57(38.00) | 130(38.81) | 1.101 | 0.942 |
| | Others | 8(5.33) | 21(6.27) | 0.436 | 0.783 |
| Severity of hearing loss | Mild | 11(7.33) | 53(15.82) | 6.284 | 0.032 |
| | Moderate | 39(26.00) | 51(15.22) | | |
| | Severe | 7(4.67) | 26(7.76) | | |
| Hearing threshold curve classification | Low-frequency hearing loss | 21(14.00) | 57(17.01) | 7.803 | 0.074 |
| | High-frequency hearing loss | 25(16.67) | 53(15.82) | | |
| | Flat hearing loss | 11(7.33) | 20(5.97) | | |
| Combined ESL + HJB | | 81(54.00) | 105(31.34) | 10.392 | 0.002 |

rate in the combined group was significantly lower than that of the non-combined group, with statistically significant differences observed between the two groups ($P < 0.05$). See Table 3.

#### Univariate analysis of factors affecting prognosis

Univariate analysis was performed after dividing the patients into the effective group (recovered + markedly effective + effective) and the ineffective group (ineffective) according to clinical efficacy. The results suggested significant differences in the severity of hearing loss ($\chi^2 = 6.284$, $P = 0.032$) and combined ESL + HJB ($\chi^2 = 10.392$, $P = 0.002$) between the effective and ineffective groups ($P < 0.05$), as shown in Table 4.

#### Binary logistic regression analysis of prognostic factors

Regression analysis was conducted using the variables statistically significant in the above univariate analysis as independent variables and whether the clinical efficacy was effective as the dependent variable. The results

**Table 5** Logistic regression analysis of prognostic factors

| Factor | β | SE | Wald | OR | *P* | 95%CI |
|---|---|---|---|---|---|---|
| Severity of hearing loss | 1.320 | 0.439 | 4.284 | 3.402 | 0.005 | 1.210 ~ 7.903 |
| Combined ESL + HJB | 1.284 | 0.472 | 3.671 | 3.184 | 0.001 | 1.114 ~ 9.025 |

revealed that the severity of hearing loss (OR = 3.402, 95CI%: 1.210–7.903) and combined ESL + HJB (OR = 3.184, 95CI%: 1.114–9.025) were independent risk factors affecting the prognosis of PT patients ($P < 0.05$). See Table 5.

## Discussion

Pulsatile tinnitus (PT) is an abnormal sound generated by organs in the head and neck, cardiovascular system, or other structures before transmitting to the inner ear through bone structures, blood vessels, or blood flow, and perceived by the patient, and its rhythm is mostly consistent with the heartbeat [13]. High jugular bulb (HJB), a congenital vascular variation that directly affects the structures of the middle and inner ear, can lead to difficult-to-treat clinical conditions [14]. Despite several studies having explored the mechanisms by which HJB causes tinnitus and specifically investigating the clinical characteristics of HJB combined with PT, there is currently a lack of research on the treatment outcomes and prognostic factors for PT patients combined with ESL and HJB.

This study included a total of 485 PT patients (M = 101, F = 384), with significantly more females than males and the right side as the predominant site of disease, which is consistent with previous studies that reported a higher incidence of PT on the right side [15]. This is due to anatomic dysplasia of the bilateral jugular veins, where the amount of blood draining from the intracranial venous system into the jugular vein is less on the left side than on the right, resulting in a higher incidence of HJB on the right side. The findings of this study indicated that the combined group primarily exhibited high-frequency hearing loss (64.63%), while the non-combined group predominantly showed low-frequency hearing loss (58.10%), possibly related to the high jugular bulb being located lateral to the basal periphery of the cochlear and the subject-perceived high-frequency sounds on the lateral of the cochlear duct [16]. Metabolic activity is higher in the cochlea's base, which corresponds to high-frequency hearing. In patients with a HJB, compromised cochlear perfusion may affect high-frequency thresholds more significantly, as these frequencies rely heavily on this area's metabolic support. Additionally, among patients with hearing loss in the combined group, the severity of hearing loss was primarily moderate (65.85%), while the non-combined group mainly exhibited mild hearing loss (49.61%), the difference between which may also be related to HJB-induced inner and middle ear lesions [17]. Since HJB serves as the confluence for the inner ear venous circulation into the internal jugular vein, the inner ear circulation will be impaired when tinnitus occurs, while the slow blood flow in HJB may further affect or exacerbate this impairment, leading to aggravation of symptoms [18]. Given that the vascular blood flow as the source of tinnitus persists and the inner ear functions normally in receiving sounds, the mastoid air cells of the temporal bone are a necessary pathway for the transmission of PT related to ethmoid sinus abnormalities, and the degree of pneumatization and gas-containing state in these cells may be critical factors affecting the occurrence of tinnitus symptoms [19].

Abnormalities of the superior and inferior segments of the sigmoid sinus region are usually observed on imaging in PT of venous origin, which mainly include elevation and enlargement of the jugular venous bulb, bone wall defects, and diverticula, sigmoid sinus antecedent, bone wall defects leading to diverticula, and enlarged malformations of the mastoid conduit vein. Among them, sigmoid sinus bone wall defect is one of the most common PT triggers [20]. It is usually believed that the anatomical abnormalities of the jugular veins lead to altered hydrodynamic characteristics of the blood flow, which produces the sound source of tinnitus. Therefore, many previous reports have proposed a variety of possible mechanisms of tinnitus vocalisation due to venous sinus abnormalities, including the blood vortex hypothesis, the hyperemic state hypothesis, the vagal blood flow hypothesis, and the venous arterial chemistry hypothesis. Overall, alterations in the kinetic characteristics of blood flow are the main factor in PT sound vocalisation. Changes in the anatomy of the venous sinus affect the flow rate of blood flow as well as the laminar flow pattern, leading to the vibration of the vessel wall [21]. Du et al. [22] analysed that the reconstructed intact sigmoid sinus bone wall cuts off the path of beat sound conduction to the inner ear through the temporal bone airspace as the mechanism of surgical treatment of PT.

Prognosis significantly impacts the quality of life for PT patients. It has been demonstrated that the more severe the hearing loss in patients with sudden deafness, the poorer the prognosis of their tinnitus [23]. Additionally, numerous scientific studies have shown that PT can improve with the treatment of conductive hearing loss [24, 25]. The findings of this study indicate that the severity of hearing impairment is related to the prognosis of PT, primarily due to the fact that people with hearing loss generally experience organic damage to the auditory

system, while those with normal hearing may suffer functional disorders, making it relatively easier for the latter to eliminate the tinnitus. Meanwhile, external noise can mask PT tinnitus, helping patients achieve a more relaxed mental state [26]. People with normal hearing are more perceptive to external noise, while those with hearing loss experience a diminished sensory function for noises in specific frequency bands, leading to insufficient masking effects. This results in patients paying more attention to the tinnitus and preventing emotional release, thereby making it challenging to eliminate the tinnitus.

However, this study also comes with limitations: (1) Due to objective constraints, only one hospital was selected for research, and the sample size was limited, which may lead to bias in the results; (2) Since hearing tests are subject to subjective factors, occult hearing loss was not tested, which could lead to errors; (3) Hemodynamic data from patients were not collected. Therefore, hemodynamic assessments will be performed in future research, along with the collection of more objective indicators, so as to gain a more comprehensive understanding of the prognostic factors affecting PT.

## Conclusion

In conclusion, PT patients are predominantly affected on the right side, primarily manifested as intermittent tinnitus, and the overall response rate of drug treatment in the combined group is lower than that in the non-combined group. Additionally, the severity of hearing loss and the combined ESL + HJB are independent factors affecting the prognosis of PT patients. Clinically, the effect of ESL + HJB should be considered for diagnosis and treatment of tinnitus and hearing loss. Moreover, the diagnosis and treatment of PT patients involve multiple disciplines such as otolaryngology, neurosurgery, and radiology while requiring collaboration among various departments, thereby providing standardized, safe, and effective diagnosis and treatment for PT patients.

**Acknowledgements**
Not applicable.

**Author contributions**
Study conception and design: ZHW, ZZM, WZ. Data collection: ZX, WLY, YXQ, HJW. Data analysis and interpretation: WL, CYJ, WZY, FXM, ZZQ. Drafting of the article: ZHW, ZZM, WZ Critical revision of the article: All authors.

**Funding**
Not applicable.

**Data availability**
All data generated or analyzed during this study are included in this published article.

## Declarations

**Ethics approval and consent to participate**
This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Baoding NO.2 Hospital.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

Received: 11 September 2024 / Accepted: 16 November 2024
Published online: 20 February 2025

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