

Is There Any Association between Jugular Venous Reflux and Nonpulsatile Subjective Tinnitus? A Preliminary Study of Four-Dimensional Magnetic Resonance Angiography

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INTRODUCTION

Tinnitus is the perception of sound when no real external noise is present. While it is commonly referred as “ringing in the ears,” tinnitus can manifest as many different perceptions of sound including buzzing, hissing, whistling, swooshing, and clicking.^[1-4] Tinnitus is commonly seen as a result of exposure to acoustic trauma or advanced age. While tinnitus is not a life-threatening symptom, it influences many daily activities including sleeping and working, thus might lead to deterioration in the quality of life.^[1-4] Tinnitus

ABSTRACT

Objective: To demonstrate whether there is an association between jugular venous reflux and nonpulsatile subjective tinnitus (NST) using real-time four-dimensional magnetic resonance imaging (MRI) angiography. **Materials and Methods:** Patients with unilateral NST who underwent contrast-enhanced MRI with a special protocol were included in the study. Thick slab dynamic maximum intensity projection images were obtained including interleaved stochastic trajectories (TWIST)-MRI examination. All patients were requested to perform Valsalva maneuver during the sequence. Jugular venous reflux grading was performed as follows: absence of reflux or if reflux does not reach the base of the skull: grade 0; if reflux reaches the jugular bulb, but no intracranial contrast is observed: grade 1; and if reflux extends into the intracranial cortical veins and/or the cavernous sinus above the jugular bulb: Grade 2. **Results:** A total number of 30 patients, 23 male and 7 female, were included in the study. Jugular venous reflux was not identified (Grade 0) in 20 patients. Grade 1 reflux was determined in 7 cases and Grade 2 reflux was observed in 3 cases. Notably, only patients with Grade 2 reflux described worsening of their tinnitus symptoms during the examination and their daily activities as well. **Conclusions:** NST might also be associated with hemodynamic problems of the venous system and the MRI protocol starting with TWIST accompanied with Valsalva maneuver is not well-known, yet seems to be a feasible and beneficial method to detect potential jugular venous reflux in NST patients.

KEYWORDS: Four-dimensional magnetic resonance-angiography, magnetic resonance imaging, tinnitus, TWIST, Valsalva maneuver, venous reflux

is mainly divided into two principal types: objective and subjective.^[1-4] The most common type of tinnitus is nonpulsatile subjective tinnitus (NST).^[1-4] While another person might hear objective tinnitus when the subject is approached, subjective tinnitus is audible only to the

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person affected.^[1-4] According to the most up-to-date literature, in the nonpulsatile form of tinnitus, a problem in the sound coding and transmission pathways has been proposed as a cause, yet exact mechanism has not been revealed.^[5] On the other hand, direct pressure from arteries, jugular vein, and dural venous sinuses or presence of jugular bulb or sigmoid-plated dehiscence, diverticulum placement, venous sinus anomalies, and arteriovenous fistulas are the most commonly accused factors in the pulsatile forms of tinnitus.^[6,7]

Abnormal jugular vein and venous reflux have been demonstrated as a cause of various intracranial pathologies including multiple sclerosis, transient global amnesia, and chronic cerebrospinal venous insufficiency (CCSVI).^[8-14] Furthermore, jugular venous reflux is assumed to increase ocular venous pressure; thus, disturbing ocular venous circulation and eventually causing transient monocular blindness.^[15] Some of these studies used Valsalva maneuver to induce jugular venous reflux since Valsalva maneuver might lead to jugular venous reflux by increasing thoracic pressure and reducing the venous flow from superior vena cava to the right atrium.^[8-15] Besides from these studies that demonstrated the association between the jugular venous reflux and various intracranial pathologies, in our clinical practice, some patients with known NST described exaggeration of their symptoms in daily activities such as defecation/micturition, squatting, and coughing, which all are associated with Valsalva maneuver. Therefore, one could suggest that jugular venous reflux emerging during these activities might be the primary factor that worsens the tinnitus symptoms of the patients. Moreover, recently, Bektas and Caylan^[16] hypothesized that NST without hearing loss might be caused by undetectable sounds originating from venous system of the brain since most NST patients experience their symptoms at night while lying in the horizontal position.

Based on the findings of the aforementioned studies and our clinical observations, we considered the potential role of jugular venous reflux in patients with NST in worsening of their symptoms. Therefore, we have created a dynamic magnetic resonance imaging (MRI) protocol, which includes Valsalva maneuver and four-dimensional (4D) MR angiography, to evaluate the venous reflux might have a role in the etiology of NST.

MATERIALS AND METHODS

The institutional review board approved this study. A total of 33 patients with unilateral NST were investigated. One patient with parietal dural arteriovenous fistula in the left hemisphere on the time-resolved angiography

with interleaved stochastic trajectories (TWIST) images, one patient with left transverse sinus aplasia, and one patient with aneurysmatic dilatation in the bulbous of the right jugular vein (3 cases in total) were excluded since the presence of an accompanying venous pathology other than jugular vein reflux would complicate assessment. Examinations were performed on a 3 Tesla unit (Siemens Magnetom skyra 3T, Erlangen, Germany). During the procedure, 0.1 mmol/kg gadolinium-based contrast agent (0.1 mmol/kg gadoterate meglumine, via the antecubital vein with a 20 gauge angiocut at a speed of 2 ml/s followed by 15 ml normal saline flush) was employed. The forearm veins which were contralateral to the tinnitus were used for contrast agent injections. The procedure was carried out in the supine position. Before the examination, all patients were instructed regarding how to perform the Valsalva maneuver, and a test trial was conducted to see whether the patients were clearly understood the procedure or not. The sequence was initiated with intravenous contrast injection, and all cases were requested to hold their breath and intermittently perform Valsalva maneuver during the sequence.

Imaging parameters of TWIST sequence were TR, 3.3 ms; TE, 1.3 ms; flip angle, 25°; rectangular field of view, 246 mm × 375 mm; matrix, 210 × 320; 88 partitions; voxel size after zero interpolation, 1.2 mm × 1.2 mm × 1.2 mm (true voxel size, 1.2 mm × 1.2 mm × 2.0 mm); and acceleration factor, 2. Thick slab dynamic maximum intensity projection images were obtained following short imaging with TWIST-MRI lasting a total of 90–110 s. Jugular venous reflux grading was performed as follows: absence of reflux or if reflux does not reach the base of the skull: grade 0; if reflux reaches the jugular bulb, but no intracranial venous contrast is observed: grade 1; and if reflux extends into the intracranial cortical veins and/or the cavernous sinus after the jugular bulb: grade 2. Figure 1 demonstrates reflux grading in TWIST sequence.

RESULTS

Finally, 30 patients, 23 male and 7 female, with unilateral tinnitus were included in the study. The mean age of the patients was 49 years (range: 17–74 years). Tinnitus was on the right side in 21 patients while on the left in 9 patients. There was no anatomic anomaly, diverticula, or dilatation, in the jugular vein suggesting dehiscence.

Venous reflux was Grade 0 in 20 cases [Figure 1]. We identified no contrast signal in the jugular vein in favor of reflux in the FOV area (20 channel head and neck coil

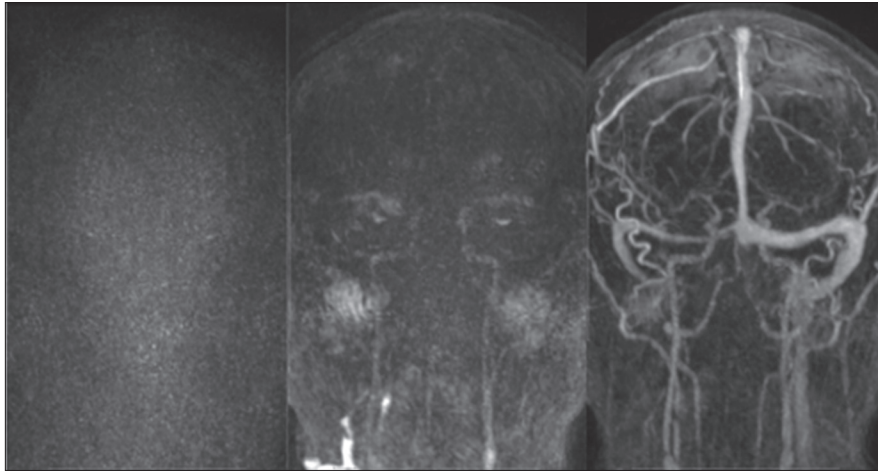


Figure 1: Reflux does not reach to the skull base (Grade 0)

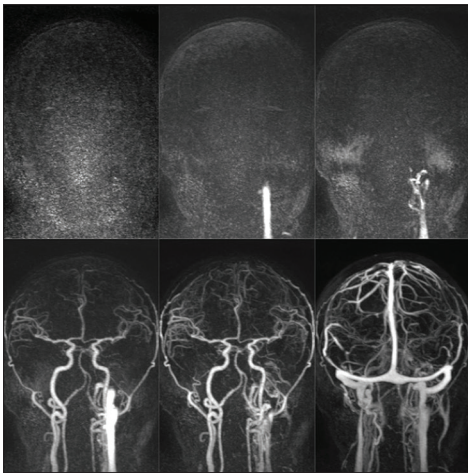


Figure 2: Jugular venous reflux reaches the jugular bulb, but no intracranial venous branch enhancement is observed on the right side (Grade 1)

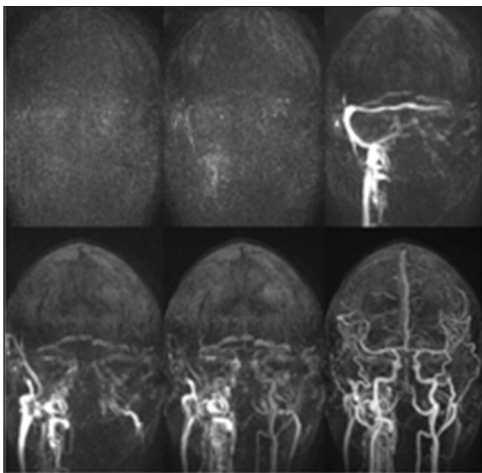


Figure 3: Jugular venous reflux extends into the intracranial temporal cortical veins and also beyond the right cavernous sinus on the right side (Grade 2)

field) in 11 of 20 patients. In remaining Grade 0 cases, reflux was observed on the right side in 3 cases and the

left side in 6 cases. Grade 1 reflux was determined in 7 cases (5 in the right and 2 in the left side) [Figure 2]. Grade 2 reflux was observed in 3 cases (2 in the left and 1 in the right side) [Figure 3].

All cases were subjected to Chi-square analysis regarding the relations between the reflux and the tinnitus sides. There was no significant difference between the right and left side in terms of reflux and tinnitus ($P = 0.763$). None of the patients with Grade 0 and 1 reflux reported worsening of their symptoms neither with Valsalva maneuver during the MRI examination nor with also their routine daily activities. On the other hand, all patients with Grade 2 reflux have a significant increase in tinnitus severity with Valsalva maneuver during the examination and in their routine daily activities as well. In this preliminary study, we aimed to investigate the relationship between tinnitus and related symptoms with jugular venous reflux. For this purpose, we included unilateral tinnitus cases only. We saw that there is no association with tinnitus in patients with Grade 0 and Grade 1 reflux. In patients with Grade 2 reflux, we saw that the side with tinnitus and reflux was the same, and the symptoms were aggravated with Valsalva.

DISCUSSION

Apart from studies focused on morphological anatomy, we investigated functional relationships, primarily by evaluating the presence of jugular venous reflux without additional sinus aplasia, dehiscence, or high diverticular bulb conjugation. Hence, the focus of our study was to investigate the presence of pathologic hemodynamic changes in the venous system in NST patients during the Valsalva maneuver. Furthermore, we questioned whether Valsalva maneuver aggravates the unpleasant sensation of tinnitus. Thus, we established a different MRI protocol that can successfully test the condition that causes this

symptom rather than standard imaging to evaluate the tinnitus; therefore, we asked patients to perform Valsalva maneuver during dynamic MR angiography imaging. To the best of our knowledge, we conducted the first study, in which the association between the jugular venous reflux and NST has been demonstrated with the help of Valsalva maneuver and reformat studies of 4D-TWIST MR angiography. In our study, by the help of 4D-TWIST MR angiography, we demonstrated venous reflux in the intracranial corticosubcortical small veins in the patients, in whom the aggravated symptoms of tinnitus could not be explained by conventional MRI imaging. Therefore, we suggest that the hypoxia induced by venous reflux secondary to the effect of these hemodynamic anomalies might lead to the formation or facilitation of tinnitus via its association with the peritemporal corticosubcortical neural parenchymal area.

In the last decades, many authors claimed that interrupted venous drainage has a potential to make some changes in endolymph circulation and volume.^[17,18] A recent study of Kariya *et al.*^[19] demonstrated the abnormalities in the microvascular anatomy of the stria vascularis with a histological examination in Meniere disease, which is an inner ear disease characterized by vertigo, hearing loss, and tinnitus. Furthermore, the relationship between Meniere disease and CCSVI has also been demonstrated.^[20,21] These studies strongly propound the role of venous pathologies in the etiology of Meniere disease. Hence, one could suggest that the association between the tinnitus, which is also related to inner ear and also one of the symptoms of Meniere disease, and the venous reflux should not be an unexpected entity, as we have demonstrated in some of our patients. Therefore, we highlight that the whole inner ear compartment should be evaluated together with the venous anatomy and function in NST patients since hemodynamic anomalies of the venous system might have a vital role in the etiology of NST. Despite the large number of studies have been done related to jugular vein reflux previously, they did not need to grade reflux. However, we found that this reflux did not cause any symptoms if it did not overflow into the intracranial venous system and we felt the need for grading. Therefore, we can emphasize that when Grade 2 reflux is detected, it should be valued.^[22] Recent studies have also shown that contrast reflux to the intracranial area can lead to global amnesia-like symptoms. Previously, although several studies have been conducted on jugular vein reflux, grading of reflux was not needed. However, we have seen that this reflux does not cause symptoms if it does not overflow into the intracranial venous system, so we need to make grading. Therefore, we can emphasize that when Grade 2 reflux is detected,

it should be valuable.^[22] In recent studies, it has been shown that contrast reflux to the intracranial area can lead to global amnesia-like symptoms.^[23]

We had several limitations in our study. First, and most important according to us, our study consisted of relatively small numbers of patients. Low number of cases is a limitation. However, we considered this study as a preliminary study. Selection of patients who have only unilateral and reflux disease caused this limitation. We think that we will work in a wider group as the series expands. Second, the MRI artifacts occurred secondary to movements of the patients during Valsalva maneuver; however, we substantially surpassed these artifacts with the high temporal resolution of the MRI sequence that we use.

CONCLUSIONS

Apart from the neurological background, NST might also be associated with the hemodynamic problems in the venous system, and the MRI protocol starting with TWIST accompanied with Valsalva maneuver seems to be a feasible and beneficial adjunct for the diagnosis of tinnitus by its ability to detect venous reflux. In this study, we saw that none of the patients with Grade 0 and 1 reflux reported worsening of their symptoms with Valsalva maneuver during the MRI. In patients with Grade 2 reflux, we saw that the side with tinnitus and reflux was the same, and the symptoms were aggravated with Valsalva.

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Conflicts of interest

There are no conflicts of interest.

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