Original article

Hounsfield unit-to-hematocrit ratio as a quantitative marker for cerebral venous sinus thrombosis: A retrospective diagnostic study

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Abstract. *Background and Aim:* Cerebral Venous Sinus Thrombosis (CVST) is a rare but potentially life-threatening condition that requires advanced imaging modalities, such as magnetic resonance venography (MRV) or computed tomography venography (CTV), for diagnosis. However, access to these diagnostic tools is often limited in resource-constrained settings. There is an unmet need for simpler, cost-effective, and rapid diagnostic methods to facilitate early detection of CVST. This study aims to evaluate the utility of the Hounsfield unit (HU)/hematocrit (Hct) ratio derived from non-contrast CT imaging as a novel diagnostic marker for CVST and explore its correlation with hematological parameters, while identifying common symptoms and demographic patterns. *Methods:* This cross-sectional study was conducted between September and October 2024. Data were collected retrospectively from patients diagnosed with CVST between January 2022 and August 2024 at a tertiary care center. The study variables included Hct, platelet count (Plt), HU values from CT scans, and the HU/Hct ratio. Data were analyzed and presented in summary tables, focusing on the relationship between imaging and hematological parameters. *Results:* A total of 93 patients with CVST were identified, with 74.2% being female and a mean age of 40 years. After applying inclusion criteria, 34 patients were analyzed. The study revealed a significant negative correlation between Hct and the HU/Hct ratio ($p = 0.001$). No significant correlation was observed between Plt and HU or the HU/Hct ratio. Common clinical presentations included headache (84%) and dizziness (35%), with CVST predominantly affecting women of reproductive age. *Conclusion:* The HU/Hct ratio demonstrates potential as an accessible and reliable diagnostic marker for CVST, particularly in resource-limited settings where advanced imaging is unavailable. This quantitative parameter could complement existing diagnostic workflows and aid in the early detection of CVST. Further validation through multicenter studies is recommended to establish its broader applicability. (www.actabiomedica.it)

Key words: cerebral venous sinus thrombosis, hu/hct ratio, hounsfield unit, hematocrit, platelet count, headache, dizziness

Introduction

Cerebral Venous Sinus Thrombosis (CVST) is a rare and potentially fatal cerebrovascular disease with an incidence of about 0.5%–1% in all stroke cases and 10%–20% in younger populations. CVST is a pathology with its origins in the cerebral venous sinuses causing obstruction of venous drainage leading to increased intracranial pressure (ICP) and possible complications such as cerebral edema, infarction, or hemorrhage. It is a condition that can be associated with significant morbidity and mortality if not diagnosed and managed in a timely manner. The clinical picture is extremely heterogeneous, ranging from nonspecific manifestations such as headache, nausea, and dizziness to more severe neurological deficits including focal motor weakness, cranial nerve palsies, aphasia, seizures, and altered mental status. Because of its spectrum of clinical phenotypes, CVST is frequently misdiagnosed or addressed late, highlighting the need for rapid imaging-based recognition (1-4). The global incidence of CVST among individuals aged 18–64 years is estimated to be between 2.45 and 3.16 per 100,000 person years and is roughly similar in the hospitalized patient population in the United States. Risk factors of CVST are multifactorial (e.g. prothrombotic state, pregnancy and puerperium, use of oral contraceptives, neoplasms, infections and inflammatory diseases). Early identification and intervention are key in reducing long-term risk of neurological sequelae and disability (5-7). Neuroimaging is considered the gold standard for CVST diagnosis. Magnetic Resonance Venography (MRV), Computed Tomography Venography (CTV), and Cerebral Digital Subtraction Angiography (C-DSA) are the gold standard diagnostic techniques as they visualize the venous anatomy and identify filling defects consistent with thrombosis (8). These imaging modalities are, however, expensive and rely upon specialized equipment and expertise, often not available in resource limited settings. For this reason, non-contrast computed tomography (NCCT) is still the most widely performed first imaging grade in emergency clinical practice given its speed, cost-effective utilization, and accessibility (9). Although NCCT is easily available, it is limited in its ability to diagnose CVST with a high sensitivity and specificity. Traditionally, the hyperdense appearance of thrombosed venous sinuses, also known as the "cord sign," is used as a marker of acute thrombosis, but this finding is qualitative in nature and subject to interobserver variability. Additionally, the lack of direct thrombus visualization on NCCT frequently leads to the need for other imaging to confirm (10). Hounsfield Unit (HU) measurement has been studied as a quantitative parameter of thrombus density to improve diagnostic accuracy. The HU value indicates the radiodensity of the thrombus affected mainly by its composition and primarily by hemoglobin concentration. Studies indicate that hematocrit (Hct) has a significant effect on HU values, which may lead to diagnostic discrepancies (11,12). The HU/Hct ratio has been proposed as an adjunct in the detection of CVST on NCCT. This ratio, expressed as HU on Hct, takes into account physiological differences in blood density, increasing the sensitivity and specificity of NCCT for CVST diagnosis. Owing to its enhanced objectivity, recent studies have demonstrated that elevated HU/Hct ratio is better correlated with the existence of CVST; therefore, it is also a more reliable diagnostic marker especially in locations where more advanced imaging modalities are inaccessible (9). The aim of this study was to address the aforementioned diagnostic challenges of CVST by investigating the impact of HU/Hct ratio on improving the accuracy of NCCT. In particular, this study aims to explore if the combination of hematological parameters improves the diagnostic yield of NCCT, to allow early and more accurate diagnosis of CVST. In addition, the study reports the epidemiological and clinical features of CVST such as predominance in females in reproductive age group and headache as the most common presenting symptom. The basic assumption here is that using the HU/Hct ratio greatly enhances the diagnostic efficacy of NCCT in the condition of CVST, mainly in areas of limited resources where MRV, CTV, and C-DSA are unavailable.

Material and Methods

Study design

This study utilized an analytic observational method with a retrospective cross-sectional research design held at Wahidin Sudirohusodo Hospital in the September - October 2024 period. Data collection was limited to two-month periods, given its retrospective nature, as it incorporated medical records from January 2022 to August 2024. The study was cross-sectional but used this method to manage for time constraints while ensuring the reliability and thoroughness of the data analysis. An a priori sample size of 30 subjects was determined to yield adequate statistical power to conduct correlation analyses.

Sample criteria

All CVST patients confirmed by MRV, CTV, or C-DSA were included in the study population from January 2022 to August 2024. Eligibility criteria based on confirmed diagnosis of CVST and available NCCT based radiological imaging for analysis. In order to minimize the counfounding and ensure the quality of data, exclusion criteria were also applied. Patients who had incomplete medical data, had head trauma or intracranial haemorrhage or calvaria fractures that could potentially affect CT imaging interpretation were excluded from the study. Other exclusion criteria were previous surgery of head, severe anaemia, essential thrombocytosis or contrast agents for other imaging studies in the 3 days preceding the CT scan. Such a thorough selection process provided a homogeneous and representative study population for the assessment of diagnostic and clinical features associated with CVST.

Research procedures

Data were carefully collected from a physician's medical records of patients fulfilling the previously established inclusion and exclusion criteria. Radiological evaluations were based on NCCT, where quantitative parameters were assessed to help with the diagnosis of CVST. In detail, haematological variables included Hct levels and the counts of platelet (Plt) in the system, and the attribution of HU values to the cerebral venous sinuses was through axial NCCT imaging. The HU/Hct ratio was subsequently estimated from the data, a derived parameter we hypothesized could improve imaging-based diagnostic accuracy for CVST (7). The CT imaging protocol was performed using 0.62 mm slice thickness on a 128-slice CT scanner (Siemens SOMATOM Definition AS+) in the axial plane. Hounsfield Unit: These were measured by placing standardized regions of interest (ROI) within thrombosed sinuses, as determined by a neuroradiologist. Measurements were performed to limit variability and to allow reproducibility (8). Details of the study flow are shown below in Figure 1 which outlines the methodology followed for the study.

Data and statistical analysis

Quantitative data, including Hct levels, Plt counts, HU values, and HU/Hct ratios, were subjected to detailed statistical analysis to explore potential relationships and assess diagnostic accuracy. The data were first tested for normality using the Kolmogorov-Smirnov test, appropriate for the sample size exceeding 30 participants. Statistical analyses were conducted using SPSS software version 25.0, with significance determined at a p-value of less than 0.05. For data exhibiting a normal distribution, Pearson's correlation method was applied to evaluate the relationships between variables, whereas Spearman's correlation method was used for non-normally distributed data.

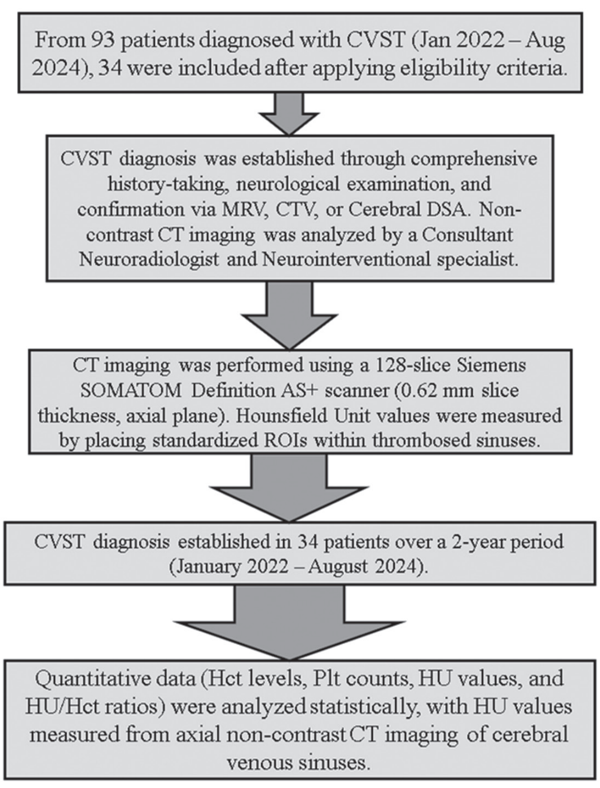

Figure 1. Study flow of Hematocrit, Platelets, and Hounsfield Units of CVST.

These statistical approaches were carefully selected based on the distributional properties of the data, ensuring robust and reliable analysis.

Results

A retrospective cross-sectional study was conducted by analysing the relationship of Hct and Plt count to neuroimaging images with increased attenuation of head NCCT scans in patients with CVST (Figure 2).

Table 1 presents the characteristics of patients diagnosed with CVST from January 2022 to August 2024. After applying the inclusion and exclusion criteria, 34 patients met the study requirements. Initially, 93 patients were diagnosed with CVST before the selection criteria were implemented.

The study sample characteristics include sex, age, Hct levels, Plt count, symptom onset, HU scale, and the HU/Hct ratio. Among the included patients, 6 (17.65%) were male, and 28 (82.35%) were female. The youngest patient was 18 years old, while the oldest was 67 years old, with a mean age of 40 ± 12.70 years. The mean Hct level among the 34 patients was 39.19 ± 4.36. The average symptom onset duration for CVST patients was 14.32 days. The mean HU value among

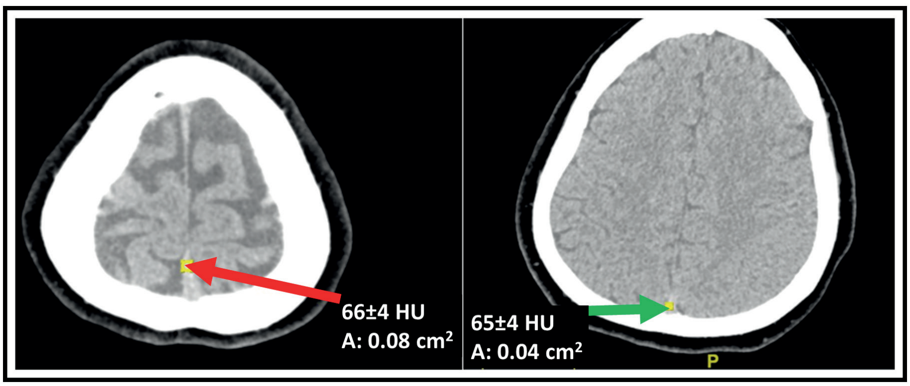

Figure 2. Non-contrast CT imaging of the superior sagittal sinus (red arrow) and confluence of sinuses (green arrow) demonstrating hyperdense thrombosis, with measured Hounsfield unit (HU) values of 66 and 65. The hyper density reflects the presence of an acute thrombus, a characteristic radiological feature of cerebral venous sinus thrombosis (CVST).

Table 1. Characteristics of CVST Patient Population for the Period 2022 – 2024

Variable	Frequency	Mean	Standard Deviation	%
Sample Characteristics				
Sex				
Male	6			17.65
Female	28			82.35
Age	34	40	12.70	100
Onset	34	14.32	11.44	100
Clinical Profile				
Hematocrit/Hct	34	39.19	4.36	100
Platelet/Plt	34	304×10^9/L	54.5	100
Hounsfield Unit/HU	34	68.68	8.06	100
HU/Hct	34	1.76	0.3	100

Table 2. Symptoms and Clinical Signs of CVST Patients

Symptom	n (%)
Headache	28 (84 %)*
Dizziness	12 (35 %)
Seizure	1 (3 %)
Vomit	6 (18 %)
Motor deficit	6 (18 %)
Sensorics Deficit	1 (3 %)
Decreased consciousness	1 (3 %)
Diplopia	2 (6 %)

Table 3. The correlation of Hct and Plt to HU and HU/Hct

	HU		HU/Hct	
Parameter	r value	p value	r value	P value
Hct	-0.255	0.145	-0.667	0.001**
Plt	-0.296	0.089	-0.255	0.145

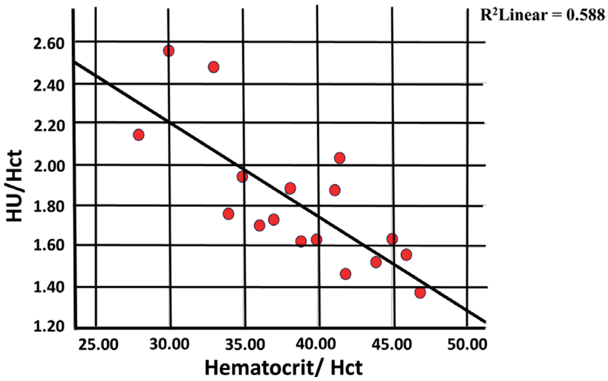

Figure 3. Scatter plot illustrating the correlation between Hct levels and the HU/Hct ratio. The data points demonstrate an inverse relationship, as indicated by a negative correlation coefficient (r = -0.667). This suggests that as Hct levels increase, the HU/Hct ratio tends to decrease. The statistical analysis yielded a p-value of 0.001, confirming that this correlation is statistically significant ($p < 0.05$). The distribution of data points and the regression trend line further emphasize the strength and direction of this negative correlation.

the study subjects was 68.68 ± 8.06. The HU/Hct ratio had a mean value of 1.76 ± 0.3. The mean Plt count of the study subjects was 304×10^9/L.

Table 2 presents the distribution of clinical symptoms observed in 34 patients diagnosed with CVST. Headache was the most frequently reported symptom, occurring in 84% of cases, highlighting its prominence as a primary manifestation of CVST. In contrast, decreased consciousness, seizures, and sensory deficits were the least common symptoms, each observed in only 3% of patients. Furthermore, the data indicate that the majority of CVST patients (more than 50%) presented with a single clinical symptom, whereas fewer than 50% exhibited multiple concurrent symptoms. This distribution underscores the variability in clinical presentation among CVST patients, with some experiencing isolated symptoms while others develop additional neurological deficits.

Table 3 the correlation coefficient displayed with an r value of 0.035 indicates a weak correlation with a positive direction. From the statistical test results, a p value of 0.844 (>0.05) was obtained which means that there is no correlation between Hct and HU. The correlation coefficient displayed with an r value of -0.296 indicates a weak correlation with a negative direction. From the statistical test results, a p value of 0.089 (>0.05) was obtained, which means that there is no correlation between Plt and HU. The correlation coefficient displayed with an r value of -0.667 indicates a weak correlation with a negative direction. From the statistical test results, a p value of 0.001 (<0.05) was obtained, which means that there is a correlation between Hct and HU/Hct. The correlation coefficient displayed with an r value of -0.255 indicates a weak correlation with a negative direction. From the statistical test results, the p value is 0.145 (>0.05) which means there is no correlation between Plt and HU/Hct. Figure 3 show the correlation of Hct and HU/Hct ratio.

Discussion

The results of this study support the role of hyperdense dural venous sinuses as a valuable radiological diagnostic feature of CVST but note that qualitative assessment alone needs to be interpreted with caution due to differing sensitivity. Several studies have previously documented the relationship between effective communication and the healthcare setting: Roland et al., Zaheer et al., and Linn et al. non-contrast CT has reported sensitivities of 63–73% to detect hyperdense sinuses (13-16). Previous literature suggests that while hyper density can point to a diagnosis, its clinical utility is enhanced in combination with an analysis of Hounsfield units (HU) (17). Quantifying objective measurement of HU have enhanced diagnosis accuracy mainly in contrast enhanced CT (Zaheer et al.), and Digge et al. (16,17). This is consistent with previous recommendations that suggest the analysis of HU (Hounsfield unit) as a more reliable indicator of CVST. The demographic analysis in this study showed a striking female predominance (82.35%), which is consistent with the established epidemiological profile of CVST. Previous studies such as Uluduz et al. Coutinho et al., also found a predominance of female sex among patients with CVST, with female patients constituting 75% of described cases (6,16). This gender difference is ascribed to factors like hormones like pregnancy, use of oral contraceptives, and postpartum periods that have been shown to be prominent risk factors for venous thromboembolism, included CVST (17). Despite this, these findings are in line with recent meta-analyses supporting the implication of estrogenic effects in the pathogenesis of CVST. In this study, patients with CVST had a mean age of 40 ± 12.70 years; previous studies also found that CVST primarily occurs in patients younger than 55 years (18). Yaxi Luo et al. reinforced that the peak incidence of CVST is in young adults, with a peak between ages 30 and 41 years, particularly in women of childbearing age (19). The median time from symptom onset to CVST of 14.32 days in this study is also consistent with previous reports from Furie et al., whose data suggested that about half of patients present with CVST from 2 to 30 days after symptom onset (20). This reemphasizes heterogeneity in the progression of CVST symptoms, which calls for alertness for early detection and diagnosis. Headache was the most common symptom reported (84%), consistent with previous studies from Dhanani et al. and Idiculla et al. with headache being the most common presentation owing to the high intracranial pressure of venous outflow obstruction (3,21). The importance of neuroimaging at early phases of CVST is highlighted in a recent systematic review identified headache as the most common symptom in patients with CVST and recommending neuroimaging in patients with unexplained headache if risk factors for venous thrombosis are present. The mean HU value of CVST patients in this study was 68.68 ± 8.06, consistent with the 60–85 HU range previously reported by Buyck et al. and Shaygafnar et al. (7,8,12,22). After all, the mean HU/Hct ratio in this study was 1.76 ± 0.3, similar to the threshold of 1.69 determined in this study by Chetana et al. and the mean value reported by Shaygafnar et al. of 1.42 (22). The HU/Hct ratio is being identified more and more as a reliable parameter for definitive CVST diagnosis as it accounts for hematocrit level variability that would bias absolute HU measurements. This measure has emerged recently in the literature as a complementary tool for reducing the incidence of false positives and increasing the specificity of a CT non-contrast examination. The weak positive correlation between HU and hematocrit ($r = 0.035$, $p = 0.844$) in this study is consistent with previous results reported by Yang et al. and Shaygafnar et al. indicating that, although hematocrit may affect HU, its effect is not statistically significant (22-24). However, Buyck et al. has provided further justification for the need for the HU/Hct ratio to optimize sensitivity toward detection of intravascular hyperdense sinuses, as elevated hematocrit levels have been correlated with false-positive hyperdense sinuses (11). The study's notable negative correlation of hematocrit with the HU/Hct ratio ($r = -0.667$, $p = 0.001$) highlights the need for future studies to investigate the implications of hematocrit variations in CVST imaging variables. We found no significant correlation of platelet count with HU ($r = -0.296$, $p = 0.089$) or HU/Hct ratio ($r = -0.255$, $p = 0.145$), which is in line with the previously reported study in Nurmin et al. suggesting that platelet count does not play a substantial role in thrombus attenuation for patients with CVST (25,26). Similarly, Madieni et al. reported no significant influence of mean platelet volume (MPV) and platelet crit on CVST risk, and only in severe cases platelet distribution width (PDW) was relevant (27). These results support the idea that platelet parameters' utility for predicting CVST in clinical practice may be limited. Though promising, it is important to note several limitations. However, the sample size (n=34) limits the ability to generalize the results and larger multicenter studies are needed to validate the diagnostic utility of the HU/Hct ratio. The lack of a control group of non-CVST patients precludes specificity analyses, preempting the opportunity to distinguish false-positive cases. Moreover, potential confounding factors including hydration status, thrombus size, and duration of thrombosis were not controlled for, which may have different impacts on HU. Previous studies highlighted the impact of hydration status on HU values and warranting further studies (28). The clinical implications of using the HU/Hct ratio in diagnostic algorithms should be further investigated. Due to its capacity to consider the effects of hematocrit, this ratio might potentially present as an accessory parameter for the detection of AMI in emergency environments, where differential diagnosis has to be conducted promptly. Further studies should be conducted to incorporate this metric into CVST standard diagnostic protocols for clinical utility in different patient populations. Moreover, machine learning based algorithms using the HU/Hct ratio could improve automated CVST detection and provide a quantifiable and reproducible tool for clinicians. Some limitations of this study should be recognized. The small sample size (n=34) renders limited generalizability of the data, with a larger multicenter study needed to confirm the diagnostic utility of the HU/Hct ratio. Non-cMvST patients were enrolled in a control group missing, which would have improved specificity analyses. In addition, other confounding factors, including hydration status, thrombus size, and duration of thrombosis, were not controlled for, which may have contributed to the detected HU measurements. Akhavan et al., with the leading one being the influence of hydration status on HU values, which warranted further investigations with respect to this parameter (28). Lastly, from the study's retrospective nature, causal interpretation is limited, thus prospective studies would be needed to confirm how Hct plays a mechanistic role in CVST pathophysiology. In conclusion, this study reinforces the diagnostic utility of the HU/Hct ratio in CVST detection, demonstrating its potential to enhance the accuracy of non-contrast CT imaging. Future research should focus on refining diagnostic thresholds and integrating this parameter into clinical decision-making algorithms to optimize patient outcomes.

Conclusion

The diagnosis of cerebral venous sinus thrombosis (CVST) is known to be difficult using non-contrast CT owing to the variable sensitivity of hyperdense signs. Objective quantitative imaging parameters such as the mean HU value of 68.68 and the HU/Hct ratio of 1.76, can enhance diagnostic accuracy. In particular, the HU/Hct ratio allows discrimination between true and false cases of CVST that are due to differences in haematocrit. CVST occurs primarily in reproductive-aged women, and headache is the most common presenting sign. Although the analysis did not show any significant correlation between haematological parameters such as Hct or platelets and HU values, the significant inverse correlation between Hct and HU/Hct ratio may indicate that haematocrit may also have a role in influencing CT attenuation in patients with CVST. Additional higher sample size and prospective studies could be adopted to better validate the diagnostic performance and the clinical applicability of the HU/Hct ratio in a real-world setting.

Ethic Approval: All research designs were reviewed and approved by the Health Research Ethics Committee of Dr Wahidin Sudirohusodo Hospital – Faculty of Medicine, Hasanuddin University (783/UN4.6.4.5.31/ PP36/2024) on September 25, 2024.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: MYA (Concept, Design, Supervision, Resources, Materials, Data Collection and Processing, Analysis and Interpretation, Literature Search, Writing Manuscript), MFH (Concept, Design, Analysis and Interpretation, Literature Search, Writing Manuscript), and MA, AKB, IH (Concept, Design, Analysis and Interpretation, Literature Search). All authors read and approved the final version of the manuscript.

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