



Diagnostic Sensitivity of Unenhanced CT for Cerebral Venous Thrombosis: Can Clot Density Measurement Replace CT Venogram?

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Abstract

Objectives Cerebral venous sinus thrombosis is an important cause of stroke in young adults. Noncontrast-enhanced CT head (NECT) is almost always the first investigation. Our objectives were as follows:

1. How accurately does venous sinus density on NECT predict the presence of clot on CT venogram (CTV)?
2. Whether repeated measurements changed the confidence?
3. How many venous sinus thrombus would be missed if we do not do a CTV?
4. Can clot density measurement replace CTV?

Methods Multicenter case–control study was designed with data from seven hospitals. Inclusion criteria: all CT and magnetic resonance imaging venograms with a prior NECT, performed between 1.1.2018 and 31.12.2018 (12 months), were included. Hounsfield unit (HU) values were calculated at the site of highest density on the NECT. Logistic regression analysis was performed using STATA.

Result Two-hundred seventy-seven cases met the criteria with 33 positive cerebral venous thrombosis (density on NECT 60–92 HU) and 244 negative examinations (density on NECT 31–68 HU). Area under the curve for average clot density on NECT was 0.9984.

Conclusion We found a strong relationship between sinus density on NECT and outcome of CTV. Repeating density measurements did not add any predictive value or changed outcome.

Advances in Knowledge Density 70 HU or higher on NECT always resulted in a positive CTV but would miss a fifth of the positives. Cutoff at 60 HU would not miss any but result in significant false positives. An efficient option could be to limit CTV to sinus densities 60 to 70 HU only. However, a larger study would be required for such change in practice.

Keywords

- CT
- density
- head
- unenhanced
- venogram

Introduction

Cerebral venous sinus thrombosis is an important cause of stroke in young adults with a female preponderance¹ accounting for 0.5 to 1.0% of unselected stroke admissions.² Noncontrast-enhanced computed tomographic scan (NECT) of head is almost always the first imaging offered to patients with suspected stroke or in acute headache in most hospitals.³

The classic finding of sinus thrombosis on unenhanced CT images is a hyperattenuating thrombus in an occluded sinus (hyperdense dural sinus or delta sign)⁴

Earlier studies reported poor sensitivity of NECT in identifying such thrombus.^{2,5} However, more recent studies have shown more promise in specificity of clot density measurement with a range to proposed density cutoff values, and statistically significant density differences between non-thrombosed and thrombosed cerebral veins.^{6–9}

With ever increasing demand of emergency CT heads in and out of hours and time pressured reporting, it would be useful to have a simple reproducible parameter that could predict the presence of cerebral venous sinus thrombus. We retrospectively evaluated the current diagnostic sensitivity of NECT head for cerebral venous sinus thrombosis and assess the CT attenuation of the thrombosed vein on the NECT in patients with confirmed cerebral venous sinus thrombosis.

The aim of the study was to confirm how accurately the Hounsfield unit (HU) value of the venous sinus measured on NECT predict the outcome of the subsequent venogram. A further aim of the study was to assess whether repeated measurements of clot density changed the confidence on nonenhanced CT and to assess how many venous sinus thrombus would be missed if we choose not to do a CT venogram based on clot density on NECT? We wanted to assess if clot density measurement can indeed replace CT venogram.

Methodology

A multicenter case–control study was designed with retrospective data collection by trainees under supervision of a consultant radiologist, as an early project (phase 2 roll out) of the Royal College of Radiologists, Radiology Academic Network for Trainees committee of Merseyside. Data was collected from seven hospitals in the region covering two university hospitals (Hospital A [Toshiba Aquilion Prime], Hospital B [Siemens Somatom Definition Flash and Toshiba Aquilion Prime]), two District General Hospital's (Hospital C [GE Medical Systems Revolution Evo], Hospital D [Philips Ingenuity, Canon Medical Systems Aquilion One]) and, three specialty-specific hospitals (Hospital E [Siemens Somatom Force], Hospital F [Toshiba Aquilion One, Canon Medical Systems Aquilion Lightning], and Hospital G [Philips Ingenuity]).

Inclusion criteria were all CT and magnetic resonance imaging (MRI) venograms that *had* a prior noncontrast CT performed, performed between January 2018 1, and December 31, 2018 over a period of 12 months (all the noncontrast

CTs were performed within 72 hours of the venogram apart from two cases where the venogram was performed on day 7 and day 9 post-NECT). Noncontrast CTs were performed at all sites using standard trauma brain protocol helical images with soft tissue and bone algorithm image reconstruction. There were vendor-specific variations in basic helical CT head protocol across sites that have been presented for information to demonstrate the variation in modern CT technology (–Table 1).

Exclusion criteria were known chronic and repeat CT venograms, post-surgical, and post-traumatic CT venograms and scans degraded severely by artefact. Venogram studies without a prior noncontrast CT head were also excluded.

For all the positive cases of cerebral venous sinus thrombosis, HU values were calculated at the site of highest perceived density on the NECT corresponding to the site of thrombosis confirmed on the later CT/MR venogram studies. Three separate measurements were performed and recorded (one by the trainee and twice by the supervising consultant on separate occasions) on all positive cases corresponding to the perceived highest densities. On all occasions, the density was measured using a standard circle region of interest tool on Carestream PACS version 12.2 on standard reporting workstations, with the average density recorded (–Figs. 1 and 2).

For all the negative cases, HU values were calculated at the torcula/confluence of the venous sinuses or perceived area of highest density on the scan, if brighter than torcula (e.g., superior sagittal sinus or sigmoid sinus).

Results

A total of 277 cases of CT or MRI venogram were identified across all sites that had a prior NECT head performed; there were 33 positive cases of cerebral venous thrombosis (CVT) and 244 negative examinations. The patients with a positive CT venogram study ranged from 16 to 79 years in age (average 50.2 years) with 13 males and 20 females in the group. The patients with a negative study ranged from 4 to 91 years in age (average 40.4 years) with 65 male and 179 females in this group.

The sinus attenuation measured on the positive scans ranged from 60 HU to 92 HU with a mean of 73.6 HU. The sinus attenuation measured on the negative scans ranged from 31 HU to 68 HU with a mean of 49 HU. Standard deviation was 6.7 HU for both groups.

Statistical Analysis

There were three questions: A. How accurately does venous sinus density on NECT predict the presence of clot on CT venogram/outcome of the CT venogram? B. Does multiple measurements of sinus density on NECT predict the outcome any better than one single measurement in the positive cases? And C. How many venous sinus thrombus would be missed if we choose not to do a CT venogram based on the measurement of clot density on NECT?

A logistic regression analysis was performed using STATA with robust standard errors; with the variable (clot density) coded 1-0 with 1 indicating a positive CT venogram showing

Table 1 Variations in scanners across multiple sites (anonymized)

	A	B	C	D	E	F	G	H
Body part	Head	Brain	Head	Brain	Head	Brain	Head	Brain
Scan option	Helical	Helical	Helical	Helical	Helical	Helical	Helical	Helical
Slice thickness	1.0	1.0	1.0	1.0	0.625	0.5	0.5	1.0
Spacing between slices		0.75			0.625			0.5
Kvp	120	120	120	120	120	120	120	100
Data collection diameter	240	500	500	500	320	320	320	500
Reconstruction diameter	220	250	254	231	250	220	247.50	214
Gantry detector tilt	0	0	0	0	0	0	0	0
Exposure time	750	1252	1000	1000	1460	1000	750	1056
X-ray tube current	238	214	128	158	154	200	217	124
Filter type	Medium	IMR	Flat	Flat	Head	Small	Medium	UB
Focal spot	0.9/0.8		1.2	1.2	1.2	0.9/0.7	0.9/0.8	
Convolution Kernel	✓	✓	✓	✓	✓	✓	✓	✓
Revolution time	0.75	0.5			0.8	1	0.75	0.4
Single collimation width	0.5	0.625	0.6	0.6	0.625	0.5	0.5	0.625
Total collimation width	20	40	19.2	12	20	20	20	40
Table feed per rotation	12.5	25.6	10.5	7.2	10.6	12.5	12.5	25.5
Spiral pitch factor	0.625	0.4	0.55	0.6	0.53	0.625	0.625	0.39
Number of images	862	841	370	399	916	701	2680	857
Samples per pixel	1	1	1	1	1	1	1	1
Photometric interpretation	Monochrome2	Monochrome2	Monochrome2	Monochrome2	Monochrome2	Monochrome2	Monochrome2	Monochrome2
Rows	512	512	512	512	512	512	512	512
Columns	512	512	512	512	512	512	512	512
Pixel spacing	0.43/0.43	0.49/0.49	0.49/0.49	0.45/0.45	0.48/0.48	0.43/0.43	0.48/0.48	0.42/0.42
Window center	40	30	35	35	35	35	35	40
Window width	80	75	100	100	85	85	80	80

Note: Our aim is not to compare standardized vendor-specific protocols but to display the variation in scanning protocols/parameters across multiple sites.

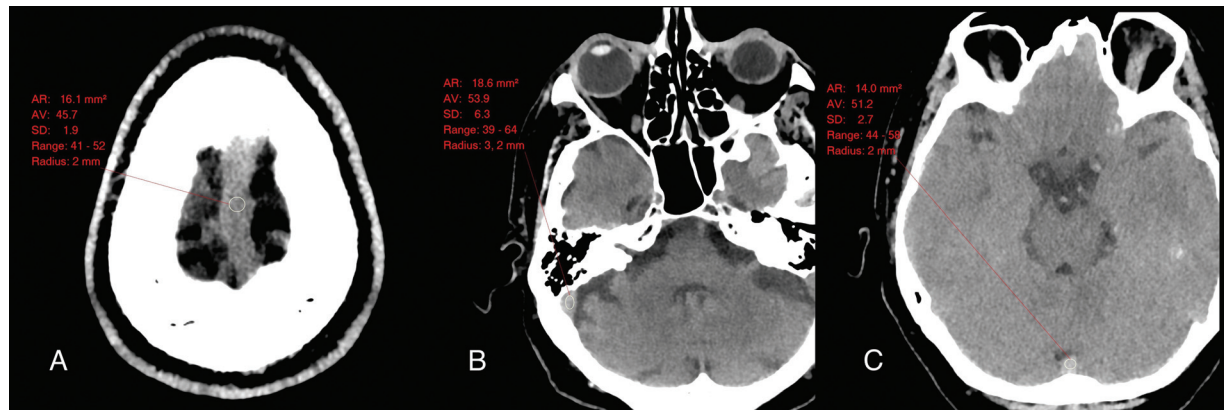


Fig. 1 Axial unenhanced computed tomography (CT) images of three different patients with negative CT venogram, showing density assessment with ROI (region of interest) tool at the superior sagittal sinus (A), right sigmoid sinus (B), and at the level of the torcula (C).

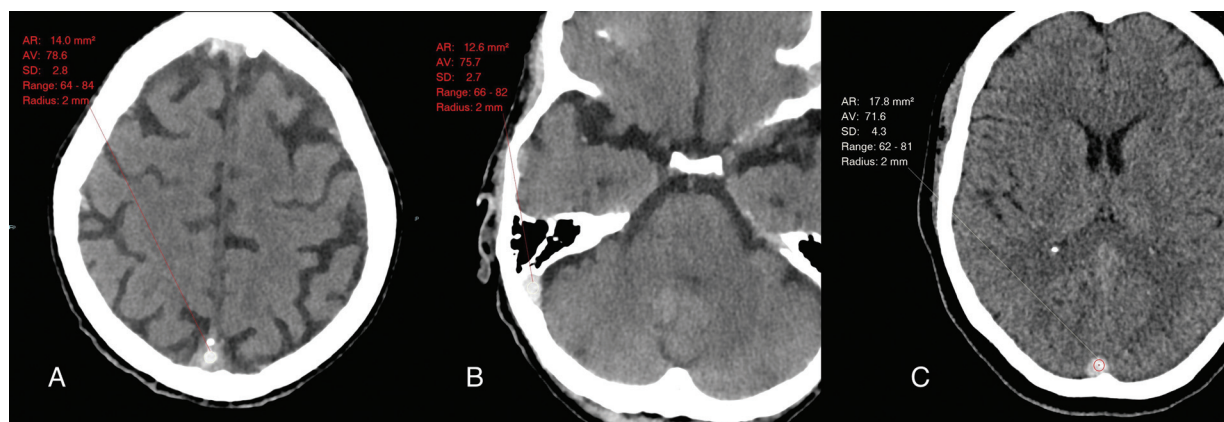
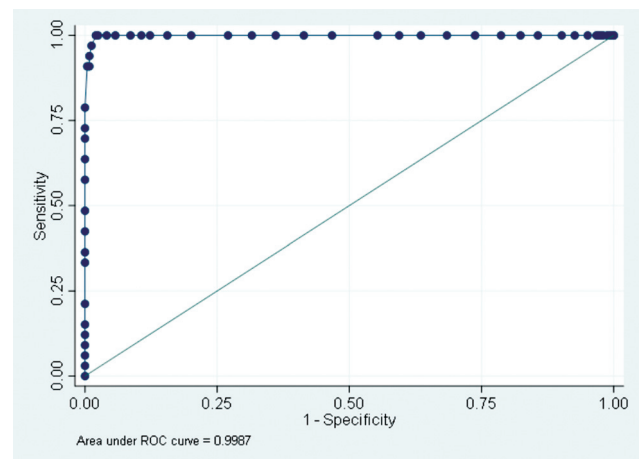


Fig. 2 Axial unenhanced computed tomography (CT) images of three different patients with positive CT venogram, showing density assessment with ROI (region of interest) tool at the superior sagittal sinus (A), right sigmoid sinus (B), and at the level of the torcula (C).

thrombus and 0 when the CT venogram was negative for thrombus. The logistic command reports the results in terms of an odds ratio. The results for the first density measurement for patients with a proven venous thrombus in the subsequent CT venogram (positive cases) was compared with the result for the average of the three density measurements. There was a very strong relationship between clot density on the NECT and the CT venogram with an odds ratio of 2.166 for the first density measurement and an odds ratio of 2.016 for the average density measurement. Receiver operating characteristic (ROC) curve was used to assess how well the density measurements of the NECT predicted the outcome of the CT venogram.

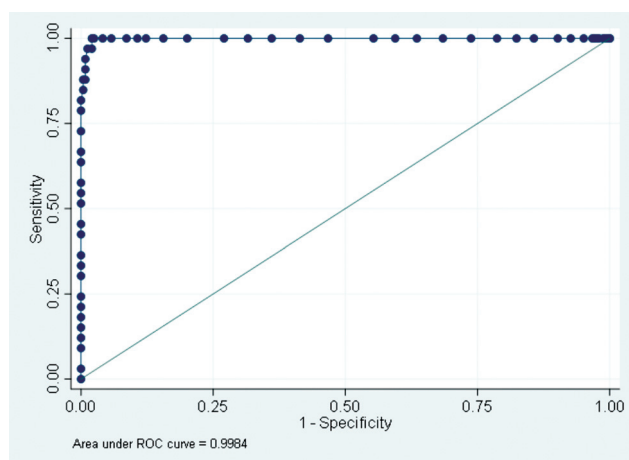
The first density measurement performed marginally better than the average density measurement with the area under the curve (AUC) being 0.9987 (95% confidence interval [CI]: 0.9968–1.000) for the first density measurement compared to 0.9984 (95% CI: 0.9961–1.000) for the average (**Graphs 1–3**). The difference was not statistically significant ($p=0.514$). The second (AUC of 0.9958; 95% CI: 0.9911–1.000) and third (AUC of 0.9972; 95% CI: 0.9939–1.000) density measurements on the NECT performed a little worse than the average (AUC of 0.9984; 95% CI: 0.9961–1.000); however, in neither case was the difference statisti-



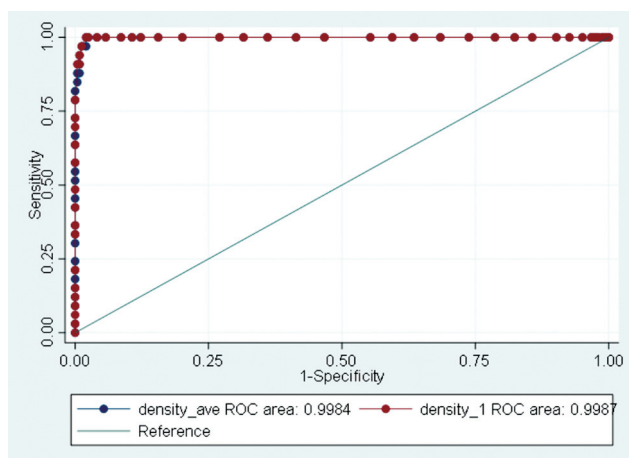
Graph 1 Area under receiver operating characteristic (ROC) curve for the first-density measurement.

cally significant ($p=0.1154$ and $p=0.2137$ for the second and thirds measurements, respectively)

So, in summary we found a very strong relationship between density measurements on NECT and the outcome of the CT venogram test, which is in agreement with findings of various other papers as detailed in the discussion section.



Graph 2 Area under receiver operating characteristic (ROC) curve for the average-density measurement.



Graph 3 Area under receiver operating characteristic (ROC) curve for the first-density measurement compared with average-density measurement.

We found that there was no evidence that repeating the density measurements on the NECT added any significant predictive value or changed the outcome.

In order to answer the third question, we calculated the percentage of true positives for multiple “density cut offs” based on the NECT. This calculation was performed using the average density measurement on the NECT and we have also included 95% confidence intervals using the Binomial exact calculation (**Graph 4**; **Table 2**). In this sample, a density score of 70 or above perfectly predicted a positive Venogram test, even when the density measurements are repeated (this is true because none of the normal cases ever recorded a clot density of 70 or more). However, if we used 70 as the cutoff for diagnosing venous sinus thrombosis, we would only have identified 26 of the 33 positive cases and miss the remaining 7 cases. Put another way, a density score cutoff of 70 would have resulted in zero false positives but about 20% of true positives being missed. On the other hand, if we used a clot density of 65 on the NECT as cutoff, we would have identified 32 of the 33 positive cases but would have falsely diagnosed

three patients. Finally, using a clot density of 60 on the NECT as cutoff would have resulted in correctly identifying all 33 of the positive cases of venous sinus thrombosis (i.e., none of the true positives would be missed) but at the expense of falsely diagnosing 14 patients.

Discussion

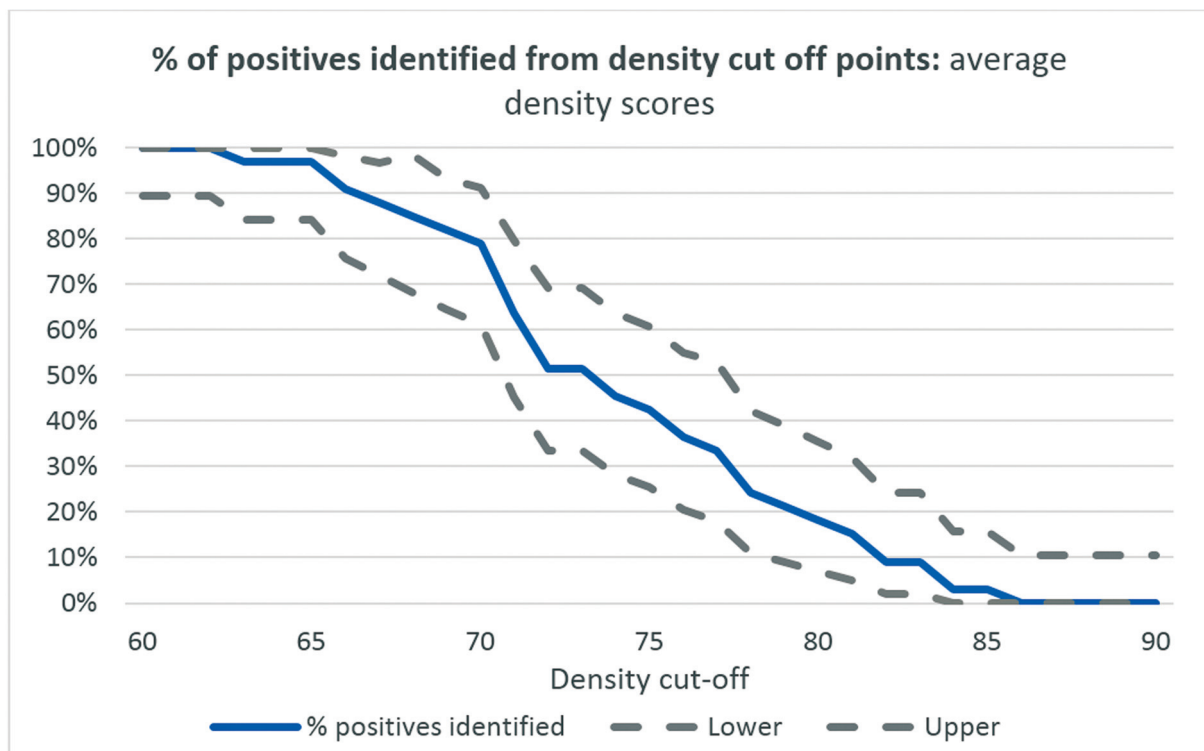
Cerebral venous sinus thrombosis is an important cause of stroke in young adults with a female preponderance (1) accounting for 0.5 to 1.0% of unselected stroke admissions (2). They present with a wide range of symptoms, some nonspecific, ranging from minor headache to life threatening ones, depending on the sinuses involved, duration of occlusion, extent of brain parenchymal injury, and the effect on intracranial pressure. (3) Suspicion of cerebral venous sinus thrombosis requires prompt neuroimaging, which almost always is a noncontrast CT head in the first instance. Early diagnosis is critical for early therapeutic intervention.

The classic finding of sinus thrombosis on unenhanced CT images is a hyperattenuating thrombus in an occluded sinus (hyperdense dural sinus or delta sign)⁴ However, it is well recognized that CT can be read normal in up to third of such patients and even if abnormal, they are not specific. The European Stroke Organization (ESO) guidelines advocate contrast MRI or CT for diagnosis of suspected cerebral venous sinus thrombosis.¹⁰ CT venogram has an excellent diagnostic performance CT venography with a sensitivity of 95% and specificity of 91%.¹¹ More recent studies have shown sensitivity and specificity as high as 100% (95% CI: 88–100 for sensitivity and 95–100 for specificity)¹²

Having said that, NECT of head is almost always the first imaging offered to patients with suspected stroke or in acute headache in most hospitals.³ With that in mind several studies have looked at the performance of NECT in diagnosing cerebral venous sinus thrombosis. The reported accuracy ranges from a sensitivity of 50 to 100% and a specificity of 83 to 100%.^{7,12–15} A reason for such wide variation is variation in technologies, image acquisition, advances in image reconstruction/image quality, not to mention the various causes of false-positive and false-negative interpretation.¹⁶

Recently, a meta-analysis summarizing the diagnostic accuracy of CT (noncontrast-and contrast-enhanced) for CVT has been published. Overall, CT was found to have a reasonable diagnostic accuracy with a pooled sensitivity of 79% (95% CI: 76–82%) and a pooled specificity of 90% (95% CI: 89–91%).

Over the last decade, several studies have looked at the attenuation of a thrombosed cerebral venous sinus and nonthrombosed venous sinus on unenhanced CT, showing statistically significant difference in attenuation between thrombosed and nonthrombosed sinuses ($p < 0.0001$)^{6–9,17–19} and ($p < 0.05$).^{15,20} ROC analysis and AUC have been used to predict cutoff values for the attenuation of thrombus. Statistically, a range of cutoffs have been suggested ranging from 58 HU in a study exclusively on pediatric population¹⁹ and 60 to 70 HU in other age groups.^{6–9,13,15,17,18,20–24} At the start of the last decade, a



Graph 4 Percentage of positive cases of cerebral venous sinus thrombus identified from density cutoff points based on average density score on the nonenhanced computed tomography (To be read with ►Table 2).

Table 2 Number of true positive cases of venous sinus thrombosis identified at different cutoff points based on our density measurement on noncontrast CT head, that is, in essence, the number of cases of venous sinus thrombosis missed if used the “cutoffs” to diagnose thrombus, and chose not to do a confirmatory CT venogram

Density cutoff points based on measurement on NECT	Percentage of positive cases of venous sinus thrombosis identified	Percentage of cases of venous sinus thrombosis missed	95% Confidence intervals
60	100.0%	0.0%	89.4–100.0%
65	97.0%	3.0%	84.2–99.9%
70	78.8%	21.2%	61.1–91.0%
75	42.4%	57.6%	25.5–60.8%
80	18.2%	81.8%	7.0–35.5%
85	3.0%	97.0%	0.1–15.8%

Abbreviation: NECT, nonenhanced computed tomography.

study looking at eight patients had suggested a cutoff of 70 HU as being 100% specific, as none of normal patients had a sinus attenuation 70 or more.²⁴ Then a multicentric retrospective study on CVT probability based on visual assessment of spontaneous hyperdensity of cerebral venous system, performed by four blinded radiologists, with 14 positive patients with CVT showed an AUC of 0.992 and density of more than 70 HU only seen in thrombosed segments bar horizontal section of superior sagittal sinus.¹⁵ More recently, in a study looking at 36 patients with CVT, ROC curve analysis of HU showed an AUC of 1.0 with cutoff of 70 HU being 92% sensitive and 100% specific.²⁰ Whereas a similar study looking at 114 patients, with an AUC of 0.82

(0.72–0.93) suggested a cutoff of 60 HU as 94% specific but only 70% sensitive.²² A further recent study looking at 35 patients with CVT suggested 60.4 HU was the best optimal cutoff with AUC of 0.918 (0.848–0.962) to be 100% specific, although 71.4% sensitive.¹⁸ Whereas another study looking at 48 patients suggested a cutoff of 63 HU to be 88% specific but only 52% sensitive, based on ROC analysis.⁸

It is recognized that the attenuation of blood and hematocrit bears a linear relationship.²⁴ Based on that several studies have assessed the diagnostic accuracy of attenuation of the clot and attenuation compared to the hematocrit (H:H ratio). There is no significant increase in sensitivity (64–95%) or specificity (54–100%) compared to clot density

alone^{7,9,13,20–22,25} hence, for the purpose of our study, we simply assessed the clot density (to be routinely useful, in most acute scenarios it will not be feasible for the reporting radiologist to determine H:H ratio during a busy on call shift)

Our study shows that the density of the cerebral venous sinus reliably predicts the outcome of the CT venogram and there is no evidence that repeating the density measurements on the NECT added any significant predictive value or changed the outcome. Further, in this sample, a density score of 70 HU or above perfectly predicted a positive Venogram test, even when the density measurements are repeated. However, if we use 70 HU as the cutoff to diagnose cerebral venous sinus thrombosis, and not perform a CT venogram, we will miss 21.2% of the positive cases (7 out of 33 of our positive cases of cerebral venous sinus thrombosis). If, on the other hand, we used 60 HU as the cutoff for density on the NECT, we will not miss any of the true cases of venous sinus thrombosis, but we will have some false positives. One option could be to limit CT venogram to those patients who have a perceived highest venous sinus density of 60 to 70 HU (i.e., considering all cases with value above 70 HU as positive and all cases with values less than 60 HU as negative). This will certainly improve efficiency by significantly reducing the number of unnecessary scans (88%, i.e., 244/277 negative studies in our cohort). It will also reduce total scanning burden, cost, save scanner time, radiation exposure, and improve resource utilization, particularly in view of ever-increasing demand on imaging. However, since the number of positive cases are low in our study group, it will need a much larger multicenter data collection to change practice.

Limitations

A primary limitation of the study design is its retrospective nature; there is bias introduced by the fact that the authors knew where to measure the maximum density on the positive scans based on the subsequent CT venogram. To compensate, as mentioned in the methodology, the authors measured the density of the sinus on the NECTs at the perceived brightest location, not just the torcula or superior sagittal sinus. Another limitation was that the authors did not look at the hematocrit of the patient or the whether the patients were on any treatment like anticoagulants. The authors did not look at venobasilar ratio and difference in attenuation difference between normal and abnormal sinus in the same patient. However, the authors believe that the above, possibly, imitates real time on call reporting scenario as closely as possible (allowing for the artificial setup of a study of this nature); since such details may not be available to the reporting general radiologist prospectively. A limitation in statistical evaluation is the low number of true positive cases of 33.

Conclusion

Cerebral venous sinus thrombosis is an important cause of stroke in young adults. Noncontrast-enhanced CT scan of

head is almost always the first imaging offered to most patients presenting with stroke or headache. With ever increasing demand of emergency CT heads in and out of hours, it would be useful to have a simple reproducible parameter that could predict the presence of cerebral venous sinus thrombus. In agreement with multiple previous papers, we found that in our patient cohort, measured attenuation value of sinus on NECT was indeed a simple and reproducible indicator of presence or absence of venous sinus thrombosis. In addition, we found no evidence that repeating the density measurements on the NECT added any significant predictive value or changed the outcome.

We also demonstrated the trade-off between missing true cases of thrombus and false diagnoses from imposing a particular density score cutoff value before performing a confirmatory CT venogram. In our sample, a density score of 70 or above would have perfectly predicted a positive venogram test. However, using 70 HU as a cutoff would have meant missing a fifth of the positive cases. A lower cutoff point of 60 HU would have meant that all positive cases were correctly diagnosed but would have resulted in a significant number of false positives. A more efficient option could be to limit CT venogram to those patients who have a perceived highest venous sinus density of 60 to 70 HU. This has the potential to reduce scanning burden, cost, radiation exposure and improve efficiency, resource utilization, particularly in view of ever-increasing demand on imaging, in particular out of hours. However, considering the low number of positive cases in our study group, a larger multicenter study would be required to provide greater confidence for such a change in practice.

Funding

None.

Conflict of Interest

None declared.

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