Supplementary

Appendix 1

Materials and methods

Participants

Diagnostic criteria of subjective tinnitus

The diagnostic criteria of subjective tinnitus included the following: (I) unilateral or bilateral non pulsatile sound (sustainable or non-sustainable); (II) no abnormalities of hearing structures, including the auditory conduction pathway, inner ear hearing organs, auditory nerve, temporal lobe and brain parenchyma, found by imaging; (III) no causes of objective tinnitus resulting from ear trauma, vascular abnormalities, new organisms, etc. (1,2).

Diagnostic criteria of dominant drainage and high jugular bulb

Dominant drainage of transverse-sigmoid sinus is defined as the transverse sinus on one side, and the diameter of sigmoid sinus is more than 1.5 times that of the opposite side (17). High jugular bulb is defined as the basal rotation of the jugular bulb up to the ipsilateral cochlea (18) (*Figure S1*).

Hemodynamic analysis

CVI-42 has been used to post process the 4D Flow MRI data of all participants, and the specific processing process was as follows. First, the whole processing procedure was based on the small vessel algorithm provided by the software developer to analyze the data. After importing the image data into CVI, the software automatically detected the range of blood flow and performed preprocessing. The software used the offset correction and phase unwrapping function to further optimize the accuracy of blood flow region detection. Secondly, the vessels of interest were segmented and outlined. The vascular segment in this study was sinus confluence to transverse sinus to sigmoid sinus to jugular bulb to internal jugular vein. After the segmentation of vessels, in order to ensure the accuracy of blood flow measurements, the centerlines of blood vessels of interest were further tracked. Using the vessel centerline tracking function of the software, we respectively selected the sinus confluence and internal jugular vein as the start and end points of the centerline. After automatic tracking, we conducted careful inspection and correction to ensure the reliability of the centerline. Thirdly, hemodynamic analysis was performed. At this time, the software showed the segmented vessels' hemodynamic features, including the morphologies of the vessels of interest and the internal blood flow. The visualization of the streamline could help clarify the accuracy of blood flow direction setting. Blood flow abnormalities could be identified according to the changes of streamline color and shape.

Results

Hemodynamic abnormalities in the venous sinus of patients with VPT

There was no significant difference in the TV of the six planes among the three groups, but there were significant differences in the PV and MWSS of the six planes among the three groups (*Table S1*).

Relationship among hemodynamic factors, bone dehiscence, and severity of tinnitus

Plane 3 with the largest variability of blood flow was selected as the appropriate measurement plane to explore the relationship between hemodynamic parameters and the BD in patients with VPT. The TV (r=0.31, P=0.028), PV (r=0.62, P<0.001), MWSS (r=0.49, P<0.001), and MEL (r=0.54, P<0.001) were positively related to the size of BD as shown in *Figures S2,S3*. THI scale was used to evaluate the severity of tinnitus symptoms in patients with VPT. The TV (r=0.38, P=0.007), PV (r=0.63, P<0.001), MWSS (r=0.36, P=0.010), and MEL (r=0.57, P<0.001) on plane 3 were positively correlated with the THI scores. The size of BD in patients with VPT was also positively correlated with the THI score (r=0.47, P=0.002) (as shown in *Figures S2,S4*).

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In addition, the results showed that there were no statistically significant correlation between THI and TV (r=0.320, P=0.074), PV (r=−0.058, P=0.753), MWSS (r=0.009, P=0.960), and MEL (r=−0.108, P=0.556) (as shown in *Figure S5*).

The blue band shows the relationship between bone dehiscence and hemodynamics. The PV, MWSS, and MEL were positively correlated with the size of BD. The correlation between the PV and the size of BD was the strongest. The correlation between the TV and the size of BD was the weakest. The pink band shows the relationship between the severity of tinnitus, hemodynamics, and bone dehiscence, the correlation between the PV and THI was the strongest. The correlation between the MWSS and THI was the weakest.

The effect of BD on PT severity is mediated by hemodynamic factors

The MEL and PV showed complete mediation effects between the effect of BD and THI, as shown in *Figure 5A,5B* and *Table S2*. However, when the TV and MWSS were used as mediation variables, the model was invalid (*Figure S6*).

The BD a complete mediation effect between MWSS and THI, as shown in *Figure 5C* and *Table S3*. However, no significant mediation effect existed between the TV, PV, and THI when the BD was used as a mediation variable (*Figure S7*).

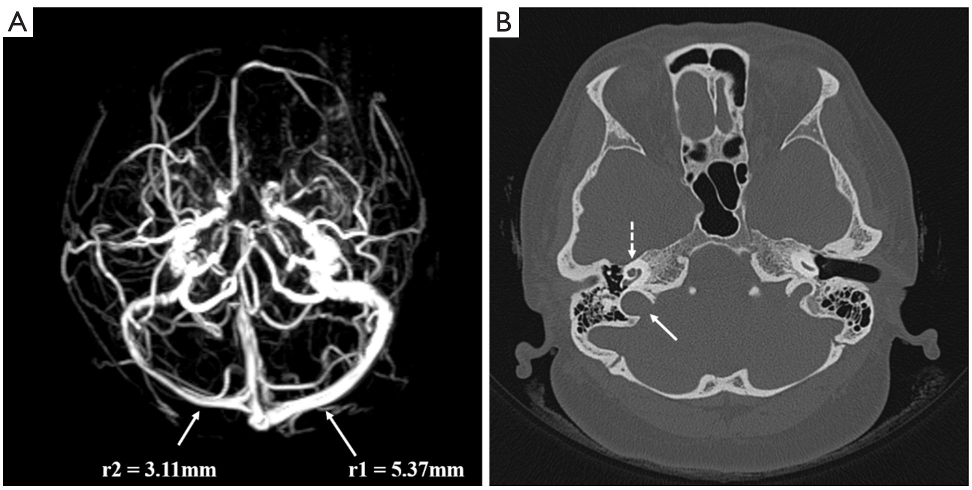

Figure S1 Diagnostic criteria of dominant drainage and high jugular bull. Dominant drainage was defined as the diameter of the vein on the dominant side was 1.5 times greater than that on the contralateral side. The high jugular bull was defined as the level of the jugular bulb reaching the bottom of cochlea on the same side.

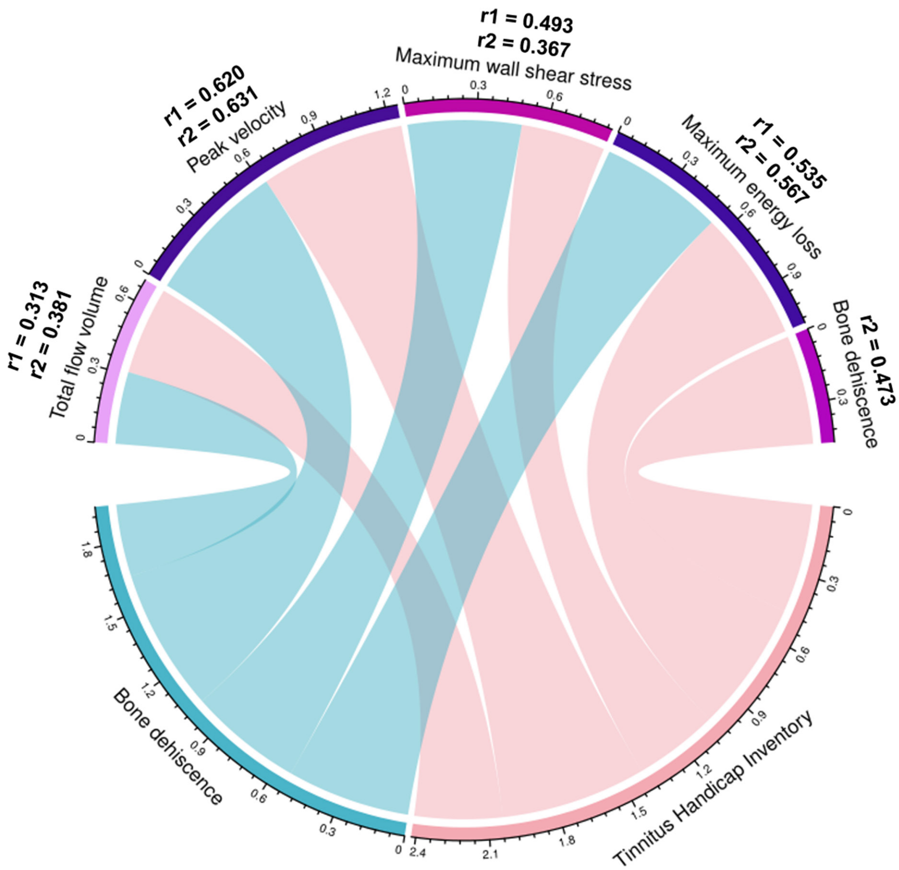

Figure S2 Correlations between the bone dehiscence, hemodynamic parameters, and severity of tinnitus in patients with VPT. VPT, venous pulsatile tinnitus.

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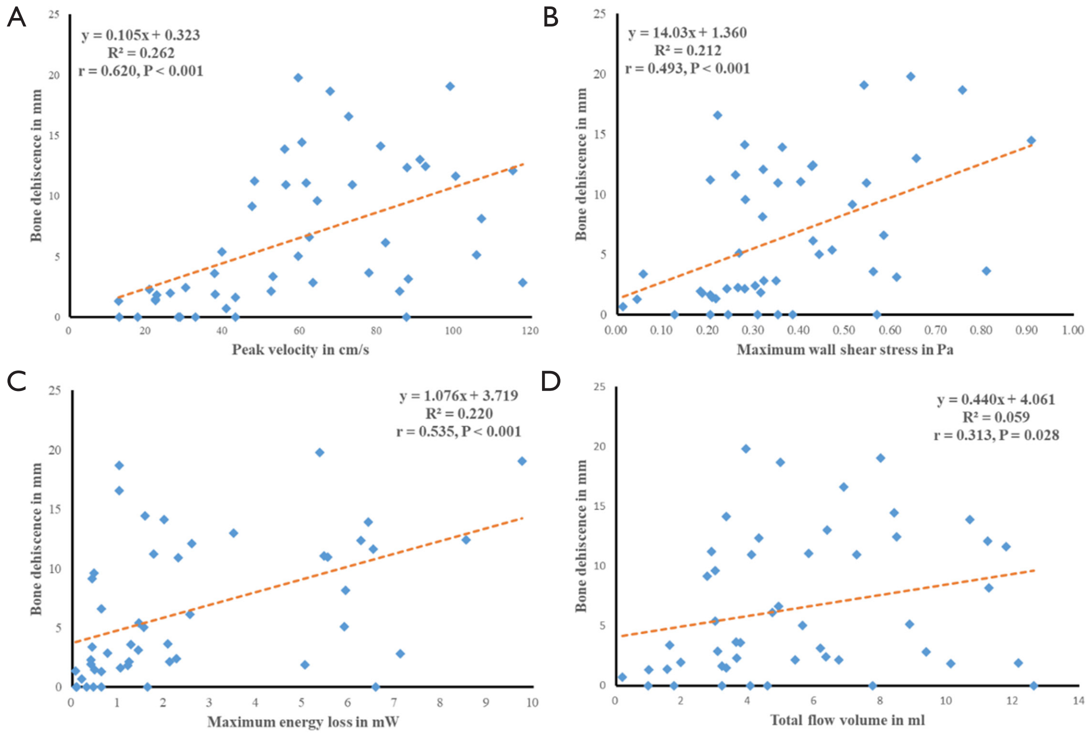

Figure S3 Correlations between bone dehiscence and hemodynamics in PT patients. PV, MWSS and MEL were positively correlated with the size of bone dehiscence. PT, pulsatile tinnitus; PV, peak velocity; MWSS, maximum wall shear stress; MEL, maximum energy loss.

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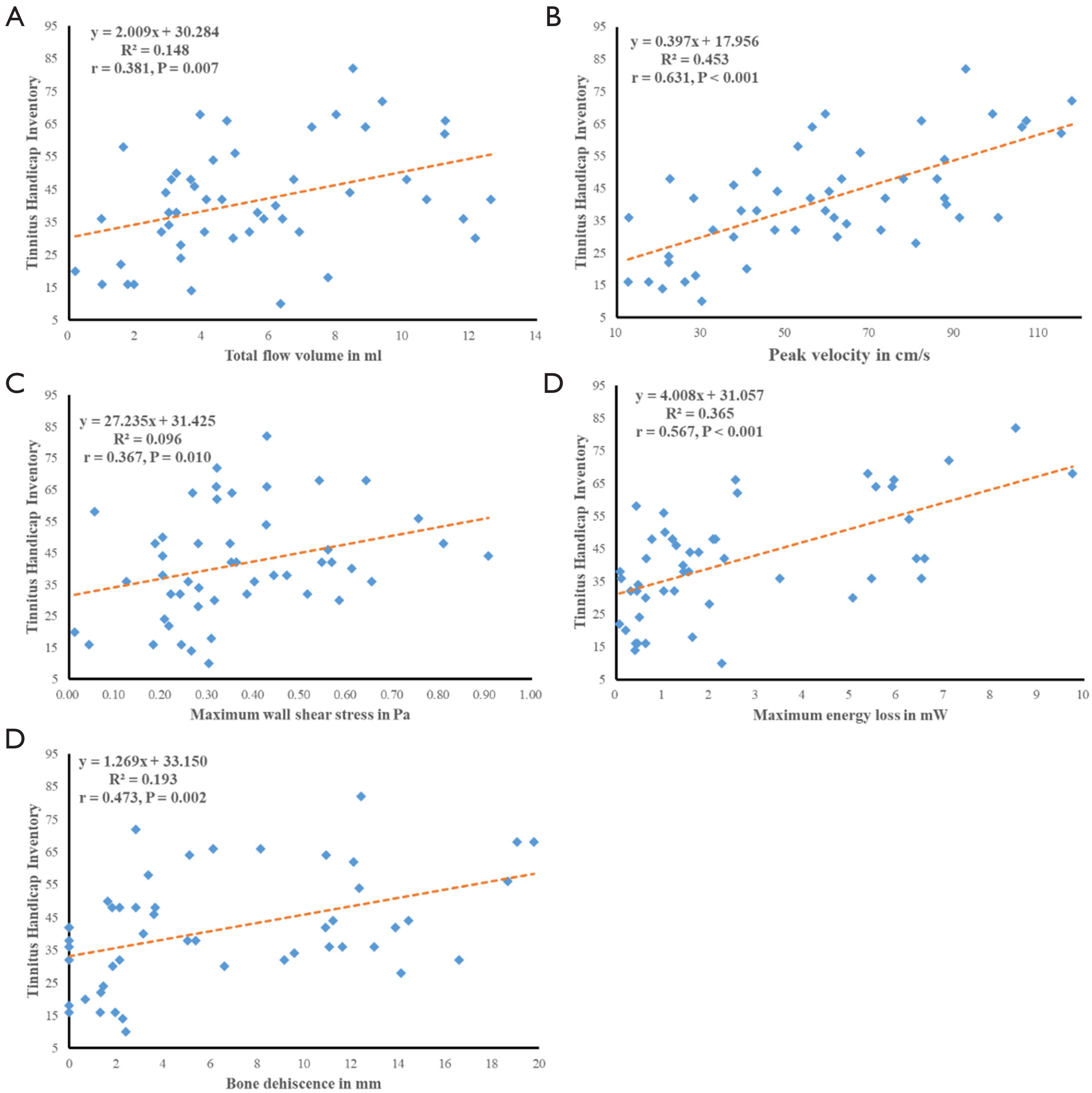

Figure S4 Associations of Tinnitus Handicap Inventory score with hemodynamics and bone dehiscence in PT patients. TV, PV, MWSS and MEL were positively correlated with Tinnitus Handicap Inventory score. The size of bone dehiscence was positively correlated with Tinnitus Handicap Inventory score. PT, pulsatile tinnitus; TV, total blood flow volume; PV, peak velocity; MWSS, maximum wall shear stress; MEL, maximum energy loss.

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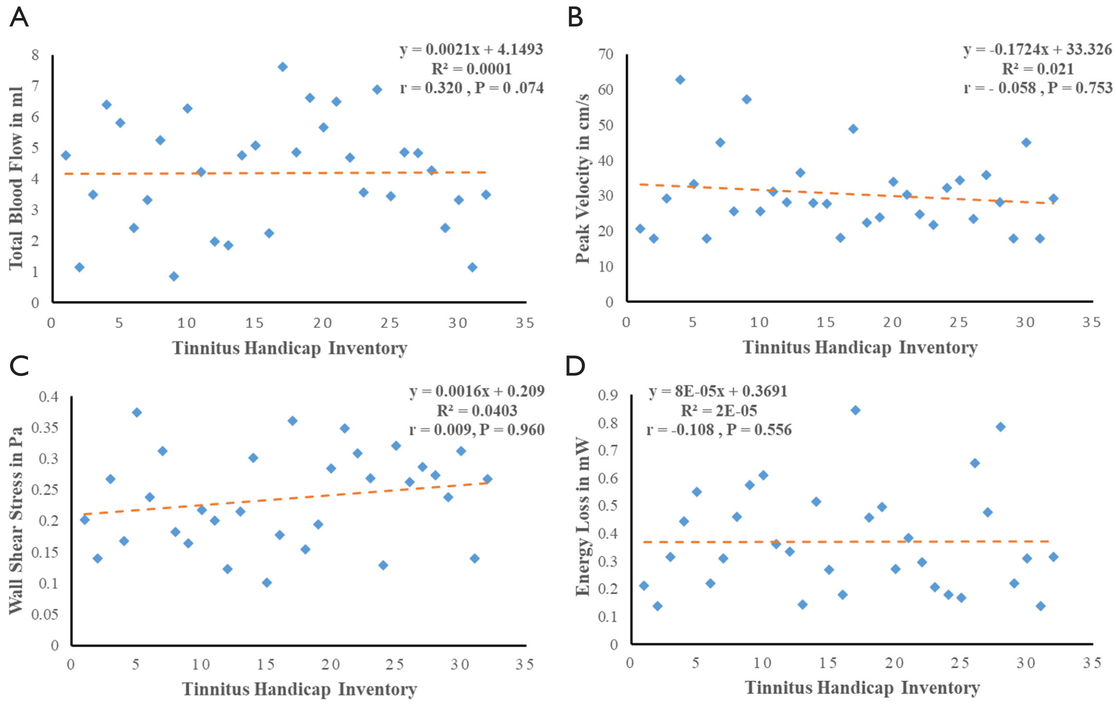

Figure S5 Associations of Tinnitus Handicap Inventory score with hemodynamics and bone dehiscence in ST patients. TV, PV, MWSS and MEL have no obvious correlation with Tinnitus Handicap Inventory score. ST, subjective tinnitus; TV, total blood flow volume; PV, peak velocity; MWSS, maximum wall shear stress; MEL, maximum energy loss.

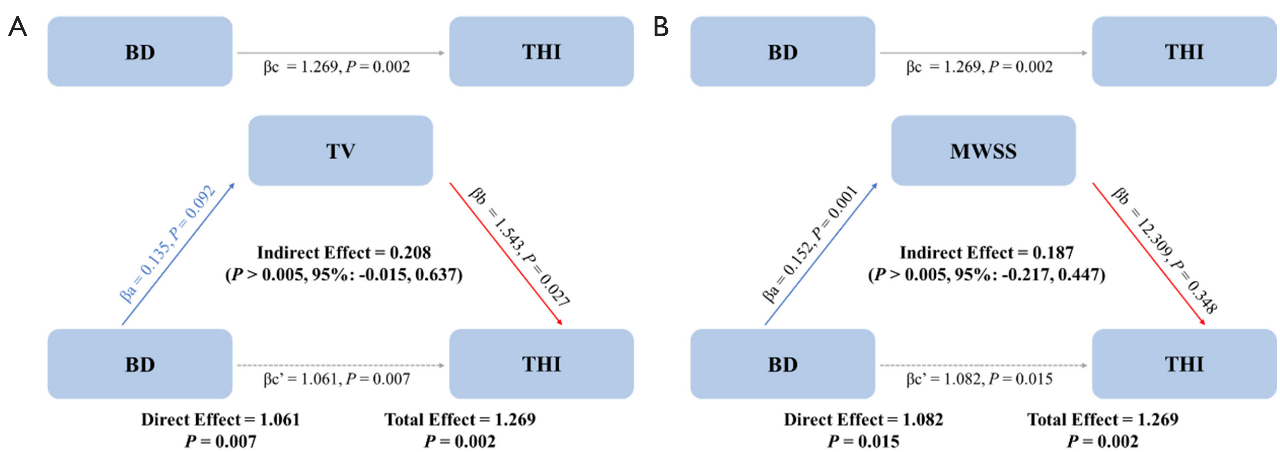

Figure S6 Two non-significant mediation analysis models for hemodynamic parameters in regulating the relationship between BD and THI. BD, bone dehiscence; THI, Tinnitus Handicap Inventory; TV, total blood flow volume; MWSS, maximum wall shear stress.

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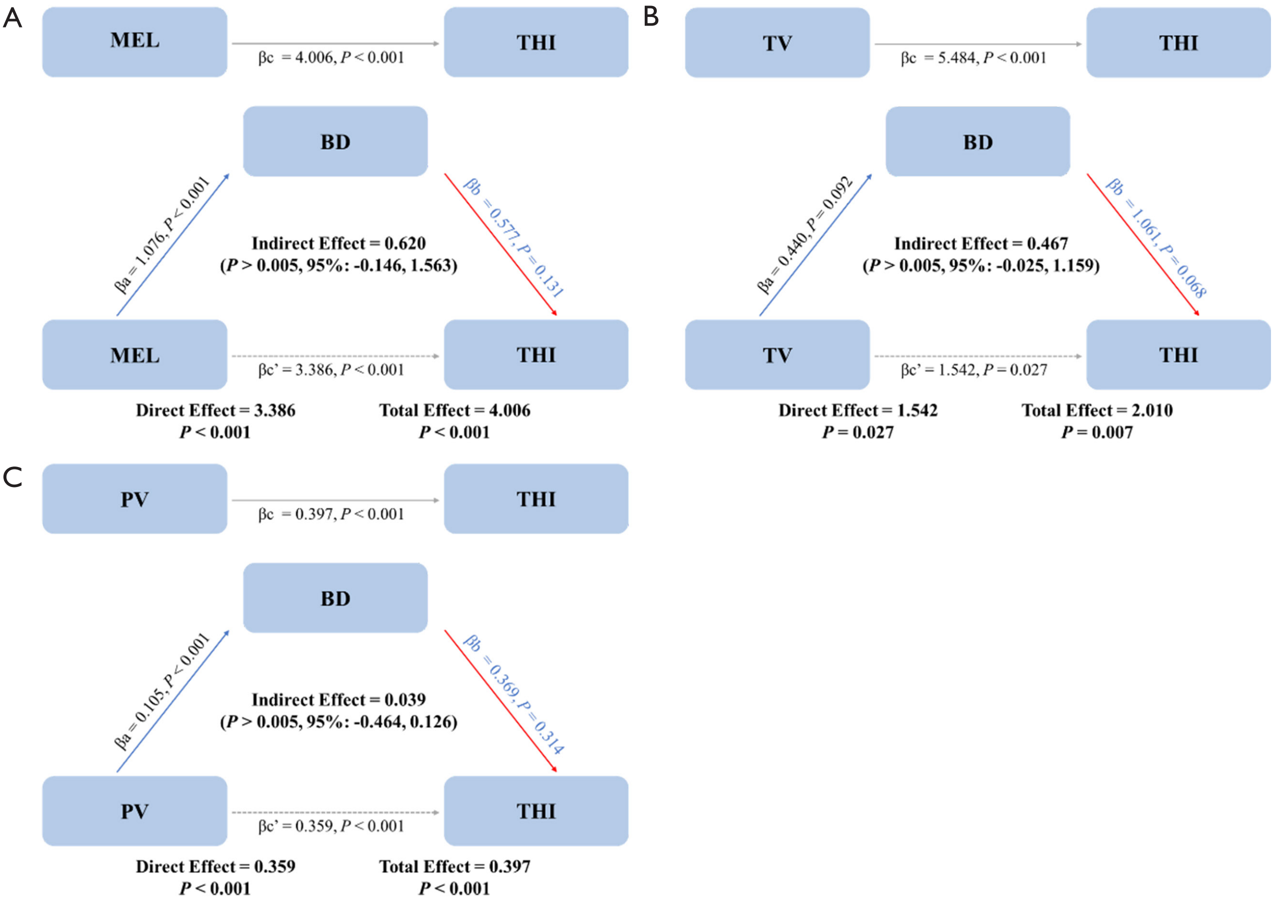

Figure S7 Non-significant mediation analysis models for BD in regulating the relationship between hemodynamics and THI. MEL, maximum energy loss; THI, Tinnitus Handicap Inventory; BD, bone dehiscence; TV, total blood flow volume; PV, peak velocity.

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Table S1 Hemodynamic differences in the different planes of transverse-sigmoid sinus in three groups

	Plane 1	Plane 2	Plane 3	Plane 4	Plane 5	Plane 6	F value	P value
VPT								
TV (mL)	4.52 (2.73–6.63)	4.55 (2.47–6.59)	4.73 (2.99–7.87)	4.72 (3.15–7.10)	4.76 (2.47–6.63)	3.29 (2.11–5.29)	10.079	0.073
PV (cm/s)	25.80 (20.77–39.25)	40.68 (29.17–63.48)	59.27 (35.11–83.91)	44.34 (35.23–62.30)	38.56 (34.17–49.22)	26.95 (19.28–30.81)	71.204	<0.001‡
MWSS (Pa)	0.23 (0.19–0.30)	0.51 (0.28–0.73)	0.32 (0.24–0.49)	0.38 (0.27–0.44)	0.28 (0.23–0.38)	0.21 (0.16–0.28)	66.589	<0.001‡
MEL (mW)	1.55 (0.56–5.21)	–	–	–	–			
HC								
TV (mL)	4.44 (2.88–5.60)	4.15 (2.93–5.11)	3.94 (2.81–5.98)	3.92 (2.80–5.11)	4.10 (3.25–5.72)	3.12 (2.35–5.26)	8.415	0.135
PV (cm/s)	24.47 (19.49–34.58)	31.73 (22.44–38.91)	25.41 (20.78–33.60)	25.78 (21.80–33.94)	28.75 (24.76–35.53)	24.82 (21.27–28.56)	16.365	0.006†
MWSS (Pa)	0.25 (0.10–0.31)	0.40 (0.32–0.51)	0.23 (0.19–0.27)	0.28 (0.24–0.32)	0.29 (0.25–0.34)	0.21 (0.17–0.25)	89.742	<0.001‡
MEL (mW)	0.30 (0.67–1.20)	–	–	–	–			
ST								
TV (mL)	4.81 (3.63–5.97)	4.15 (2.31–5.61)	4.50 (2.64–5.56)	4.20 (3.05–5.78)	4.53 (3.46–6.21)	3.58 (2.60–4.65)	8.098	0.151
PV (cm/s)	25.60 (20.43–30.89)	29.25 (23.91–35.00)	28.20 (22.63–34.28)	26.02 (22.94–32.67)	32.58 (28.62–40.54)	35.02 (21.24–31.10)	20.913	0.001†
MWSS (Pa)	0.25 (0.22–0.31)	0.43 (0.34–0.52)	0.27 (0.20–0.34)	0.32 (0.28–0.36)	0.32 (0.26–0.38)	0.25 (0.22–0.30)	36.473	<0.001‡
MEL (mW)	0.41 (0.29–0.68)	–	–	–	–			

†, P<0.05; ‡, P<0.001. VPT, venous pulsatile tinnitus; TV, total blood flow volume; PV, peak velocity; MWSS, maximum wall shear stress; MEL, maximum energy loss; HC, healthy control; ST, subjective tinnitus.

Table S2 Mediating efficacy with hemodynamic parameters used as mediating variables

Mediating factor	Effect	Boot SE	T	P	95% confidence interval	
					LLCI	ULCI
MEL						
Total effect	1.269	0.379	3.350	0.002	0.507	2.031
Direct effect	0.577	0.375	1.538	0.131	–0.178	1.331
Indirect effect	0.692	0.300	–	–	0.201	1.377
PV						
Total effect	1.269	0.379	3.350	0.002	0.507	2.031
Direct effect	0.369	0.363	1.018	0.314	–0.361	1.100
Indirect effect	0.899	0.295	–	–	0.406	1.582

SE, standard error; LLCI, lower limit of the confidence interval; ULCI, upper limit of the confidence interval; MEL, maximum energy loss; PV, peak velocity.

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Table S3 Mediating efficacy with bone dehiscence used as an independent variable

Mediating factor	Effect	Boot SE	T	P	95% confidence interval	
					LLCI	ULCI
BD						
Total effect	27.489	12.170	2.259	0.029	3.008	51.971
Direct effect	12.309	12.993	0.947	0.348	–13.844	38.462
Indirect effect	15.181	8.417	–	–	3.448	35.493

SE, standard error; LLCI, lower limit of the confidence interval; ULCI, upper limit of the confidence interval; BD, bone dehiscence.

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