Morphology and Hemodynamic Characteristics of Internal Jugular Vein Hypoplasia and Relation with Cerebral Venous Sinus Stenosis

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Objective: The characteristics of Internal jugular vein (IJV) morphology and hemodynamics of IJV hypoplasia have not been well illustrated.

Methods: Seventy-three cases with IJV hypoplasia diagnosed by MR and/or CT venous angiography and 126 healthy control were recruited. Ultrasound was performed to examine the J1-J3 segments of IJV. The diameter and mean flow volume (FVm) of bilateral IJV were compared. The linear regression of bilateral diameter ratio and FVm ratio were analyzed. The optimal cut-off values of diameter and flow volume of different segment of IJVs were determined by receiver operating characteristic (ROC) analysis. Furthermore, the correlation between the IJV hypoplasia and cerebral venous sinus stenosis were analyzed.

Results: There were 91.8% (67/73) cases with left IJV hypoplasia. The diameter and FVm of hypoplasia IJV were lower than the contralateral side (P < 0.001). The bilateral J1 diameter ratio was linear correlation with the FVm ratio, with a coefficient 0.720. The optimal cut-off diameter ratio of J1-J3 hypoplasia/dominant side were 0.70, 0.80 and 0.75 respectively and the optimal cut-off FVm ratio of three segments were all 0.50. The side of IJV hypoplasia was highly correlated with the side of transverse sinus and/or sigmoid sinus stenosis with an overall coincidence rate of 68.5%.

Conclusion: The left IJV was vulnerable for hypoplasia. IJV hypoplasia was correlated with ipsilateral cerebral venous sinus stenosis. Ultrasound is a reliable modality for evaluating IJV hypoplasia.

Key words: Internal jugular vein; Hypoplasia; Ultrasound; Diameter; Flow volume; Cerebral venous sinus

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Recently, accumulating evidences have suggested that cerebral venous (sinus) system not only reserves and drainages the cerebral blood flow but also maintains the cerebral perfusion, regulates the cerebrospinal fluid and adjusts the intracranial pressure [1]. Internal jugular veins (IJV) are the main outflow pathway of cerebral venous sinuses. Several studies have demonstrated that the IJV abnormalities were related with multiple neurological diseases, such as cerebral venous sinus thrombosis, idiopathic intracranial hypertension, transient global amnesia, transient monocular blindness, and multiple sclerosis [2-6]. IJV hypoplasia was one type of IJV abnormalities. Ultrasound is the modality for screening the morphology and hemodynamics alteration of IJV [2]. While, there is few reports on the morphology and hemodynamics of IJV hypoplasia evaluated by ultrasound. In this study, with healthy individuals as control, the characteristics of venous morphology and...
hemodynamics were evaluated by ultrasound in patients with IJV hypoplasia and its relationship with cerebral venous sinus stenosis was further investigated.

**Patients and Methods**

**Patients**

This study protocol was approved by the Institutional Review Board. From October 2017 to June 2018, 73 patients (study group) who were with symptoms of headache, tinnitus, tinnitus cerebri and et al, diagnosed as unilateral IJV hypoplasia by MR venous angiography (MRV) and/or CT venous angiography (CTV) in our institution were recruited. In addition, these patients were categorized as two subgroups: combined with \( n=50 \) cases or without \( n=23 \) cases cerebral venous sinus stenosis. At the same time, 126 healthy individuals (control group) were selected as control.

Patients’ inclusion criteria: (1) patients with age 18-80 years old, (2) patients with the symptoms of headache, tinnitus, tinnitus cerebri and et al. and clinic suspected with cerebral venous insufficiency, (3) MRV and/or CTV showed the unilateral IJV hypoplasia. Exclusion criterial: (1) cerebral venous sinus thrombosis, (2) IJV thrombosis, anomalous valve, (3) congenital heart disease, atrial fibrillation, and cardiac dysfunction, (4) extracranial and intracranial arteries with moderate, severe stenosis or occlusion detected by carotid artery ultrasound and transcranial color-coded sonography (TCCS), (5) IJV cannulation, (6) artery-venous fistula at the upper limb for dialysis, (7) tinnitus and tinnitus cerebri with definite etiology, such as otogenic disease.

Control inclusion criterial: (1) age 18-80 years old. (2) Without symptoms of headache, tinnitus and tinnitus cerebri. (3) Without hypertension or history of cerebrovascular or heart diseases. (4) Heart morphology and function were normal detected by echocardiography. (5) Bilateral IJV and cerebral venous sinuses were symmetrical evaluated by MRV and/or CTV.

**IJV ultrasonography**

Hitachi Ascendus ultrasound system (Hitachi, Inc., Tokyo, Japan) with a 4-8MHz microcurvilinear array probe was used to examine the IJV. The examinations were performed by experienced sonographers (with more than 10 years of experiences) according to the protocol we previously reported [2]. The diameters and hemodynamics parameters of the following three segments of IJV were measured: J1 (the level of IJV influx into the innominate vein), J2 (the level at which the superior thyroid vein influx into IJV) and J3 segment (the IJV level representing for the bifurcation level of common carotid artery). The parameters included: (1) the maximum diameters and cross-section areas at the end-expiration during smooth breath period. (2) Under the pulsed wave doppler mode, through auto-enveloping five “M” shape spectrums above the baseline and selecting one of the stable phase with the maximum velocity, then, the maximum, minimal velocity (Vmax and Vmin) and the mean flow volume (FVm) were measured.

**MRV and CTV examinations**

MagnetomVerio3.0 T MRI station (Siemens Inc., Germany) with head and neck 8-channel coils was used to perform MRV examination. The screening ranges were from aorta arch to the top of head. The magnevist (Bayer pharmaceutical Inc., Levekusen, Germany) were used as the contrast. Before injection of the contrast, routine scan and triple-phase contrast-enhanced scan were performed. Then 3-D head and neck veins images were reconstructed by the maximum intensity projection (MIP) processing [7]. In patients with contraindication for MRV examination (such as with metal materials), CTV examination was performed to evaluated the IJV and cerebral venous sinuses. IJV hypoplasia was defined as: the diameter of one side of IJV was obvious smaller than the other side of IJV detected by MRV and/or CTV (the whole length of one side IJV was moderate to severe stenosis) [8]. The transverse sinus and/or sigmoid sinus hypoplasia was defined as the difference of bilateral diameters of sinuses was > 50% [9].

**Statistical analysis**

The Statistical Package for Social Sciences (SPSS version 22.0) software was used for the statistical analysis. Numerical values with normal distribution were shown as mean ± SD and with non-normal distribution shown as median (interquartile range). Paired t test was used to compare the parameters of bilateral IJV in both study and control group. Two-independent sample t test was used to compare the parameters between the study and control group and between the two subgroups. Linear regression was used to analyze the correlation between the parameter of diameter ratio and FVm ratio and a linear regression equation was established. The optimal cut-off values of diameter and flow volumes of different segment of IJVs were determined by receiver operating characteristic (ROC) analysis. \( P < 0.05 \) was considered statistically significant.

**Results**

**The baseline characteristics of the two groups**

There were 126 healthy individuals in the control group, with 103 individuals (83.7%) were women. There were 73 cases with unilateral IJV hypoplasia in the study
group, with 46 cases (63.0%) were women. There was no difference of age between these two groups (55.5±13.8 years vs. 57.1±13.5 years, t=0.795, P=0.428). The main symptoms of study groups were tinnitus cerebri (45 cases, 61.6%), tinnitus (14 cases, 19.2%), headache (10 cases, 13.7%) and others (4 cases, 5.5%). The median time for the symptoms duration were two months (interquartile range 1-7 months).

The comparison of diameter and flow volume between the two groups

In control groups, the diameter and FVm of on the left IJV were smaller than that of right IJV (P < 0.001, Table 1). There were no difference of diameter ratio and FVm ratio either in control group or in the study group (data not shown). In the study group, there were 67 cases (91.8%) were with left IJV hypoplasia and 6 cases were with right IJV hypoplasia. The diameter and FVm of all three segments on the hypoplasia side were significantly lower than that on the dominant side, and were lower than the parameters of left (non-dominant) side of control group (P < 0.001, Table 1). The diameter of J1 and FVm of all three segments of IJV on the dominant side in study group were obviously higher than that of the right (dominant) side in control group, suggesting the compensation of dominant IJV (P < 0.05, Table 1).

In study group, the J1 diameter ratio between the hypoplasia side to dominant side were linear correlation with the J1 FVm ratio, with a coefficient 0.720 (P < 0.001, Fig. 2). The linear regression equation was: FVm ratio=0.794×diameter ratio-0.212.

The optimal cut-off values of the diameters and flow volumes of IJV hypoplasia by ROC analysis

Fig 3 showed the ROC curves of J1-J3 diameter (with the area under the curve AUC 0.826-0.887) and FVm (with the AUC 0.904-0.960) (all P < 0.05). Then the optimal cut-off values of diameters and FVm for identifying IJV hypoplasia were determined, with the diameter ratio (hypoplasia/dominant side) of J1-J3 segment 0.70, 0.80, 0.75 respectively and with the FVm ratio either in control group or in the study group (data not shown). In the study group, there were 67 cases (91.8%) were with left IJV hypoplasia and 6 cases were with right IJV hypoplasia. The diameter and FVm of all three segments on the hypoplasia side were significantly lower than that on the dominant side, and were lower than the parameters of left (non-dominant) side of control group (P < 0.001, Table 1). The diameter of J1 and FVm of all three segments of IJV on the dominant side in study group were obviously higher than that of the right (dominant) side in control group, suggesting the compensation of dominant IJV (P < 0.05, Table 1). Fig 1 showed the ultrasound images and MRV images of a patient with unilateral IJV hypoplasia.

Table 1 Bilateral J1 diameter and blood flow volume of the two groups

| Parameter | Control group | Study group |
|-----------|---------------|-------------|
|           | Right | Left | Left/Right | t value | P value | Dominant | Hypoplasia | Hypoplasia/ Dominant | t value | P value |
| Diameter (mm) | 9.29±1.32 | 8.35±1.05 | 0.91±0.17 | 6.697 | <0.001 | 9.97±1.26 | 6.33±1.40 | 0.65±0.17 | 16.599 | <0.001 |
| FVm (ml/min)  | 926±252 | 764±229 | 0.86±0.39 | 5.604 | <0.001 | 1235±397 | 354±217 | 0.30±0.18 | 18.240 | <0.001 |

Note: FVm: mean flow volume. a: compared with the right side of control group, P < 0.05, b: compared with the left side of control group, P < 0.05. c: compared with the left/right ratio of control group, P < 0.001.

Figure 1 Ultrasound and MRV IJV images of a 55-year-old man A, The spectrum of right J1 with a diameter 12.61mm and FVm 1.26 L/min B, The spectrum of left J1 with a diameter 6.44mm and FVm 0.23 L/min C, MRV image showed the left transverse sinus and sigmoid sinus stenosis and left IJV hypoplasia.

Figure 2 The linear correlation of the J1 diameter ratio and FVm ratio.
ratio (hypoplasia/dominant side) of all three segments
0.50. In addition, the accuracy of FVm ratio was higher
than that of diameters ratio (Table 3).

**The correlation of IJV hypoplasia and cerebral venous sinus stenosis**
In 67 cases with left IJV hypoplasia, there were
45 cases (67.2%) with left side transverse sinus and/
or sigmoid sinus stenosis. In 6 cases with right IJV
hypoplasia, there were 5 cases (83.3%) with right side
transverse sinus and/or sigmoid sinus stenosis. The side
of IJV hypoplasia were highly correlated with the side
of transverse sinus and/or sigmoid sinus stenosis, with
an overall coincidence rate of 68.5% (50/73 cases).
However, the diameter ratio and flow volume ratio of
IJV hypoplasia/dominant side had no differences
between the two subgroups with and without cerebral
venous sinus stenosis (all \( P > 0.05 \), Table 4).

| Table 2 | The AUC of diameter ratio and FVm ratio (hypoplasia/dominant) of IJV hypoplasia |
|---------|---------------------------------------------|
| Parameter | Diameter ratio | FVm ratio |
|          | AUC | 95% CI | SE | P value | AUC | 95% CI | SE | P value |
| J1       | 0.871 | 0.820-0.922 | 0.026 | <0.001 | 0.960 | 0.936-0.94 | 0.012 | <0.001 |
| J2       | 0.826 | 0.765-0.887 | 0.031 | <0.001 | 0.904 | 0.864-0.945 | 0.021 | <0.001 |
| J3       | 0.887 | 0.836-0.939 | 0.026 | <0.001 | 0.948 | 0.916-0.980 | 0.016 | <0.001 |

Note: FVm: mean flow volume.

| Table 3 | The optimal cut-off values of diameter ration and FVm ratio for identifying IJV hypoplasia |
|---------|---------------------------------------------|
| Parameter | Diameter ratio | FVm ratio |
|          | Cut-off value | Sensitivity (%) | Specificity (%) | Youden’s index | Cut-off value | Sensitivity (%) | Specificity (%) | Youden’s index |
| J1       | 0.70 | 92.1 | 64.4 | 0.565 | 0.50 | 92.1 | 86.3 | 0.784 |
| J2       | 0.80 | 80.2 | 72.6 | 0.528 | 0.50 | 77.0 | 82.2 | 0.592 |
| J3       | 0.75 | 81.7 | 82.2 | 0.639 | 0.50 | 84.1 | 94.5 | 0.786 |

Note: FVm: mean flow volume.

| Table 4 | The diameter ratio and FVm ratio of IJV between subgroups with and without cerebral venous sinus stenosis |
|---------|---------------------------------------------|
| Parameters | Cerebral venous sinus symmetry (n=23) | Cerebral venous sinus stenosis (n=50) | t value | P value |
| J1 diameter ratio | 0.65±0.19 | 0.64±0.16 | 0.194 | 0.847 |
| J2 diameter ratio | 0.72±0.20 | 0.69±0.18 | 0.567 | 0.572 |
| J3 diameter ratio | 0.57±0.29 | 0.55±0.22 | 0.464 | 0.644 |
| J1 FVm ratio | 0.30±0.19 | 0.30±0.18 | 0.314 | 0.755 |
| J2 FVm ratio | 0.26±0.20 | 0.30±0.19 | 0.772 | 0.443 |
| J3 FVm ratio | 0.24±0.29 | 0.21±0.16 | 0.469 | 0.640 |

**Discussion**
The present study indicated that the diameter and
FVm of right side were higher than the left side in
healthy control group. In addition, in study group,
most of the cases (93.8%) of the IJV hypoplasia were
on the left side. These findings showed that the right
IJV was the dominant side, which were consistent with
the previous studies [10-12]. The outflow difference
between the bilateral IJV related to its anatomic
variations: (1) the left side of IJV-innominate vein-
superior vena cava pathway is longer than the right
side. Moreover, the angle of innominate vein influxes
into the superior vena cava on the left side is larger than
that on the right side. These anatomy characteristics
determine that the outflow pathway on the right side
is much smoother than the left side. (2) In healthy
population, the sizes of bilateral jugular foreman were
asymmetry. Freitas et al reported that in 30 autopsy samples, 73.3% right jugular foramen size was larger than the left side [13]. 3) IJV size was related to the variation of the superior sagittal sinus influx into transverse sinus. Saiki et al found that 73.6% superior sagittal sinus influx into the right transverse sinus, meanwhile, the size of right transverse sinus and IJV was larger than that of the left side [14].

In this study, the diameter ratio and FVm ratio of the study group were significantly lower than the control group, which contributed to the symptoms of cerebral venous insufficiency. The mechanism of cerebral venous insufficiency induced clinical symptoms might be it induced the venous sinus pressure increase and leaded to the turbulence of venous flow [15]. Moreover, the diameter and FVm of dominant IJV in study group were higher than that of right (dominate) IJV in the control group, suggesting the compensation of the morphology and hemodynamics existed.

The main findings of this study was that established the optimal cut-off values of diameter ratio and flow volume ratio for identifying IJV hypoplasia. The hypoplasia/dominant ratio of diameter and flow volume were used in order to avoid the individual variant. The optimal cut-off diameter ratio of J1-J3 hypoplasia/dominant side were 0.70, 0.80 and 0.75 respectively and the optimal cut-off flow volume ratio of three segments were all 0.50. In addition, a linear regression equation (J1 FVm ratio=0.794×diameter ratio-0.212) was established. According to this equation, the FVm of the hypoplasia side would be 50% of the contralateral side when the diameter ratio was 0.896. However, the FVm ratio would be only 0.185 when the diameter ratio was 0.5. Recently, West et al found that 30-35% stenosis of transverse sinus would lead to symptomatic intracranial hypertension [16]. These findings suggested that the venous hemodynamic parameter (FVm) alteration was more sensitively than the morphology parameter (diameter), i.e. the smaller diameter alteration would lead to obvious hemodynamics change. The study also found out the accuracy and AUC of FVm ratio was higher than that of the diameter ratio for identifying hypoplasia. Thus, when evaluating hypoplasia, physicians should pay more attention to the hemodynamic alteration. It is known that the rate of diameter stenosis ≥ 50% could induce significant hemodynamic alteration in artery system. These difference of relationships of morphology and hemodynamics between artery and venous system might relate to the difference of vessel wall constituent, with the venous had thinner smooth muscle cells and lower compliance and elasticity [17].

Furthermore, the side of IJV hypoplasia were highly correlated with the side of transverse sinus and/or sigmoid sinus stenosis, which was consistent with the findings of Chao’s study [17]. Chao et al reported that IJV hypoplasia was related to transverse sinus stenosis. When the J3 dominant/hypoplasia area ratio was 1.55 (i.e. the hypoplasia/dominant area ratio 0.64 or the diameter ratio 0.80), it can predict the transverse sinsus hypoplasia [7]. The cut-off values of this present study (J3 diameter ratio cut-off value 0.75) was similar with that. It should be noted that there were still 31.5% cases in study group with the bilateral cerebral venous sinus symmetry and the diameter ratio and FVm ratio of IJV hypoplasia side/dominant side had no differences between the two subgroups with and without cerebral venous sinus stenosis. Zhou et al demonstrated that only IJV stenosis (without venous sinus stenosis) would lead to intracranial hypertension [3]. Thus, when there was IJV hypoplasia or stenosis, it is still necessary to use MRV/CTV to...
examine the cerebral venous sinus in order to develop an integral therapeutic regimen.

For imaging evaluation IJV hypoplasia, physicians should pay more attention to the hemodynamics evaluation besides the morphology difference, including the contralateral compensation ability. As demonstrated in this study, the accuracy of FVm ratio was higher than that of the diameter ratio for identifying hypoplasia. Ultrasound can evaluate both the morphology and hemodynamics of IJV, which is the advantage of ultrasound. In addition, as a real-time, dynamic modality, ultrasound can view alteration of diameter and flow volume along with the respiration, which is the advantage of ultrasound over CTV or MRV. The advantage of CTV and MRV are they can evaluate the IJV and the cerebral venous sinus morphology at the same time.

The limitation of this study was it was a relatively small sample thus sub-analysis on age was absent. However, there was no difference on the age between study group and control group. In addition, diameter ratio and FVm ratio were used to minimize the individual variations. In the coming project, the venous sinus stenosis cases with and without IJV hypoplasia will be recruited to compare the parameters pre- and post treatment (cerebral venous intervention and/or IJV intervention) and further demonstrate the correlation mechanism of IJV hypoplasia and cerebral venous sinus stenosis.

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Conflict of Interest
The authors have no conflict of interest to declare.

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