The Effect of Vertebral Venous Collaterals on Intracranial Hypertension and Related Symptoms in Patients with Bilateral Transverse Sinus Stenosis

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Research article

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Abstract

Background: Vertebral venous collaterals (VVC) were often found in patients with bilateral transverse sinus stenosis (BTSS). The purpose of this study was to investigate the physiological role of VVC in BTSS patients.

Methods: The index of TSS was used in the assessment of BTSS severity. Subjects underwent a standard lumbar puncture to measure the intracranial pressure (ICP). Papilledema and tinnitus were evaluated by using Frisén's grade and questionnaires for tinnitus handicap inventory (THI), respectively. The intensity and impact of headache was assessed by using 10-point Numeric Pain Rating Scale (NPRS) and six-item Headache Impact Test (HIT-6).

Results: BTSS group had more patients with severe intracranial hypertension (IH) and less patients with normal ICP. BTSS patients had higher ICP than normal controls. Further analysis on VVC showed that VVC decreased the elevated ICP in BTSS patients and exerted no impact on ICP in normal controls. A similar incidence of VVC in BTSS patients and normal controls were found. BTSS patients with normal ICP and mild IH exhibited a higher incidence of VVC compared with those with severe IH. VVC, rather than the severity of BTSS, regulated the ICP. Furthermore, VVC alleviated IH-related clinical manifestations including papilledema and tinnitus in BTSS patients.

Conclusions: The present study demonstrated BTSS is correlated with IH. The presence of VVC, which is postulated to be congenitally formed, normalizes the elevated ICP and alleviated IH-related symptoms in BTSS patients. VVC may be used as an indicator of relatively low ICP in BTSS patients.

Trial registration: This study was registered retrospectively on 07/28/2020 (NCT04492332).

Background

Bilateral transverse sinus stenosis (BTSS) is characterized by narrowing of bilateral transverse sinus which resulted in obstruction of venous reflux [1]. The majority of BTSS patients exhibited with intracranial hypertension (IH) which manifested as a triad of headaches, tinnitus and papilledema [2, 3]. Stenting improved the symptoms in patients with transverse sinus stenosis (TSS) and reduced the elevated intracranial pressure (ICP) [4]. It is suggested that BTSS is one of the etiologies of IH.

Since an alternative pattern of venous reflux was observed in patients with occluded superior sagittal sinus, it is postulated that altered pattern of venous reflux also exists in the presence of BTSS [5]. The drainage of cerebral veins consists of two major pathways: transverse sinus-sigmoid sinus-internal jugular vein and vertebral venous plexus [6]. Vertebral venous plexus is an extensive paravertebral system that provides direct venous communication between peritoneum and cranial cavity [7]. The presence of vertebral venous collaterals (VVC) was reported in 108 consecutive patients [6]. However, whether VVC is of physiological significance in BTSS patients remained unknown.

This article was aimed to investigate the physiological role of VVC and whether it is involved in the regulation of IH and related clinical symptoms in BTSS patients.

Methods

Subjects recruitment

BTSS patients were recruited from the neurology department and neurosurgery department of Xuanwu Hospital from January 2014 to December 2018. The normal controls were recruited from health examination center of Xuanwu hospital. This study was approved by the Ethnic Board of Xuanwu Hospital.

The inclusion criteria were BTSS confirmed by two of magnetic resonance venography (MRV), computed tomography venography (CTV) or digital subtraction angiography (DSA). Normal controls had no history of neurological diseases and no neurological signs.

The exclusion criteria involved: 1) systemic inflammation; 2) medicine related intracranial hypertension; 3) moderate to severe stenosis in intracranial or jugular veins other than transverse sinus; 4) moderate to severe stenosis in intracranial, carotid or vertebral arteries; 5) intracranial lesions.

Experimental Design

Subjects underwent a standard lumbar puncture to measure ICP. It is reported that 95% reference interval for ICP was 100 to 250 mmH2O in healthy adults [8]. ICP above 250 mmH2O was considered IH [9, 10]. However, there is an overlap between normal and elevated ICP ranging from 200 to 250 mmH2O [11, 12]. In this article, Normal ICP was defined as 100 to 200 mmH2O. Mild IH was defined as an ICP ranging from 200 to 250 mmH2O whereas severe IH was defined as an ICP above 250 mmH2O.

Triad of IH were also evaluated. Fundus photography was conducted and the papilledema was graded by using modified Frisén's grade [13, 14]. The intensity of headache was assessed by using 10-point Numeric Pain Rating Scale (NPRS) [15]. The six-item Headache Impact Test (HIT-6) was used to measure the impact of headache [16]. The impact of tinnitus was evaluated by using questionnaires for tinnitus handicap inventory (THI) [17].

The index of TSS (ITSS) score was a useful tool for the assessment of BTSS severity. The degree of stenosis was graded from 0 to 4 based on the following scale: 0 = normal; 1 = stenosis up to 1/3; 2 = stenosis between 1/3 and 2/3; 3 = stenosis >2/3; and 4 = hypoplasia. ITSS was calculated as degree of right TSS × degree of left TSS [18].

Statistical analysis

All clinical data were collected by Dr. Chaobo Bai and Dr. Jingkun Sun. Dr. Min Li independently analyzed the clinical data in a blinded manner. The data are expressed as mean ± standard error (SE). Rates were compared by using chi-square test. Numerical values between two and three groups were compared by using Student's t test and one way-Analysis of Variance (ANOVA) followed by Student-Newman-Keuls (SNK) test, respectively. Correlations were performed with Pearson correlation coefficients or linear regression. $P < 0.05$ was defined as statistically significant. All analyses were performed using the SPSS software (version 19.0, SPSS, USA) and GraphPad Software (Version 7.0, GraphPad Prism, USA).

Results

92 normal controls and 45 BTSS patients were enrolled. The listed clinical characteristics in normal controls and BTSS patients were similar (Table 1). 37.77% of BTSS patients and 75% of normal controls had normal ICP. 17.77% of BTSS patients and 25% of normal controls had mild IH. 44.44% of BTSS patients had severe IH. A series of studies reported a correlation between TSS and IH [19–21]. Data from the present study confirmed the aforementioned results. BTSS patients had higher ICP compared with normal controls (Fig. 1A). ICP was significantly lower in BTSS patients with VVC compared with those without VVC. No significant difference in ICP was found between normal controls with VVC and those without VVC (Fig. 1A). It is suggested that VVC decreased the elevated ICP in BTSS patients and exerted no impact on ICP in normal controls.

Table 1
Demographic features of the normal controls and BTSS patients.

Characteristics	Normal controls (n = 92)	Patients with BTSS (n = 45)	p value
Age (years)	53.24 ± 14.23	50.87 ± 16.10	0.174
Female, n (%)	60 (65.22%)	34 (75.56%)	0.221
BMI	24.56 ± 3.25	25.16 ± 3.94	0.289
Premedical history, n (%)			
Hypertension	32 (34.78%)	14 (31.11%)	0.669
Diabetes mellitus	12 (13.04%)	2 (4.44%)	0.119
Coronary artery disease	9 (9.78%)	5 (11.11%)	0.809
Hyperlipidemia	21 (22.83%)	10 (22.22%)	0.859
Hyperuricemia	1 (1.09%)	2 (4.44%)	0.207
Smoking	11 (11.96%)	3 (6.67%)	0.337
Alcohol	12 (13.04%)	2 (4.44%)	0.119
Vital signs at admission			
Systolic pressure (mmHg)	124.42 ± 13.17	127.16 ± 14.07	0.292
Diastolic pressure (mmHg)	76.13 ± 9.35	77.87 ± 10.19	0.179
Heart rate (bpm)	78.31 ± 10.80	77.20 ± 9.33	0.592
Respiratory rate (/min)	19.49 ± 1.25	19.16 ± 1.61	0.302
Body temperature (°C)	36.44 ± 0.30	36.45 ± 0.29	0.978
ICP			
100–200 cmH_2O	69 (75%)	17 (37.77%)	0.000*
201–250 cmH_2O	23 (25%)	8 (17.77%)	0.343
> 250 cmH_2O	0 (0%)	20 (44.44%)	0.000*

* indicated statistically significant. BTSS, bilateral transverse sinus stenosis; BMI, body mass index; ICP, intracranial pressure.

The incidence of VVC between BTSS patients and normal controls were compared. 51.6% of BTSS patients and 48.6% of normal controls had VVC (Fig. 1B). Interestingly, BTSS patients with normal ICP and mild IH exhibited a higher incidence of VVC compared with those with severe IH (Fig. 1B). These findings indicated that severe IH in BTSS patients may be due to the absence of VVC.

Since BTSS was correlated with IH, it is hypothesized that severity of BTSS may influence the ICP. However, further analysis revealed that ICP was not affected by the severity of BTSS graded by ITSS score. VVC was found to be the only factor that influence the ICP (Table 2). Furthermore, we assessed the correlation between ITSS score and incidence of VVC. Results showed that incidence of VVC was irrelevant with ITSS score (Fig. 2). It is demonstrated that VVC, rather than the severity of BTSS, plays the key role in regulating ICP.

Table 2
The presence of VVC, instead of the severity of bilateral transverse sinus stenosis, was associated with the ICP.

Multivariate linear regression						
Independent variables	Dependent variables	Coefficient	SD	P	95% CI	
					Lower	Upper
ITSS score	ICP	1.921	4.344	0.662	-7.009	10.851
VVC		-76.443	26.925	0.009*	-131.787	-21.099

* indicated statistically significant. ITSS, index of transverse sinus stenosis; ICP, intracranial pressure; CI, confidence interval; VVC, vertebral venous collaterals; SD, standard deviation.

The correlation between VVC and triad of IH symptoms was analyzed. The papilledema was assessed by Frisén's grade. Pearson correlation analysis showed that ICP was positively associated with the score of Frisén's grade (Fig. 3A). BTSS patients with VVC had significantly lower score of Frisén's grade than those without VVC (Fig. 3B). However, VVC exerted no influence on headache either assessed by NPRS or HIT-6 score in BTSS patients (Table 3). THI was used to evaluate tinnitus. BTSS patients with VVC had significantly lower THI score than those without VVC (Table 3). Taken together, the presence of VVC attenuates papilledema and tinnitus in BTSS patients.

Table 3

A reduced THI score, rather than NPRS score and HIT-6 score, was observed in BTSS patients with VVC.

Univariate linear regression						
Independent variables	Dependent variables	Coefficient	SD	P	95% CI	
					Lower	Upper
VVC	NPRS score	0.694	1.705	0.687	-2.810	4.198
VVC	HIT-6 score	3.730	13.990	0.792	-25.028	32.488
VVC	THI score	-24.284	9.886	0.021*	-44.605	-3.963

* indicated statistically significant. ITSS, index of transverse sinus stenosis; ICP, intracranial pressure; SD, standard deviation; CI, confidence interval; VVC, vertebral venous collaterals; NPRS, numeric pain rating scale; HIT-6, six-item Headache Impact Test; THI, Tinnitus Handicap Inventory.

Discussion

Farb et al reported that bilateral sinovenous stenoses were seen in 27 of 29 patients with IH [2]. Bono et al suggested that BTSS patients had higher ICP than normal controls [22]. In this study, BTSS group had more patients with severe IH and less patients with normal ICP (Table 1). Consistent with previous findings [11, 12], our results also demonstrated that ICP ranging from 200 to 250 mmH2O is an overlap between normal and elevated ICP (Table 1). BTSS patients had an average ICP of 246.6 ± 80.7 (Fig. 1A). It is demonstrated that BTSS is associated with elevated ICP.

The presence of VVC was observed in our clinical practice. However, it has been very confusing that whether these collaterals were congenitally formed or acquired after BTSS. A higher incidence of VVC in BTSS patients compared with normal controls and in BTSS patients with elevated ICP compared with those with normal ICP suggests that VVC may be acquired after BTSS. Otherwise, it is indicated that VVC may be congenital. The present study showed a similar incidence of VVC between BTSS patients and normal controls. Moreover, the incidence of VVC in BTSS patients with severe IH was no higher than those with mild IH and normal ICP (Fig. 1B). A plausible explanation for this observation is that VVC was a congenital and physiological existence.

In the meanwhile, the physiological role of VVC has not been demonstrated before. Results of this study revealed that VVC is capable of down-regulating the elevated ICP and exerted no effect on normal ICP (Fig. 1A). A negative correlation between VVC and ICP was identified after adjusted for the severity of BTSS (Table 2). Under the condition of BTSS, more venous blood drains into vertebral venous plexus. VVC allows more intracranial venous blood to pass through, thus guarantees the venous return. The presence of VVC compensated the obstruction of transverse sinus-sigmoid sinus-internal jugular vein pathway. However, the severity of BTSS was proofed to be irrelevant with ICP after adjusted for VVC (Table 2). This finding was evidenced by Bono et al [22]. This lack of association may be due to the compensatory effect of vein of Labbe and occipital sinus [23, 24].

In agreement with the regulatory effect on ICP, VVC alleviated IH-related clinical manifestations. Tinnitus, papilledema and headaches were the three major symptoms of IH [3]. VVC improved papilledema and tinnitus. However, headache was not relieved (Table 3). Since NPRS and HIT-6 is subjective, scores given by patients with distinctive pain tolerance may be inaccurate. It is indicated that NPRS and HIT-6 are more suitable in the application of self-control studies.

Conclusions

The present study demonstrated BTSS is correlated with IH. The presence of VVC, which is postulated to be congenitally formed, normalizes the elevated ICP and alleviated IH-related symptoms in BTSS patients. The presence of VVC may be used as an indicator of relatively low ICP in BTSS patients.

Abbreviations

BTSS: Bilateral transverse sinus stenosis

TSS: Transverse sinus stenosis

ICP: Intracranial pressure

VVC: Vertebral venous collaterals

MRV: Magnetic resonance venography

CTV: Computed tomography venography

DSA: Digital subtraction angiography

NPRS: Numeric Pain Rating Scale

HIT-6: Six-item Headache Impact Test

IH: Intracranial hypertension

THI: Tinnitus handicap inventory (THI)

ITSS: The index of Transverse sinus stenosis

SE: standard error

ANOVA: Analysis of variance

SNK: Student-Newman-Keuls

SD: standard deviation

CI: confidence interval

Declarations

Ethnic approval and consent to participate

This case report is approved by the Ethnic Board of Capital Medical University Xuanwu Hospital. All patients enrolled in this study signed a letter of consent for participation.

Consent for publication

All patients reported in this case series signed a letter of consent for publication.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author via E-mail upon reasonable request.

Competing interests

All authors declare that they have no conflicts of interest.

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Author contributions

ML: contributed to designing this study, analyzing clinical data and drafting the manuscript;

CBB: contributed to collecting clinical data;

JKS: contributed to collecting clinical data;

NX: contributed to English editing;

XMJ: contributed to critical revision of the manuscript;

RM: contributed to acquisition of study funding and critical revision of the manuscript.

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Figures

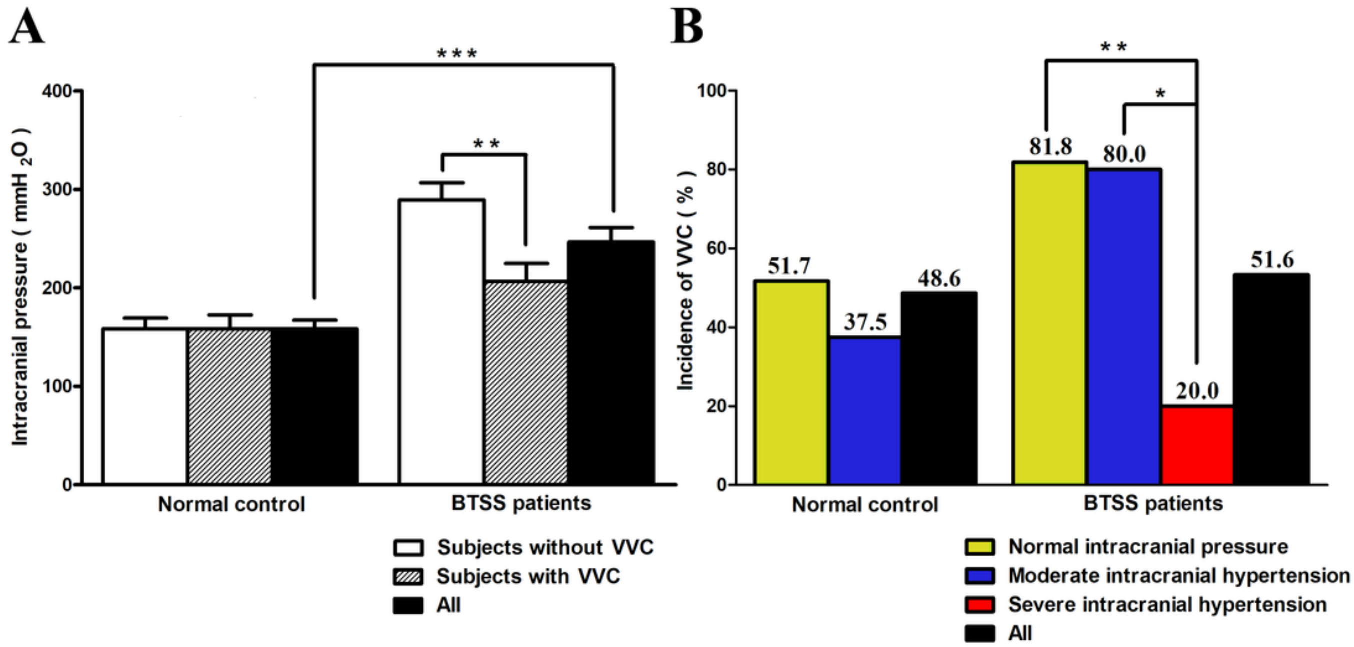

Figure 1

The presence of VVC reduced the elevated ICP in BTSS patients. The BTSS patients revealed a higher ICP than normal controls. and BTSS patients with VVC exhibited a lower ICP than those without VVC (A). The incidence of VVC was significantly higher in BTSS patients with normal ICP or mild IH than those with severe IH (B). *p < 0.05, **p < 0.01, ***p < 0.001. BTSS, bilateral transverse sinus stenosis; ICP, intracranial pressure; IH, intracranial hypertension; VVC, vertebral venous collaterals.

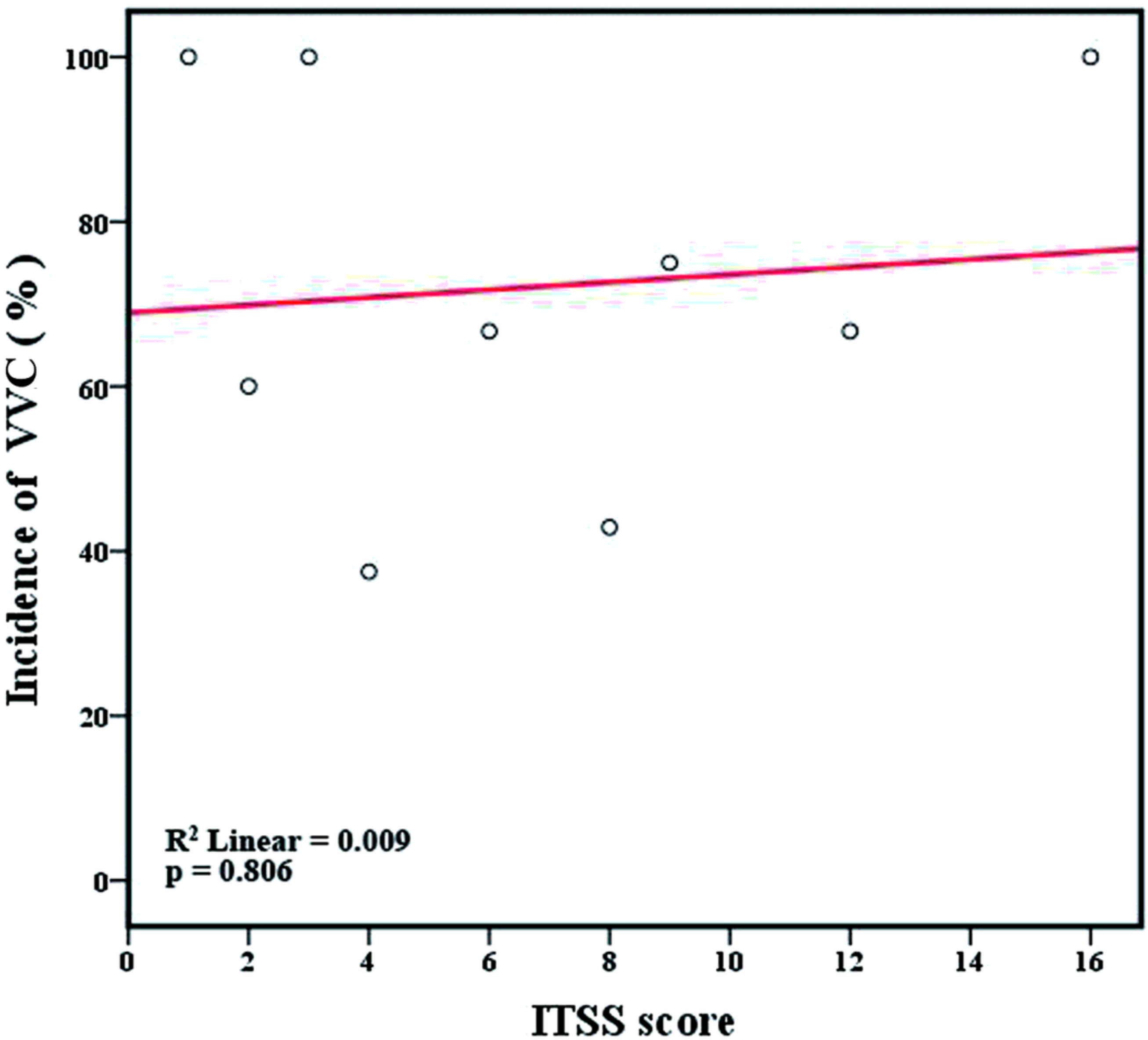

Figure 2

There was no correlation between the ITSS score and incidence of VVC. ITSS, index of transverse sinus stenosis; VVC, vertebral venous collaterals.

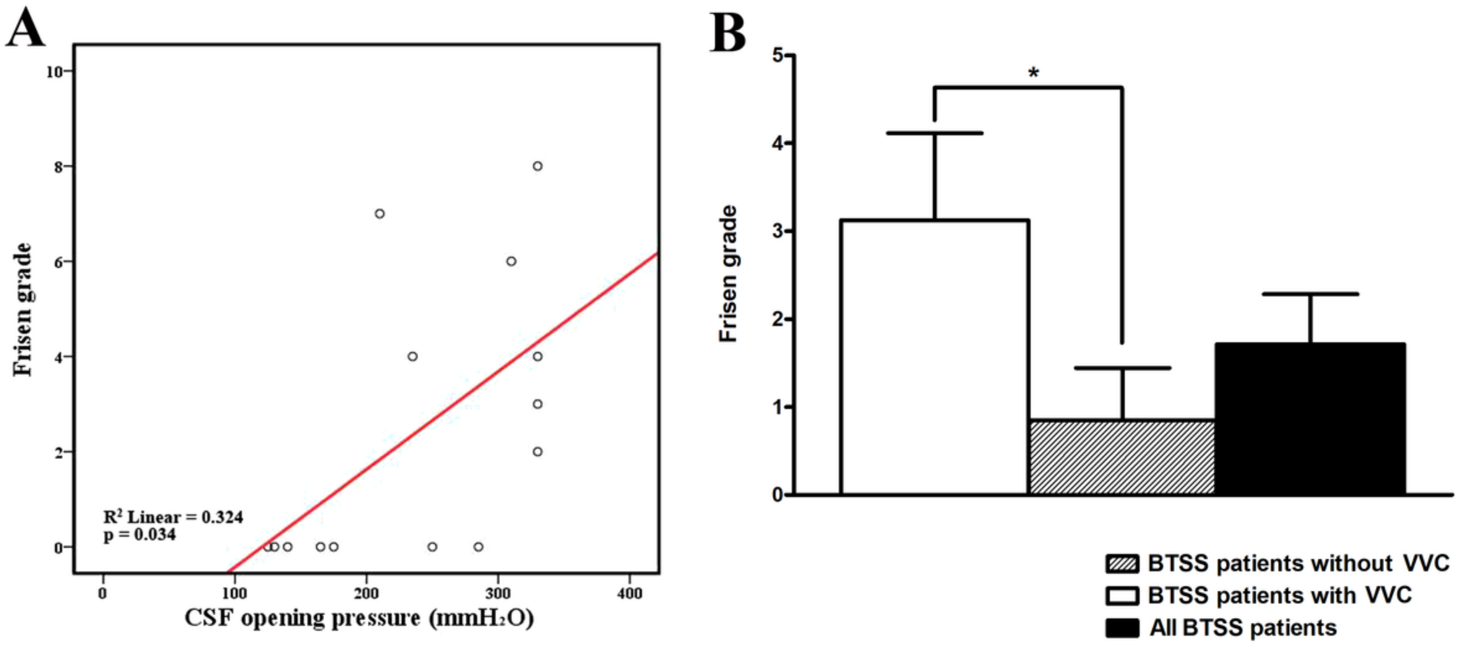

Figure 3

The presence of VVC alleviated papilledema in BTSS patients. Frisén's grade based on fundus photography was positively correlated with ICP (A). BTSS patients with VVC had a lower Frisen grade compared with those without VVC (B). *$p < 0.05$. ICP, intracranial pressure; BTSS, bilateral transverse sinus stenosis; VVC, vertebral venous collaterals.