Effects of different morphologic abnormalities on hemodynamics in patients with venous pulsatile tinnitus: A four-dimensional flow magnetic resonance imaging study

Xiaoshuai Li, MD,¹ Xiaoyu Qiu, MD,¹ Heyu Ding, MD,¹ Han Lv, MD,¹ Pengfei Zhao, MD,^{1*} Zhenghan Yang, MD,¹ Shusheng Gong, MD,² and Zhenchang Wang, MD^{1*}

The effects of morphologic abnormalities, including sigmoid sinus wall dehiscence (SSWD), transverse sinus stenosis (TSS), and sigmoid sinus diverticulum (SSD), on hemodynamics in venous pulsatile tinnitus (PT) patients have not been established. The aim of this study was to evaluate the effects of SSWD, TSS, and SSD on the hemodynamics of transversesigmoid sinus in venous PT patients. This was a prospective study with 44 venous PT patients and 12 healthy controls. A 3 T/four-dimensional (4D) flow magnetic resonance imaging with fast field echo was used. Computed tomography arteriography/venography was used to assess ipsilateral SSWD, TSS, and SSD. Maximum velocity (V_{max}), average velocity (V_{avg}), and average flow (Flow_{avg}) were measured. Blood flow patterns were independently assessed by three neuroradiologists. One-way analysis of variance or Kruskal-Wallis test was also used. On the symptomatic side, all patients had SSWD, 33 patients had TSS, and 22 patients had SSD. Compared with healthy controls, patients with TSS, without TSS, with SSD, and without SSD all showed higher V_{max} (all p < 0.050), V_{avg} (all p < 0.050), and Flow_{avg} (all p < 0.050). Patients with TSS showed higher V_{max} (p < 0.050) and V_{avg} (p < 0.050) than those without TSS, and no significant difference in Flow_{avg} was found between the two groups (p = 0.408). No significant differences in V_{max} , V_{avg} , and Flow_{avg} were found between patients with and without SSD (all p = 1.000). Jet-like flow in the stenosis and downstream of the stenosis was observed in all patients with TSS. Vortex in SSD was observed in 15 patients with SSD (68%). High blood velocity and flow may be characteristic markers of venous PT. SSWD may be a necessary condition for venous PT. TSS may further increase the blood velocity and form a jet-like flow. SSD may be related to vortex formation but had no significant effect on blood velocity and flow. Level of Evidence: 2

Technical Efficacy Stage: 3

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INTRODUCTION

Pulsatile tinnitus (PT) is characterized by a perception of vascular somatosound synchronized with cardiac pulse.^{1,2} It can be divided into the arterial, venous, and neoplastic

types, 3 and venous PT accounts for approximately 84% of all PT. 4

Transverse sinus stenosis (TSS), sigmoid sinus wall dehiscence (SSWD), and sigmoid sinus diverticulum (SSD)

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*Correspondence Pengfei Zhao and Zhenchang Wang, Department of Radiology, Beijing Friendship Hospital, Capital Medical University, No. 95, Yong'an Road, Xicheng District, Beijing 100050, China. Email: zhaopengf05@163.com and cjr.wzhch@vip.163.com

From the ¹Department of Radiology, Beijing Friendship Hospital, Capital Medical University, Beijing, China; and ²Department of Otolaryngology Head and Neck Surgery, Beijing Friendship Hospital, Capital Medical University, Beijing, China

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have proven to be the most common morphologic abnormalities in venous PT.⁵⁻⁷ TSS can not only increase the blood flow velocity but also lead to poststenotic turbulent flow.^{7,8} Stent placement can eliminate venous PT in this population.^{9,10} Simple SSWD was first confirmed as the etiology of venous PT by Eisenman because this condition could be successfully treated by sinus wall reconstruction.¹¹ It was speculated that venous PT originated from the vibration of the dehiscent sinus wall and then transmitted to the cochlea.¹¹ SSD is associated with venous PT. The perception of venous PT is considered to originate from the vortex and elevated vascular wall pressure in the diverticulum.^{6,12,13} Therefore, coil embolization of the diverticulum and sinus wall reconstruction have been demonstrated to be effective approaches for the treatment of venous PT.^{14,15} However, previous studies have mainly focused on a single pathoetiologic factor of venous PT.6,9,16

Four-dimensional (4D) flow magnetic resonance imaging (MRI) is an emerging blood flow imaging technique.⁸ It can be used to quantitatively evaluate hemodynamics and visualize blood flow patterns. This technique was initially used in the hemodynamic evaluation of arterial structures.¹⁷ Several studies have shown that 4D flow MRI has potential in studying venous PT.^{8,12,18,19} The accuracy and reliability of blood flow measurements have been confirmed.²⁰ A recent 4D flow study found that venous PT was associated with not only high blood velocity and flow but also abnormal blood flow patterns.⁸

Because the same venous PT patient may have one or more morphologic alterations simultaneously, SSWD, SSD, and TSS are not considered independent and have synergistic effects when causing venous PT.^{7,13} However, the effects of each factor on the hemodynamics in venous PT patients have not been established. The aim of this study was to use 4D flow MRI to investigate the effects of SSWD, TSS, and SSD on the hemodynamics of the transverse-sigmoid sinus in patients with venous PT.

MATERIALS AND METHODS

This prospective study was approved by the local ethics committee. Each patient provided informed consent before being entered into this study.

Subjects

Fifty-seven consecutive patients with venous PT were enrolled from the Department of Otolaryngology Head and Neck Surgery between January 2018 and December 2019. Patients were included based on the following criteria: (1) pulse-synchronous tinnitus, which disappeared by compressing the ipsilateral internal jugular vein; (2) normal audiometric and otoscopic examination results; (3) at least one piece of radiological evidence of ipsilateral SSWD, SSD, and TSS on computed tomography arteriography/venography (CTA/V); and (4) available 4D flow MRI data. Patients with other etiologies of venous PT, such as jugular bulb abnormalities, abnormal emissary veins (>4.0 mm in diameter),³ and sinus thrombosis, were excluded. Thirteen patients were excluded due to jugular bulb dehiscense, abnormal emissary vein, and incomplete 4D Flow data. Finally, 44 patients with unilateral venous PT were analyzed in this study (Figure 1). The radiological signs were independently assessed by three neuroradiologists (Han Lv, Heyu Ding, Pengfei Zhao) with 6, 8, and 12 years of experience. Discrepant cases were discussed to reach consensus. The dominance of transverse sinus was defined as 150% of the cross-sectional area on the smaller side. The location of the largest cross-sectional area of the bilateral transverse sinuses was first determined on CTV curve planar reformation. Then, the crosssectional area of the transverse sinus was measured perpendicular to



FIGURE 1: Flow chart of the inclusion for venous pulsatile tinnitus (PT) patients

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FIGURE 2: Typical examples of transverse sinus stenosis, sigmoid sinus wall dehiscence, and sigmoid sinus diverticulum. (a, b) Measurement of stenosis and adjacent stenosis in the transverse sinus; (c) right sigmoid sinus wall dehiscence (white arrow); (d) right sigmoid sinus diverticulum (white arrow)



FIGURE 3: Four-dimensional (4D) flow data processed in GTFlow software. 4D flow magnetic resonance imaging streamline visualization (a) and hemodynamic measurements within contours (b)

the vessel. TSS was defined as a local reduction in the lumen crosssectional area of at least 50% on CTV images (Figure 2a and b)). SSWD was characterized as the absence of a normal bone layer overlying the sigmoid sinus on at least three consecutive 0.6-mm sections on axial CT, without focal outpouching or irregularity¹⁴ (-Figure 2c). SSD was characterized as an irregular outpouching of the sigmoid sinus expanding into the mastoid air cell or mastoid cortex (-Figure 2d). Twelve age- and gender-matched healthy controls were included.

Imaging Technique

CTA/V was performed in all venous PT patients using a Brilliance 64-slice CT scanner (Philips, Best, The Netherlands) with a bolus tracking program (Trigger Bolus software; Philips, Best, The

Table 1. Clinical and imaging data of venous PT patients and healthy controls			
	Venous PT patients	Healthy controls	<i>p</i> -value
Gender (male/ female)	4/40	1/11	1.000 ^a
Age (year)	39 ± 10	42 ± 9	0.338 ^b
Side (left/ right)	16/28	—	-
BMI (kg/m ²)	22.66 ± 2.84	21.83 ± 2.48	0.360 ^b
PT duration (months)	24 (454)	—	-
Drainage dominance on PT side	41	—	-
SSWD	44	—	-
SSD	22	_	-
Ipsilateral TSS	33		-

Notes: Normally distributed data are expressed as the mean ± standard deviation. Nonnormally distributed data are represented as the median (range).

Abbreviations: BMI, body mass index; PT, pulsatile tinnitus; SSD, sigmoid sinus diverticulum; SSWD, sigmoid sinus wall dehiscence; TSS, transverse sinus stenosis.

^aFisher's exact test.

^bTwo-sample *t*-tests.

Netherlands). The parameters were as follows: 100 kV; 250 mAs for the arterial phase and 300 mAs for the venous phase; rotation time, 0.75 s; matrix, 512×512 ; and collimation, 64×0.625 mm. Contrast (iopamidol, 370 mg/ml iodine; Bracco, Shanghai, China) was intravenously injected at a dose of 1.5 ml/kg. Images were reconstructed on a postprocessing workstation with a thickness of 1 mm and no gap. To evaluate arterial and venous systems, standard algorithms (width 700 Hu; level 200 Hu) were applied to reconstruct the arterial and venous images. High-spatial-resolution bone algorithms (width 4000 Hu; level 700 Hu) were used to reconstruct the venous images to evaluate sigmoid sinus wall.

The MRI data of all participants were acquired on a 3.0 T MRI unit (Ingenia; Philips Healthcare, Best, Netherlands) with a 32-channel standard head coil. The parameters of the phase-contrast (PC) three-dimensional (3D) magnetic resonance venography were as follows: repetition time/echo time (TR/TE), 17/6.2 ms; velocity encoding (VENC), 15 cm/s; flip angle (FA), 10°; bandwidth, 230 Hz/pixel; field of view, $173 \times 173 \times 192 \text{ mm}^3$; matrix size, $144 \times 108 \times 120$; and acquisition time, 2 min 15 s.

The two-dimensional (2D) PC and 4D flow data were obtained with free-breathing and retrospective electrocardiographic (ECG) gating. The acquisition plane of 2D PC MRI was positioned at the distal part of the venous sinus stenosis and perpendicular to the venous sinus. The 2D PC MRI parameters were as follows: TR/TE, 10/5.8 ms; FA, 10°; acquired voxel size, $1 \times 1 \text{ mm}^2$; reconstructed voxel size: $0.31 \times 0.31 \text{ mm}^2$; bandwidth, 192 Hz/ pixel; field of view, $161 \times 161 \text{ mm}^2$; and acquisition time of each scan, 1 min 23 s. The VENC was first set to 80 cm/s. If velocity aliasing occurred (as determined by a neuroradiologist), the scan was repeated, and the VENC was adjusted in 20 cm/s increments until the aliasing disappeared.

The 4D flow MRI parameters were as follows: TR/TE, 8.5/3.9 ms; FA, 20°; acquired voxel size, $1 \times 1 \times 1 \text{ mm}^3$; reconstructed voxel size: $0.46 \times 0.46 \times 1 \text{ mm}^3$; 13 heart phases; bandwidth, 193 Hz/pixel; field of view, $161 \times 161 \times 40 \text{ mm}^3$; and acquisition time, 5 min 24 s. The final VENC setting of the 2D PC MRI was adopted to avoid velocity aliasing.

Data Analysis

The 4D flow data were processed by GTFlow software (v3.2.10, GyroTools, Switzerland), and eddy current correction, antialiasing, velocity mask application, and vessel segmentation were performed. The points of maximum velocity were first determined by one



FIGURE 4: Histograms depicting the values for maximum velocity (a), average velocity (b), and average flow (c) in healthy controls and venous pulsatile tinnitus (PT) patients with transverse sinus stenosis (TSS) and without TSS

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FIGURE 5: Histograms depicting the values for maximum velocity (a), average velocity (b), and average flow (c) in healthy controls and venous pulsatile tinnitus (PT) patients with sigmoid sinus diverticulum (SSD) and without SSD

neuroradiologist (Xiaoshuai Li) with 6 years of experience through manual inspection of the 3D streamline. Then, the measurement planes were placed perpendicular to the streamlines in all phases at the location of maximum velocity. Contours were manually drawn to measure the hemodynamic parameters flowing through the contours (Figure 3). By evaluating all voxels inside the contour, the maximum velocity (V_{max}, cm/s) was determined at the time index when peak velocity appears.^{8,21} The average velocity (V_{avg} , cm/s) and average flow (Flow_{ave}, ml/s) referred to the mean value of the average velocity and flow in an entire cardiac cycle, respectively. For fair comparison, the asymptomatic veins in venous PT patients were not included in the healthy control group. Flow patterns were characterized by streamlines, which were lines tangent to the local velocity vector field. The cine loops of the streamlines can be viewed from arbitrary directions on a monitor display of the workstation. Three neuroradiologists (Han Lv, Heyu Ding, Pengfei Zhao) with 6, 8, and 12 years of experience independently assessed the blood flow patterns of stenosis in the transverse sinus and diverticulum in the junction of the transversesigmoid sinus. Disagreements were settled by consensus. Vortex was characterized as the closed formation of concentric circular flow. Jet-like flow was characterized as a bundle of high-speed streamlines according to the color bar scale.

Statistical Analysis

SPSS 22.0 (software IBM, Chicago, IL) was used for statistical analysis. Normality was detected with the Shapiro–Wilk test. Variance homogeneity was tested using the Levene test. Continuous variables are expressed as mean \pm standard deviation (normal distribution) or median (range) (nonnormal distribution). Two-sample t-test and Fisher's exact test were used to compare the differences in clinical data between the venous PT patients and healthy controls. For multiple sets of comparisons, if the criteria of a normal distribution and variance homogeneity were met, one-way analysis of variance with post hoc Bonferroni test was applied; if not, the Kruskal–Wallis test with post hoc multiple comparison test was applied. p < 0.05 was considered statistically significant.

RESULTS

Clinical Data

Clinical and imaging data are summarized in Table 1. A total of 44 patients with unilateral venous PT and 12 healthy

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controls were analyzed in this study. Except for four cases, all patients were female. There was no significant difference in gender (p = 1.000), age (p = 0.338), and body mass index (p = 0.360) between the two groups.

Based on the ipsilateral bone and/or vascular abnormalities, the patients were divided into the following four different cohorts: SSWD + TSS (n = 20), SSWD + SSD + TSS (n = 13), SSWD + SSD (n = 9), and simple SSWD (n = 2) (Figure 1). The patients with SSWD +TSS were the most common (45%) among all venous PT patients. Forty-one patients had dominance of the transverse sinus on the PT side, and only three patients had codominance. All patients had SSWD, including 33 patients with TSS and 22 patients with SSD. According to the presence of TSS and SSD, the venous PT patients were divided as follows: patients with TSS (n = 33) and without TSS (n = 11) and patients with SSD (n = 22) and without SSD (n = 22).

Hemodynamic Measurements

In venous PT patients, 44 symptomatic veins were measured by 4D flow MRI. For healthy controls, 20 of 24 veins were included, but four veins were considered too narrow to be measured. Significant differences in V_{max} , V_{avg} , and Flow_{avg} were found among the healthy controls, and the patients with and without TSS (V_{max} : p < 0.050; V_{avg} : p < 0.050; Flow_{avg}: p < 0.050). Compared with the healthy controls, the patients with TSS and without TSS showed significantly higher V_{max} $(167.31 \pm 40.73 \text{ cm/s} \text{ vs. } 56.24 \pm 16.60, p < 0.050; 114.97 \pm$ 23.29 cm/s vs. 56.24 ± 16.60, p < 0.050), V_{avg} (64.03 ± 18.08 cm/s vs. 27.87 \pm 5.80, p < 0.050; 41.58 \pm 7.28 cm/s vs. 27.87 \pm 5.80, p < 0.050), and Flow_{avg} (7.00 \pm 3.82 ml/s vs. 4.32 ± 2.56 , p < 0.050; 8.53 ± 2.87 ml/s vs. 4.32 ± 2.56 , p < 0.050). The patients with TSS showed higher V_{max} $(167.31 \pm 40.73 \text{ cm/s vs.} 114.97 \pm 23.29, p < 0.050)$ and V_{avg} $(64.03 \pm 18.08 \text{ cm/s} \text{ vs. } 41.58 \pm 7.28, p < 0.050)$ than the patients without TSS, and no significant difference in Flow_{ave} was found between the two groups (p = 0.408) (Figure 4).

There were significant differences in V_{maxo} V_{avgs} and Flow_{avg} among the healthy controls and the patients with and without SSD (V_{max} : p < 0.050; V_{avg} : p < 0.050; Flow_{avg}:

p < 0.050). Compared with the healthy controls, the patients with SSD and without SSD showed higher V_{max} (147.58 ± 42.16 cm/s vs. 56.24 ± 16.60, p < 0.050; 160.86 ± 44.64 cm/s vs. 56.24 ± 16.60, p < 0.050), V_{avg} (55.92 ± 20.08 cm/s vs. 27.87 ± 5.80, p < 0.050; 60.92 ± 17.47 cm/s vs. 27.87 ± 5.80, p < 0.050; and Flow_{avg} (7.86 ± 4.03 ml/s vs. 4.32 ± 2.56, p < 0.050; 6.90 ± 3.22 ml/s vs. 4.32 ± 2.56, p < 0.050). No significant differences in V_{max} , V_{avg} and Flow_{avg} were found between the patients with SSD and without SSD (all p = 1.000) (Figure 5).

Visualization Evaluation

All patients with TSS showed jet-like flow in the stenosis and downstream of the stenosis according to the color bar scale. Vortex in the SSD was observed in 15 patients with SSD (68%) (Figure 6).

DISCUSSION

This study showed that high blood velocity and flow may be characteristic markers of venous PT. SSWD may be a necessary condition for PT. TSS may further increase the blood velocity and form a jet-like flow. SSD is related to vortex formation but has no effect on blood velocity and flow.

According to the clinical data, the PT side of all patients was the dominant or codominant side of the transverse sinus, indicating that the occurrence of venous PT may be related



FIGURE 6: Blood flow pattern of venous pulsatile tinnitus (PT). Streamline (a) and zoom-in images (b) show jet-like flow in stenosis and downstream of the stenosis. Streamline (c) indicates the existence of vortex in sigmoid sinus diverticulum (SSD)

to high flow. Patients with SSWD + TSS were the most common among all venous PT patients. SSWD was found in all patients in this study.

The intact sinus wall may effectively block the venous sound and vibration generated by venous sound.⁶ Once the sinus wall dehisces, the pulse-synchronized sound and vibration from the sigmoid sinus may transmit to the cochlea through the dehiscent areas.^{11,22} This mechanism is supported by an in vitro experimental study²³ and successful sinus wall reconstruction to treat venous PT due to dehiscence.^{6,14} The in vitro experimental study even found that SSWD can cause pulse-synchronized sound and vibration to increase to greater than 20 Hz regardless of the size of the dehiscence.²³ Therefore, SSWD may be a necessary condition for venous PT.

In this study, the venous PT patients showed higher $V_{\rm max}$, $V_{\rm avg}$, and Flow_{avg} compared with the healthy controls, regardless of the presence of TSS and SSD. This finding indicates that high blood velocity and high flow may be characteristic markers of venous PT, which is consistent with a previous study.8 Congenital causes, overgrowth of arachnoid granules, or septa are responsible for TSS.²⁴ This study demonstrated that the blood velocity of the patients with TSS was significantly higher than that of the patients without TSS, indicating that TSS could further increase the blood velocity of venous PT patients. This phenomenon is also confirmed by the jet-like flow associated with TSS on 4D flow MRI (Figure 6a and b). A computational fluid dynamics (CFD) study showed that stent placement significantly reduced blood velocity in venous PT patients with TSS.²⁵ These findings provide a hemodynamic basis for the treatment of venous PT by stenting in stenosis areas.

In this study, no significant differences in V_{max} , V_{avg} , and Flow_{avg} were found between the patients with SSD and without SSD. This finding demonstrates that SSD does not affect the blood velocity and flow of venous PT patients. Previous studies proposed that anomalous blood flow may be the direct cause of the formation of sigmoid sinus wall abnormalities.^{11,14,26} As jetlike flow impacts the lateral wall of the sigmoid sinus over the long term, the local sinus wall may be gradually eroded and thinned, leading to dehiscence and formation of the diverticulum.⁷ This mechanism is supported by the evidence that a jetlike flow from TSS is directed toward the opening of SSD in 4D flow MRI imaging and CFD simulation studies.¹²

In this study, significantly higher blood velocity in venous PT patients compared with healthy controls further supports this mechanism. However, the present data show that there are no significant differences in blood velocity between the patients with SSD and without SSD. It is speculated that SSD formation may be related to the location where the $V_{\rm max}$ occurs. The closer the location of $V_{\rm max}$ is to the distal transverse sinus, the greater the hemodynamic impact on the junction of the transverse-sigmoid sinus and the greater the possibility of SSD. In venous PT patients, the

fact that most TSS involves the ipsilateral distal transverse sinus⁷ also supports this hypothesis. The mechanism of SSD formation still needs further study.

Moreover, the blood flow patterns of venous PT patients were investigated in this study. Jet-like flow in the stenosis and downstream of the stenosis was observed in all patients with TSS, which is consistent with the result of CFD simulation.²⁵ This CFD simulation study also found that, after stent placement, the range of the jet-like flow was reduced, the blood flow pattern became more regular, and the flow direction improved in venous PT patients with TSS.²⁵ In addition, vortex in the SSD of venous PT patients was also observed, indicating a potential connection between the vortex and SSD. Vortex in the diverticulum may produce auditory PT.¹² After sinus wall reconstruction or coil embolization of the diverticulum, the PT disappeared, and the vortex in the diverticulum was completely resolved.^{12,15} Therefore, this abnormal blood flow pattern is closely related to the pathology of venous PT. In this study, vortex was observed in 68% of the venous PT patients with SSD, which may be related to the size, shape, and blood flow pattern of the diverticulum.

A 4D flow MRI can capture more comprehensive flow field information than other imaging technologies. Although digital subtraction angiography, CT angiography, and MR angiography can provide anatomical images of vascular stenosis, 4D flow MRI can quantitatively and visually describe the effects of different degrees of stenosis on blood flow. For venous PT patients with TSS, 4D flow MRI can help clinicians identify the location for stent placement and evaluate the hemodynamic changes before and after surgery, which is very valuable for the pathological study of venous PT.⁸ Moreover, this technique can reveal abnormal blood flow patterns in venous PT patients, such as jet-like flow related to TSS and vortex in the SSD, which may provide more information for the choice of treatment methods.¹²

Limitations

A previous study indicated that variations in the geometry of the jugular bulb can lead to different blood flow patterns associated with venous PT.¹⁸ In this study, the hemodynamics of the jugular bulb were not evaluated because covering the area of the jugular bulb would require a longer scan time. Second, the blood flow in the venous sinus may be affected by changes in breathing and posture. As all patients were in the supine position and followed free breathing during the scan, this problem was partially addressed. Third, the sample size is limited in this study, and more venous PT patients should be included in the future.

CONCLUSION

Venous PT in most patients may be caused by the synergistic effects of multiple morphologic abnormalities. High blood velocity and high flow may be characteristic markers of venous PT. SSWD may be a necessary condition for PT, and it causes noise to be transmitted to the cochlea. TSS can further increase the blood velocity of venous PT patients and form a jet-like flow. SSD is related to vortex formation but has no significant effect on blood velocity and flow. These findings have potential implications for the pathophysiology of venous PT. In the future, the weight of different morphologic abnormalities will be studied to help clinicians identify the most critical factor of venous PT and choose the best treatment method.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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