Factors Contributing to Attenuation of Cerebral Venous Sinus in Brain Noncontrast Computed Tomography Scan

Sima Fallah Arzpeyma[1]   Ehsan Kazemnezhad-Leili[2]   Hosna Rashidi[1]   Samaneh Ghorbani-Shirkouhi[3]
Alia Saberi[4]

[1] Department of Radiology, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[2] Clinical Statistics, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[3] Neuroscience Research Center, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[4] Neuroscience Research Center, Department of Neurology, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

Address for correspondence Alia Saberi, Professor of Neurology, Neuroscience Research Center, Department of Neurology, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran (e-mail: Alia.saberi.1@gmail.com).

Abstract

Background/Aim   In noncontrast computed tomography (NCCT), an apparently hyper-attenuated cerebral venous sinus (CVS) may lead to suspicion of CVS thrombosis. Understanding the factors affecting attenuation of CVS can guide us toward true diagnosis. Hence, the aim of the study was to determine the effect of different factors such as hematocrit, hemoglobin, age, blood urea nitrogen (BUN), creatinine, leukocyte and platelet count, and sex on the attenuation of CVS on brain NCCT.

Material and Methods   Total 1,680 patients were included in this study, and their demographic and laboratory data and brain NCCT were reviewed. In their brain NCCT, the average attenuation of superior sagittal sinus and both right and left sigmoid sinuses was measured. Data analysis was conducted using the Statistical Package for the Social Sciences version 21.0 software by Kolmogorov-Smirnov, Spearman's correlation coefficient, and multiple linear regression tests. The significance level was considered less than 0.05.

Results   Hematocrit (B $= 0.251$, $p < 0.001$), hemoglobin (B $= 0.533$, $p < 0.001$), and creatinine (B $= -0.270$, $p = 0.048$) were determined as predictors of attenuation of superior sagittal sinus. For both sigmoid sinuses, hematocrit ($p < 0.001$) and hemoglobin ($p < 0.001$) were determined as positive predictors, and creatinine ($p < 0.001$) and BUN ($p < 0.002$) were determined as negative and positive predictors, respectively.

Conclusion   Hemoglobin, hematocrit, creatinine, and BUN are the main factors that should be considered in the assessment of CVS density on brain NCCT. As with increasing hematocrit and hemoglobin of the subject, the CVS density in NCCT increases, and with increasing creatinine and in some instance decreasing BUN of the subject, the CVS density in NCCT decreases.

Keywords
► attenuation
► cerebral venous sinus thrombosis
► creatinine
► density
► hemoglobin
► noncontrast computed tomography

Introduction

Noncontrast computed tomography (NCCT) scan of brain is mainly used as the primary neuroimaging method in patients with new-onset neurological symptoms attending emergency wards such as headache, seizure, focal neurological deficits, and altered conscousness.[1]

Cerebral venous sinus thrombosis (CVST) is an important neurological disorder responsible for 0.5% of stroke cases worldwide.[2] Symptoms and signs of this disorder are widely different and are usually initiated by headache and papilledema and in clinically suspected cases, it is established by imaging.[3] The clinical course is usually subclinical with the mean diagnostic delay of nearly 7 days.[4,5] Delayed diagnosis may result in cerebral venous type of stroke or occasionally leads to symptoms of intracranial hypertension and seizure.[5] Despite its low incidence rate, it is seen in two to seven cases per million annually.[6] Janghorbani et al reported that the annual frequency of CVST in a population of 2,472,751 in Isfahan, Iran, was 12.3 (95% confidence interval: 10.1, 14.5) per million.[7] Although CVST mortality rate has been significantly reduced by improvements in treatment and diagnostic techniques, the mortality rate of severe CVST remains as high as 34.2%. Therefore, prompt diagnosis and treatment are crucial.[8] Delta and cord signs in computed tomography (CT) scan with and without contrast show the intraluminal thrombosis in superior sagittal and transverse sinuses, respectively, and they are seen in nearly 40% of patients with CVST.[9,10] The sensitivity and specificity of the cord sign for CVST have been estimated 64.6% and 97.2%, respectively, by Linn et al[4] The sensitivity of unenhanced brain CT for the diagnosis of CVST has been calculated as 73% by Roland et al; although density measurements proved to be helpful, they could not detect all cases of CVST.[11] Regarding the fact that objective assessment of radiodensity results in misdiagnosis,[6] radiologists prefer to use the Hounsfield unit to measure attenuation of cerebral venous sinus (CVS). Observation of CVS with increased Hounsfield unit may lead to suspicion of vein thrombosis. This sign is a key factor for early diagnosis of vein thrombosis that is probably accompanied by better outcomes.[12] The main limitation of this sign is that multiple factors affect the attenuation of CVS density and lead to overlap of normal and pathological conditions and result in increased false positive and negative findings in the interpretation of brain NCCT. Recognition of contributing factors can lead to a better diagnosis of suspected cases of CVST. Limited data exist on CVS attenuation related factors such as dehydration and blood concentration. Hence, in some cases, advanced techniques such as CT-venography, magnetic resonance venography (MRV), and occasionally catheter-angiography are used in suspected cases, resulting in delays in diagnosis and treatment.[13] Early intervention with systemic anticoagulants or direct injection of thrombolytic agents, and sometimes with mechanical thrombolysis, is crucial in the treatment of CVST. Accordingly, improvement in the diagnosis of CVST by brain NCCT as an early diagnostic approach is crucial in management of the patients.[14,15]

The normal CVS density is lower than 70 Hounsfield units.[16] A significant association was found between hemoglobin and hematocrit levels and blood density in brain NCCT in previous studies.[16] High hematocrit level is the most common cause of false-positive results in the diagnosis of CVST by brain NCCT.[17,18] In addition to red blood cell count, leukocyte and platelet counts may also affect the blood viscosity,[19] but their effect on the attenuation of CVS in brain NCCT has not been assessed. In this study, we assessed the effect of different factors such as hematocrit, hemoglobin, blood urea nitrogen (BUN), creatinine, leukocytes, platelets, age, and sex on the attenuation of CVS in brain NCCT. This issue can help to reduce the false positive and negative diagnoses of CVST in brain NCCT and to decrease further costs of additional tests.

Materials and Methods

This retrospective cross-sectional descriptive–comparative study was conducted on 1,680 patients attending the emergency ward in an academic hospital in Guilan, in the north of Iran, in 2018. The laboratory investigation and the brain NCCT scan performed for the subjects were registered. The proposal of the study was approved by the Ethic Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1397.274). Thereafter, data collection was initiated with permission from hospital manager. It was performed by a retrospective method and studying the existing medical documents of patients. Data were recorded in checklists. The inclusion criteria were age between 15 and 80 years, presence of complete blood count, and renal function tests done during 24 hours before and 24 hours after brain CT scan in the patient's medical documents. The exclusion criteria were bleeding/fracture of the skull near the CVS and intra/extra-axial mass or congenital abnormality of the skull; receiving injection contrast media in past 48 hours; blood transfusion in past 4 hours; current neurosurgical procedure; established CVST according to medical documents and MRV imaging; indirect symptoms of thrombosis such as an infarct in brain CT scan; presence of artifact on CVS in brain NCCT; and lesions with pressure effects on CVS, including meningioma and other tumors near the sinuses and epivenous and subvenous hematoma.

Instruments and Images

The studied variables were hemoglobin, hematocrit, BUN, creatinine, platelet count, and leukocyte count done during 24 hours before and 24 hours after brain CT scan. In addition, the age and sex were recorded. In brain NCCT, superior sagittal sinus density was measured in the posterior part in three points of upper, middle, and lower portions as well as right and left sigmoid sinuses. To reduce the difference in the measurement of the samples, a 2-mm region of interest sample in each sinus was used according to the Hounsfield unit, and finally the mean density was calculated. All CT scans were performed by a 16-slice HITACHI device, and the protocol for NCCT brain scan was as follows: thickness 7 mm, 120 kVp, and 160 mA.

Software and Analysis Method

After data collection was completed, data analysis was conducted using the Statistical Package for the Social Sciences version 21.0 software. Kolmogorov-Smirnov, Spearman linear regression, multiple linear regression, and Mann–Whitney tests were used. The significance level was considered less than 0.05.

Results

The mean age of the subjects was 47.6 ± 19.5 (range: 15–80) years, and 37.4% of them were females. ►**Table 1** shows the laboratory data and imaging measurements.

In the univariate analysis shown in ►**Table 2**, for all CVS, the mean density of CVS had significant reverse correlation with age, medium to high direct correlation with hemoglobin, and medium to high direct correlation with hematocrit of patient. The BUN had only a weak reverse significant correlation with superior sagittal sinus density. The creatinine had a weak direct significant correlation with the right sigmoid sinus density. Leukocyte count had a low direct significant correlation with the density of all sinuses. The platelet had a weak significant reverse correlation with the densities of all sinuses. Furthermore, as ►**Table 3** shows, the mean and median densities of all CVSs were significantly higher in males ($p < 0.001$).

►**Table 4** presents the regression coefficients of predictive factors based on multivariate analysis for three sinuses. Moreover, the adjusted R square for predictive factors determined for each sinus in ►**Table 4** was 0.411, 0.327, and 0.335, for superior sagittal, left sigmoid, and right sigmoid sinuses, respectively.

For the density of the superior sagittal sinus, hematocrit ($B = 0.251$, $p < 0.001$), hemoglobin ($B = 0.533$, $p < 0.001$), female sex (F/M: $B = 0.533$, $p < 0.001$), and creatinine ($B = -0.270$, $p = 0.048$) were determined as predictors. For both

Table 1 Mean laboratory and imaging measurements of subjects ($n = 1,680$)

Variable	Mean	Median	Range
Hemoglobin (g/L)	12.6 ± 2.1	12.7	3.7–39.3
Hematocrit (%)	37.2 ± 5.4	37.7	9.0–60.5
Blood urea nitrogen (mg/dL)	17.2 ± 9.8	15.0	0.8–118.0
Creatinine (mg/dL)	1.0 ± 0.6	0.9	0.1–11.0
Leukocyte ($\times 10^3$/mL)	10.0 ± 4.2	9.2	0.7–51.5
Platelet ($\times 10^3$/mL)	222.4 ± 89.5	208.0	12.4–1,119.0
Density of superior sagittal sinus (Hu)	48.2 ± 4.2	48.0	5.0–61.0
Density of left sigmoid sinus (Hu)	46.8 ± 5.0	47.0	26.0–66.0
Density of right sigmoid sinus (Hu)	46.3 ± 5.1	47.0	17.0–65.0

Table 2 Correlation of mean density of venous sinuses and background variables

		Density of superior sagittal sinus	Density of left sigmoid sinus	Density of right sigmoid sinus
Age	Correlation coefficient	−0.216	−0.165	−0.157
	p-Value	0.000	0.000	0.000
Hemoglobin	Correlation coefficient	0.653	0.543	0.550
	p-Value	0.000	0.000	0.000
Hematocrit	Correlation coefficient	0.629	0.524	0.528
	p-Value	0.000	0.000	0.000
Blood urea nitrogen	Correlation coefficient	−0.063	0.001	0.018
	p-Value	0.010	0.957	0.466
Creatinine	Correlation coefficient	0.030	0.047	0.051
	p-Value	0.220	0.055	0.036
Leukocyte	Correlation coefficient	0.104	0.115	0.105
	p-Value	0.000	0.000	0.000
Platelet	Correlation coefficient	−0.083	−0.088	0.070
	p-Value	0.001	0.000	0.004
Spearman's correlation coefficient				

Table 3 Correlation of sinus measurements and sex

		Density of superior sagittal sinus			
		Mean ± standard deviation	Median	Mean rank	p-Value
Sex	Male	49.4 ± 4.1	50.0	1,001.2	<0.001
	Female	46.1 ± 3.3	46.0	571.3	
		Density of left sigmoid sinus			
		Mean ± standard deviation	Median	Mean rank	p-Value
	Male	48.2 ± 4.8	49.0	990.9	<0.001
	Female	44.4 ± 4.3	45.0	588.5	
		Density of right sigmoid sinus			
		Mean ± standard deviation	Median	Mean rank	p-Value
	Male	47.8 ± 4.9	48.0	988.10	<0.001
	Female	43.9 ± 4.4	44.0	593.24	

Table 4 Predictive regression coefficients for density of superior sagittal, left sigmoid, and right sigmoid sinuses (stepwise multiple linear regression)

		Unstandardized coefficients		Standardized coefficients	p-Value	95.0% confidence interval for B		Correlations	
		B	Standard error	Beta		Lower bound	Upper bound	Zero-order	Partial
Superior sagittal	(Constant)	34.587	0.742		<0.001	33.131	36.402		
	Hematocrit	0.251	0.021	0.326	<0.001	0.210	0.292	0.579	0.281
	Hemoglobin	0.533	0.055	0.264	<0.001	0.424	0.641	0.564	0.229
	Sex (female/male)	0.533	0.055	0.264	<0.001	−1.946	−1.268	−0.382	−0.221
	Creatinine	−0.270	0.137	−0.037	0.048	−0.538	−0.002	−0.079	−0.048
Left sigmoid	(Constant)	33.273	0.988		<0.001	31.334	35.211		
	Hematocrit	0.247	0.027	0.268	<0.001	0.194	0.299	0.498	0.219
	Sex (female/male)	−2.123	0.221	−0.207	<0.001	−2.557	−1.389	−0.373	−0.228
	Hemoglobin	0.581	0.072	0.241	<0.001	0.439	0.723	0.485	0.193
	Creatinine	−0.901	0.214	−0.105	<0.001	−1.321	−0.481	−0.082	−0.102
	Blood urea nitrogen	0.051	0.013	0.100	<0.000	0.026	0.076	−0.073	0.096
Right sigmoid	(Constant)	32.073	1.008		0.000	30.095	34.051		
	Hematocrit	0.526	0.027	0.272	<0.001	0.202	0.310	0.508	0.223
	Sex (female/male)	−2.106	0.226	−0.200	<0.001	−2.549	−1.663	−0.370	−0.222
	Hemoglobin	0.617	0.074	0.249	<0.001	0.472	0.761	0.498	0.200
	Creatinine	−0.825	0.218	−0.093	<0.001	−1.253	−0.396	−0.083	−0.092
	Blood urea nitrogen	0.042	0.013	0.080	<0.002	0.016	0.067	−0.089	0.077

sigmoid sinuses, hematocrit ($p < 0.001$), hemoglobin ($p < 0.001$), and male sex ($p < 0.001$) were determined as positive predictors, and creatinine ($p < 0.001$) and BUN ($p < 0.002$) were determined as negative and positive predictors, respectively (►**Table 4**). As with increasing hematocrit and hemoglobin of patient, the CVS density increases, and with increasing creatinine, and in some instance decreasing BUN of patient, the CVS density decreases.

Discussion

In the current study, 1,680 patients were enrolled to assess the contributing factors for the density of the CVS. The results demonstrated that hemoglobin, hematocrit, creatinine, and BUN were the main factors that should be considered upon the assessment of CVS density on brain NCCT.

In the study by Black et al, the CVS density above 70 Hounsfield units was considered suspicious to CVST that required further assessments.[16] In the study by Buyck et al, the CVS density higher than 62 Hounsfield unit was considered for supplementary evaluation for CVST.[6]

In the present study, although there was a negative correlation between age and CVS density in univariate analysis, any association between age and CVS density in multivariate analysis was not found. The study by Al-Ryalat et al showed a direct and significant correlation between density and age.[3] Decreased hemoglobin and hematocrit is related to increased age.[20] And as in the present study the CVS density was correlated with hemoglobin and hematocrit, it may indirectly explain the finding of Al-Ryalat et al's study.[3] Hence, older subjects with suspected symptoms of CVST are more likely to have normal density and requirement to complementary assessments.

In the study by Al-Ryalat et al, the CVS density among men was higher.[3] In the present study, a discrepancy existed about the effect of sex on different attenuations of CVSs. As in superior sagittal sinus, female gender was determined as the predictor of attenuation of that CVS, whereas in both sigmoid sinuses, male gender was determined as the predictor of attenuation of those sinuses. Therefore, we ignored the contributing role of gender in CVS attenuation in NCCT.

In the present study, CVS density has a medium to powerful direct correlation with hemoglobin and hematocrit ($p < 0.001$). With the increase in hematocrit and hemoglobin of subject, CVS density increases. Al-Ryalat et al, Black et al, Akhavan et al, Lee et al, and Yurttutan et al[3,16,21–23] also demonstrated a significant correlation between hemoglobin and hematocrit and CVS attenuation.

In the present study, creatinine ($p < 0.001$) and BUN ($p < 0.002$) were determined as negative and positive predictors, respectively. So with the increase of creatinine and in some cases by decreasing BUN, the CVS density decreases. But in one study by Akhavan et al, although in univariate analysis, there was a significant and negative correlation between the BUN/creatinine ratio and average attenuation; in multivariate analysis, they did not find any correlation between BUN and creatinine and CVS attenuation.[21] The study by Al-Ryalat et al also showed no significant correlation for BUN and creatinine.[3]

In the present study by univariate analysis, in all three CVSs, the correlation of CVS density with leukocyte count was significant, but weak with direct pattern. Also, its correlation with platelet count was significant and weak with a reverse pattern. However, in multivariate analysis, there was no association between leukocyte and platelet counts and CVS density. We could not find any research investigating the association of leukocyte and platelet counts with CVS density.

The main potency of our study was that this study was conducted among a larger sample population. Although the study by Akhavan et al included a large sample size,[21] the present study included more than threefolds of the mentioned study (1,680 versus 550 subjects). In addition, some less-focused factors such as platelet and leukocyte counts were assessed in the present study.

One of the limitations of the study was the presence of few previous studies investigating factors contributing to CVST. Another one was that in the analysis of images, it was unclear that to what extent the diameter of CVS and the adjacent skull density affected the CVS density.

Conclusions

CVS attenuation may lead to suspicion of cerebral CVST. However, multiple factors affect the attenuation of CVS and lead to overlap of normal and pathological conditions and result in increased false positive and negative findings in the interpretation of brain NCCT. Recognition of contributing factors can help to achieve a better diagnosis of suspected cases of CVST. The results of this study demonstrated that hemoglobin, hematocrit, creatinine, and BUN were the main factors that should be regarded in the assessment of CVS density on brain NCCT. As with increasing hematocrit and hemoglobin of the subject, the CVS density in NCCT increases, and with increasing creatinine and in some instance decreasing BUN of the subject, the CVS density in NCCT decreases.

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