

ORIGINAL ARTICLE

Activated partial thromboplastin time as a predictor of hyperdense thrombus on non-contrast CT in acute cerebral venous sinus thrombosis

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ABSTRACT

Background and Aim: Cerebral venous sinus thrombosis (CVST) is an uncommon yet potentially serious cerebrovascular disorder that demands rapid diagnosis and timely treatment. Non-contrast computed tomography (NCCT) frequently shows increased thrombus attenuation, expressed in Hounsfield Units (HU), which mirrors clot composition. Activated partial thromboplastin time (APTT), a marker reflecting intrinsic coagulation pathway activity, may modulate thrombus formation dynamics. The relationship between APTT and thrombus density in acute CVST, however, has not been well characterized. We aimed to evaluate the association between APTT and HU-based thrombus density in patients with acute CVST.

Methods: We conducted a retrospective cohort study at a tertiary referral center between January 2022 and December 2023. Adult patients with acute CVST who underwent NCCT within 7 days of symptom onset and had APTT measured within 24 hours of imaging were included. Thrombus density was measured in HU using standardized region-of-interest assessment. Spearman's rank correlation was used to examine the APTT–HU relationship, and receiver operating characteristic (ROC) analysis was used to define the optimal APTT threshold for predicting higher thrombus density (HU \geq 70).



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Results: Ninety-three patients were analyzed. A moderate negative correlation was observed between APTT and thrombus density ($r = -0.408$, $p < 0.001$). ROC analysis identified an APTT threshold of ≤ 21.6 seconds for predicting $HU \geq 70$, with sensitivity 72.9%, specificity 91.1%, and an area under the curve of 0.769 ($p < 0.001$).

Conclusion: Shorter APTT values are associated with denser thrombi on NCCT in acute CVST. Combining coagulation parameters with quantitative CT measurement may strengthen early evaluation and clinical decision-making, especially in centers with limited access to advanced venous imaging. (www.actabiomedica.it)

Key words: cerebral venous sinus thrombosis, activated partial thromboplastin time, hounsfield unit, thrombus density, coagulation biomarkers

Introduction

Cerebral venous sinus thrombosis (CVST) is a comparatively uncommon but potentially life-threatening cerebrovascular disorder that mainly affects young adults, with a clear female predominance (1). Unlike arterial stroke, CVST tends to present in highly variable ways, ranging from isolated headache to focal neurological deficits, seizures, and depressed consciousness. Because the clinical picture is rarely uniform, early recognition is critical to avoid venous infarction and intracranial hemorrhage (2). Magnetic resonance venography is generally considered the imaging reference standard, yet in busy emergency departments non-contrast computed tomography (NCCT) remains the most accessible and most frequently performed initial imaging modality (3,4). On NCCT, a hyperdense sinus is among the earliest radiological clues of acute CVST. The attenuation of the thrombus, quantified in Hounsfield Units (HU), reflects clot composition, including red blood cell concentration and fibrin density (5). Earlier work suggested that thrombus density is influenced by hematocrit, clot age, and the structural pattern of the fibrin network. As such, HU measurement has been proposed as an imaging biomarker that can add pathophysiological insight beyond simple visual interpretation (6,7). Activated partial thromboplastin time (APTT) is a routinely available laboratory parameter that reflects activity in the intrinsic and common coagulation pathways. Variations in coagulation status influence how thrombi form, the architecture of the fibrin meshwork, and clot stability (8).

A hypercoagulable state typically favors the development of denser, more organized fibrin networks, while prolonged coagulation times often correspond to altered clot composition (9,10). Despite this biological plausibility, data exploring the link between routine coagulation profiles and imaging-based thrombus density in CVST remain limited. Understanding how APTT relates to thrombus density may help integrate laboratory and radiological biomarkers in CVST evaluation. The present study set out to investigate the correlation between APTT and HU-based thrombus density on NCCT in patients with acute CVST. We hypothesized that intrinsic coagulation activity, as reflected by APTT, would be associated with measurable variation in thrombus density on initial imaging.

Materials and Methods

Study design and setting

This was a single-center, retrospective cohort study conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia, a tertiary referral and academic teaching center. We reviewed medical records and radiological imaging data of patients diagnosed with acute CVST between 1 January 2022 and 31 December 2023. All eligible cases were identified through hospital electronic medical records and radiology databases. Only patients who underwent NCCT during the acute phase of presentation were considered. Laboratory data, including APTT, were retrieved from records obtained

at initial evaluation. The protocol was approved by the Ethics Committee of Hasanuddin University Faculty of Medicine and Dr. Wahidin Sudirohusodo General Hospital (Approval No. 535/UN4.6.4.5.31/PP36/2026, dated 17 April 2026). Given the retrospective design and the use of de-identified data, the requirement for written informed consent was waived.

Participants

Adult patients (≥ 18 years) diagnosed with CVST during the study period were screened. The diagnosis of CVST was confirmed by NCCT and/or magnetic resonance imaging with magnetic resonance venography (MRI/MRV), as documented in medical records. To ensure inclusion during the acute phase of thrombosis, only patients who underwent NCCT within 7 days of symptom onset were considered eligible. Patients were included when APTT was measured within 24 hours of CT imaging and when complete clinical, laboratory, and imaging data were available. Patients were excluded if they had received anticoagulant therapy before initial laboratory evaluation, had concomitant arterial ischemic stroke, primary intracranial hemorrhage unrelated to venous thrombosis, traumatic brain injury, aneurysm, or arteriovenous malformation. Cases with poor-quality CT images that prevented reliable HU measurement were also excluded. Patients with severe hepatic dysfunction or known congenital coagulation disorders that could meaningfully alter APTT were not analyzed. All eligible patients during the study window were included consecutively.

Data collection

Demographic and clinical data age, sex, and time from symptom onset to imaging were extracted from electronic medical records. APTT values were recorded in seconds as continuous variables, and only measurements obtained within 24 hours of NCCT were retained to keep laboratory and radiological data temporally consistent. Radiological data were retrieved from the hospital Picture Archiving and Communication System (PACS). NCCT studies were reviewed both for confirmation of CVST and for quantitative thrombus density assessment. All clinical, laboratory,

and imaging variables were de-identified and entered into a structured database before statistical analysis.

Imaging analysis

NCCT images were retrieved from the hospital PACS and analyzed with a standardized DICOM viewer. Thrombus density was quantified by measuring HU within the affected venous sinus. A circular region of interest (ROI) was placed manually within the most hyperdense portion of the thrombosed sinus, with care to avoid adjacent bone, calcifications, or partial-volume artifacts. Whenever feasible, measurements were taken from three contiguous axial slices at the level of maximal thrombus visualization, and the mean HU was used for analysis. ROI size was kept consistent across patients to limit variability. All imaging assessments were performed by a board-certified neuroradiologist with experience in neurovascular imaging. The reader was blinded to all laboratory results, including APTT, at the time of HU measurement. Only CT scans of adequate quality, with clear visualization of the involved sinus, were included.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics. Continuous variables were summarized as mean \pm standard deviation (SD) or median (interquartile range, IQR), depending on distribution; categorical variables were reported as frequencies and percentages. Normality of continuous variables was checked with the Shapiro–Wilk test. Because APTT and HU were not normally distributed, the correlation between APTT and HU was examined using Spearman's rank correlation. Receiver operating characteristic (ROC) curve analysis was performed to identify the optimal APTT threshold for predicting higher thrombus density. In the absence of an established HU cutoff for CVST, HU values were dichotomized at the sample median (≥ 70 HU vs < 70 HU). The area under the curve (AUC) was used to quantify discriminative ability, and the Youden index was used to select the optimal cutoff. Sensitivity, specificity, positive and negative predictive values (PPV/NPV), and positive and negative likelihood ratios (LR+ and LR-) were also computed. All tests were two-tailed; a p -value < 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 93 patients with confirmed acute CVST were analyzed. Demographic and baseline clinical features are summarized in Table 1.

The median age was 41 years (range 18–68), reflecting the typical age distribution of CVST. Female patients made up 74.2% of the cohort, consistent with the well-known female predominance of this disorder. Median thrombus density on NCCT was 70 HU (range 53–88 HU). Median APTT was 22.4 seconds (range 18.8–33.6 seconds). The distribution of HU and APTT values showed sufficient variability to support the subsequent correlation and discriminative analyses.

Correlation analysis

Spearman's rank correlation was used to assess the relationship between APTT and HU. Results are presented in Table 2.

Spearman's correlation showed a statistically significant moderate negative correlation between APTT and thrombus density ($r = -0.408$, $p < 0.001$). Shorter APTT values were associated with higher thrombus

density on NCCT, while longer APTT values tended to correspond with lower HU values.

To illustrate the relationship between APTT and HU more visually, a scatter plot with a fitted regression line is shown in Figure 1.

As shown in Figure 1, the scatter plot displays a clear downward trend, reflecting the inverse relationship between APTT and HU. Although individual data points show variability, the fitted regression line confirms a consistent negative association. This visual finding supports the statistical results, suggesting that increased intrinsic coagulation activity, reflected by shorter APTT values, may correspond to denser thrombus composition in acute CVST.

ROC curve analysis

To further evaluate the discriminative ability of APTT in identifying patients with denser thrombi, ROC curve analysis was performed. APTT showed acceptable diagnostic performance for identifying HU ≥ 70 . The optimal cutoff was ≤ 21.6 seconds, with a sensitivity of 72.9% and a specificity of 91.1%. The AUC was 0.769 ($p < 0.001$), reflecting good discriminative ability. The positive likelihood ratio (LR+) was 8.20 and the negative likelihood ratio (LR-) was 0.30. The ROC curve is shown in Figure 2.

The ROC curve clearly separates from the reference diagonal, supporting the discriminative capacity of APTT. An AUC of 0.769 suggests acceptable accuracy in distinguishing patients with higher versus lower thrombus density. The high specificity indicates that shorter APTT values are particularly useful for identifying patients with denser thrombi, while the sensitivity reflects a reasonable ability to detect most high-density cases.

Discussion

Our analysis showed a statistically significant moderate negative correlation between APTT and thrombus density on NCCT in patients with acute CVST. Shorter APTT values were linked to higher HU measurements, indicating denser thrombi. ROC analysis further showed that an APTT threshold of ≤ 21.6 seconds had acceptable discriminative ability for

Table 1. Baseline characteristics of the study population (n = 93).

Variable	Value
Age (years), mean \pm SD	40.77 \pm 12.53 (median 41; range 18–68)
Sex, n (%)	
Male	24 (25.8%)
Female	69 (74.2%)
Thrombus density (HU), mean \pm SD	69.88 \pm 7.66 (median 70; range 53–88)
APTT (seconds), mean \pm SD	23.01 \pm 4.29 (median 22.4; range 18.8–33.6)

Table 2. Correlation between APTT and thrombus density (HU).

Variables	Correlation Coefficient (r)	p-value
APTT and HU	-0.408	<0.001

*p-value calculated using Spearman's rank correlation test.

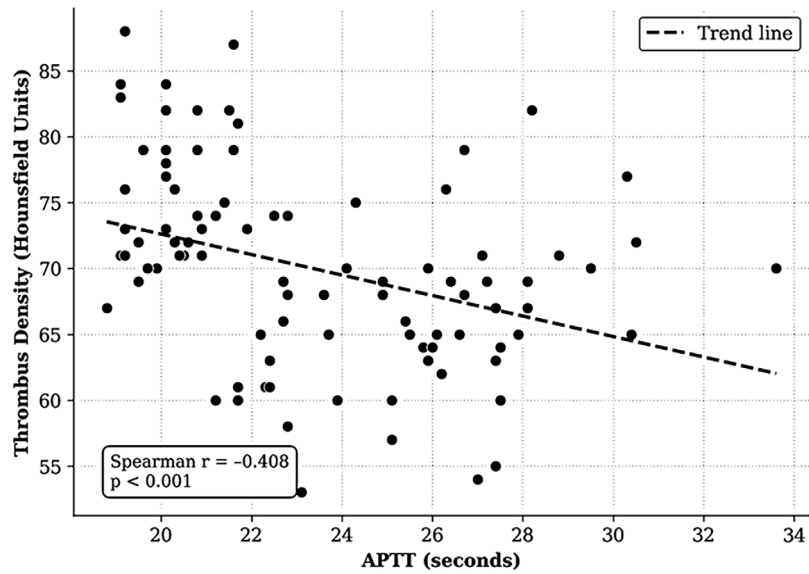


Figure 1. Scatter plot of activated partial thromboplastin time (APTT, seconds) and thrombus density (Hounsfield Units, HU) in patients with acute CVST. The dashed line represents the linear trend.

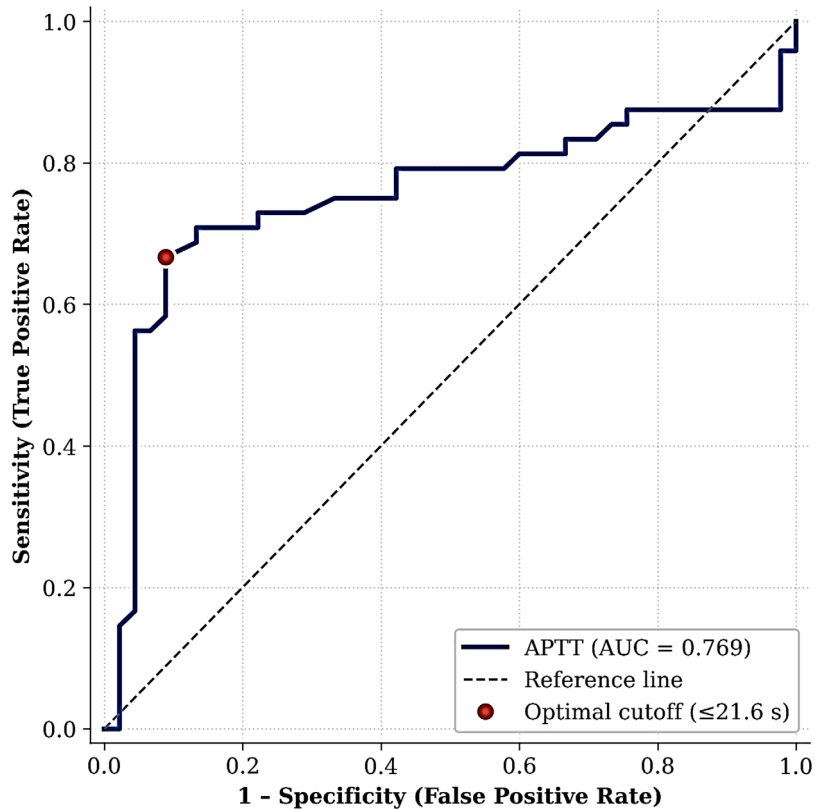
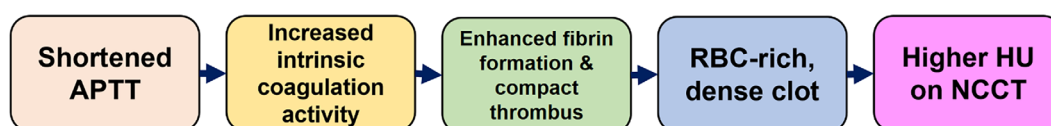


Figure 2. Receiver operating characteristic (ROC) curve of APTT for predicting higher thrombus density ($HU \geq 70$). The dot indicates the optimal cutoff value at $APTT \leq 21.6$ seconds.

predicting $HU \geq 70$, with an AUC of 0.769. Together, these findings suggest a meaningful association between intrinsic coagulation activity and imaging-based clot characteristics in the acute phase of CVST (11,12). The observed inverse relationship between APTT and thrombus density is biologically plausible. Shortened APTT can reflect heightened activity of the intrinsic coagulation pathway, which promotes more rapid fibrin generation and stabilization of clot architecture. A hypercoagulable state may favor the formation of compact, red blood cell-rich thrombi, which are known to show higher attenuation on CT (13,14). During the acute phase, increased hemoglobin concentration and dense fibrin networks both contribute to elevated HU values (15). The association we observed therefore supports the biological plausibility of routine laboratory coagulation markers correlating with structural properties of venous thrombi. The proposed pathway linking intrinsic coagulation activity and thrombus attenuation is illustrated in Figure 3.

This schematic shows the proposed biological pathway underlying the inverse association between APTT and thrombus density measured on NCCT. Shortened APTT may reflect higher intrinsic pathway activity, leading to enhanced fibrin generation and the formation of more compact, red blood cell-rich thrombi (11,16). Higher hemoglobin concentration within the thrombus likely contributes to greater attenuation, which translates into higher HU values on CT (15,17). This conceptual model is grounded in our findings and the current understanding of thrombus formation in acute CVST. Earlier work has documented the value of HU measurements in detecting acute CVST, with higher HU values often pointing to recent thrombus formation (18,19). Most prior studies, however, focused mainly on imaging features,

while the link between routine laboratory coagulation parameters and thrombus attenuation has received less attention. Studies on coagulation markers have largely concentrated on arterial stroke or risk stratification rather than on direct clot density assessment (20). To our knowledge, data specifically exploring the association between APTT and quantitative HU measurements in CVST remain scarce. Our findings therefore add novel evidence integrating laboratory and imaging biomarkers in venous stroke. From a clinical standpoint, combining APTT and NCCT findings may offer practical value, particularly in emergency settings where MRI or MRV is not immediately available (21,22). The high specificity observed here suggests that shorter APTT values may help identify patients with denser thrombi, who are likely in the acute phase of CVST. Although APTT alone cannot replace imaging confirmation, its association with thrombus density may strengthen early risk assessment and support clinical decision-making in resource-limited settings (13,15). Our study has several strengths. First, it included a relatively adequate sample size for a single-center cohort of patients with acute CVST. Second, only patients evaluated within the acute phase (≤ 7 days from symptom onset) were included, reducing variability related to thrombus evolution. Third, thrombus density was assessed quantitatively using standardized HU measurements rather than relying on qualitative reading alone. Finally, the combined use of correlation and ROC analyses provided both associative and discriminative perspectives on the APTT–HU relationship (2,17). Several limitations should be acknowledged. The retrospective design carries the risk of selection bias and limits causal inference. The single-center setting may also affect generalizability to other populations. Although we standardized HU



Inverse association: lower APTT values reflect heightened intrinsic coagulation activity, leading to denser, Red blood cell-enriched thrombi visible as higher Hounsfield Unit values on non-contrast CT.

Figure 3. Proposed conceptual mechanism linking intrinsic coagulation activity to thrombus density in acute cerebral venous sinus thrombosis. (APTT: Activated partial thromboplastin time; RBC: Red blood cell; HU: Hounsfield unit; NCCT: Non contrast computed tomography)

measurement, interobserver variability was not formally assessed. Hematocrit, which can influence CT attenuation, was not included in the primary analysis (15,23). Finally, the use of the median HU as a dichotomization threshold for ROC analysis was exploratory and may not represent a universally applicable cutoff. Future studies are warranted to validate these findings in prospective, multicenter cohorts to improve external generalizability. Adding additional laboratory parameters such as hematocrit-adjusted HU ratios or comprehensive hypercoagulability profiles may help clarify the biological mechanisms underlying thrombus density variation (15,24). Longitudinal studies linking APTT, thrombus density, and clinically relevant outcomes such as recanalization and functional recovery would also offer valuable insights into the prognostic role of these combined imaging and laboratory biomarkers.

Conclusion

Activated partial thromboplastin time is inversely associated with thrombus density on non-contrast CT in patients with acute cerebral venous sinus thrombosis. Shorter APTT values were associated with higher Hounsfield Unit measurements and showed acceptable discriminative ability for identifying patients with denser thrombi. These findings support a meaningful link between intrinsic coagulation activity and imaging-based clot characteristics. Combining laboratory coagulation parameters with quantitative CT assessment may strengthen early evaluation of CVST, particularly in settings where advanced imaging is limited.

Ethical Considerations: The study was reviewed and approved by the Health Research Ethics Committee, Faculty of Medicine, Hasanuddin University, in conjunction with Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia (Approval No. 535/UN4.6.4.5.31/PP36/2026, issued 17 April 2026). Because of the retrospective design and the use of anonymized records, written informed consent was not required. All patient data were handled confidentially and de-identified before analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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.

Author Contributions: Conceptualization, ABJ, MYA, and MA; Methodology, DCH, MYA and MA; Software, MYA; Validation, MYA, and AAZ; Formal analysis, MYA, ABJ, MA and AAZ; Investigation, MYA and ABJ; Resources, ABJ, MYA, MA and AAZ; Data Curation, ABJ, and MYA; Writing—Original Draft Preparation, ABJ, and MYA; Writing Review and Editing, MYA; Visualization, ABJ, MYA, MA, AAZ, MIB and DW; Supervision, MYA, MA and AAZ; Project Administration, ABJ. All authors have read and agreed to the published version of the manuscript.

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List of Abbreviations:

CVST: Cerebral venous sinus thrombosis
 NCCT: Non-contrast computed tomography
 HU: Hounsfield units
 APTT: Activated partial thromboplastin time
 MRI: Magnetic resonance imaging
 MRV: Magnetic resonance venography
 PACS: Picture Archiving and Communication System
 ROI: Region of interest
 ROC: Receiver operating characteristic

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