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Original Article

Radiology Section

Comparative Analysis of Diagnostic Sensitivity of Magnetic Resonance Susceptibility Sequence with Non Enhanced Computed Tomography and Magnetic Resonance Gradient Sequence in Early Haemorrhagic Transformation of Cerebral Infarction- A Cohort Study

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ABSTRACT

Introduction: Susceptibility Weighted Imaging (SWI) is a Magnetic Resonance Imaging (MRI) sequence aiming to enhance contrast in MR imaging. SWI is considered to be sensitive in detecting even minute amount of haemorrhage, putting in consideration that early detection of haemorrhage inside acute infarction restricts the use of thrombolytic drugs and minimise the development of large haematoma that need to be evacuated surgically thus, improving the prognosis of the patient.

Aim: To evaluate and compare the diagnostic sensitivity of MR SWI with Non Enhanced Computed Tomography (NECT) and Magnetic Resonance Gradient Recalled Echo (MR GRE) sequence in detecting the early Haemorrhagic Transformation (HT) of cerebral infarction.

Materials and Methods: This was a cohort study conducted from July 2018 to October 2019 on 45 patients referred to the Radiology Department of the institute with imaging findings suggestive of stroke. Apart from the NECT brain conducted on 128 slice machine and routine stroke protocol, MR SWI was also performed. MRI study was performed on 1.5 Tesla MRI scanner with a eight channel Navigator radiofrequency coil. A follow-up CT was done after 48 hours. The images obtained were subjected to radiological analysis and interpretation. Statistical Package for Social Sciences (SPSS) version 22, descriptive analysis was carried out by calculating mean±standard deviation, frequency and proportion. The collected data was compared with each other, using Chi-square test and Fisher's-exact test, correlated using Spearman Correlation test.

Results: Total 45 patients (mean age: 56 years, 31 males and 14 females) were included in the study. The diagnostic sensitivity of MR SWI in detecting early HT was high 97.5% compared to 45.0% of NECT and 82.5% of MR GRE. However, the specificity of MR SWI (33.3%) and that of MR GRE (33.33%) were very low as compared to NECT (66.67%), which had a higher specificity in detection of HT. There was a weak positive correlation between surface area of bleed in GRE and surface area of bleed in SWI (Spearman's RHO correlation 0.324, p-value 0.030).

Conclusion: MR SWI had high diagnostic sensitivity in detecting HT earlier than NECT and MR GRE sequence and hence, it could play a crucial role in the treatment of patients. One of the most dreaded complications of cerebral infarction-intracerebral haemorrhage could be prevented and thus, prognosis of the patient improves. Hence, MR SWI sequence should be added to routine stroke protocol, however it cannot replace NECT, since the specificity of NECT is high compared to MR SWI.

Keywords: Contrast, Detection, Enhance, Haemorrhagic infarct, Stroke, Susceptibility weighted imaging

INTRODUCTION

Stroke occurs due to disturbance in blood supply to the brain owing to either an ischaemic or haemorrhagic insult. Stroke is broadly classified into ischaemic and haemorrhagic based on aetiology [1]. Ischaemic stroke may lead to a complication called HT which is spectrum of brain haemorrhages related to ischemia. HT can present in any one of the forms namely, Haemorrhagic Infarction (HI) and Parenchymal Haemorrhage (PH). HI and PH are two types of HT. The HI is further classified into two types depending on position of petechiae as HI-1 and HI-2. In HI-1 the petechiae are noticed along margins of infarction whereas in HI-2 they are found inside infarcted area. PH is also classified into two types PH-1 and PH-2 depending on extent of haematoma observed in infarction. In PH-1 haematoma is found in less than 30% of infarcted area whereas in PH-2 it is found in more than 30% of infarcted area [2]. PH is better predicted by using Tmax >14s in CT perfusion imaging.

Haemorrhagic transformation is difficult to be detected by clinical symptoms because of their similarity with ischaemic stroke symptoms. Risk factors for HT of cerebral infarction include size of ischaemic stroke, area of ischaemic stroke, myocardial infarction, atrial fibrillation, diabetes, arterial hypertension, and therapeutic thrombolytic treatment [3]. Early detection of HT is important for selection of suitable treatment option because in addition to various causes related to ischemia, HT can also be caused due to thrombolytic treatment generally administered for an ischaemic stroke. Detection of HT will aid in selecting alternate courses of treatment and use intervention measures for treatment of HT. Hence, it is crucial to detect and if possible, predict HT in ischaemic stroke patients for effective treatment and management of stroke symptoms [1].

Neuroimaging is the main diagnostic method used for detection of HT in ischaemic stroke patients [4]. But there are some difficulties encountered in using standard MRI using GRE sequence and

NECT imaging in early detection of HT. In early haemorrhage, there is increased presence of intracellular oxyhaemoglobin which has no paramagnetic effect thereby, rendering diagnosis of HT difficult using conventional imaging techniques. New MRI technique using Susceptibility Weighted Sequencing (SWI) has been proved to be more accurate in detection of HT [5]. MR SWI also helps in accurate detection of cerebral microbleeds which are not detected by NECT. NECT has a low sensitivity for detecting cerebral microbleeds whose presence is considered as a contraindication for administration of thrombolytic therapy according to the present guidelines for thrombolytic therapy [6].

Previous studies have shown a correlation between existence of cerebral microbleeds and intracranial haemorrhage in ischaemic stroke patients which proved irrelevant by recent studies. Recent studies have shown that presence of cerebral microbleeds alone cannot be considered as a predictor of HT, their number, location and measures of functional outcome also must be taken into consideration [7]. MR SWI sequencing can be used to detect cerebral microbleeds, their number and size with high diagnostic sensitivity compared to other conventional MR sequences and NECT. Hence, objective of the present study was to evaluate and compare the diagnostic sensitivity of MR SWI, NECT and MR GRE in detecting the early HT of cerebral infarction.

MATERIALS AND METHODS

This was a cohort study conducted on 45 patients in the Department of Radiodiagnosis, Chettinad Hospital and Research Institute, Kelambakkam, Kanchipuram district, Tamil Nadu, India, from July 2018 to October 2019 after obtaining the Ethics Committee approval (No-116/IHEC/06-18) from the institute.

Inclusion criteria: Patients referred to Radiology Department with clinical suspicion of stroke within 12 hours of onset of symptoms (Hemiparesis/hemiplegia, slurring of speech, facial weakness or headache) and those who had imaging findings (NECT and MRI Brain) suggestive of cerebral infarction were included in the study after obtaining the written informed consent.

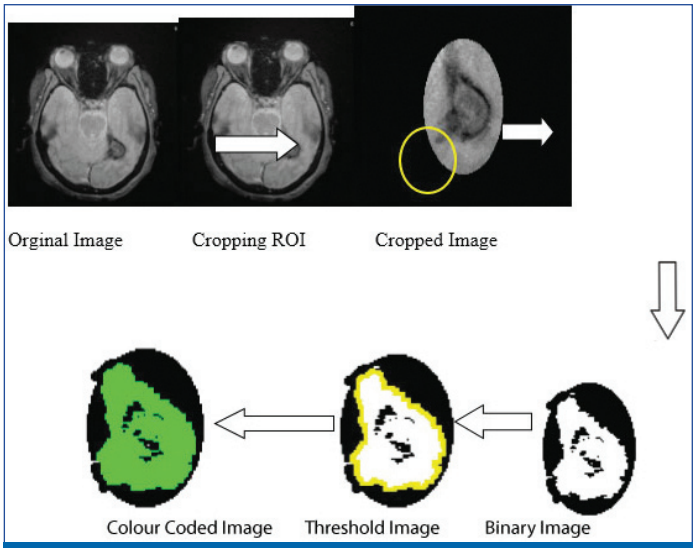
Exclusion criteria: Patients with cerebral infarcts without signs of HT in imaging, those with venous infarcts, claustrophobic or with metal implants, pacemakers and cochlear implants and female patients who were pregnant were excluded from the study.

Sample size calculation: The sample size was calculated according to following formula:

$$n = \frac{Z^2_{1-\alpha/2}\, p(1-p)}{d^2}$$

Where, P=Expected proportion (p=0.217), d=absolute precision (d=12), 1-alpha/2=desired confidence interval (95). Keeping all concerned values, required sample size came to 45.

NECT and routine MRI stroke protocol was done along with SWI sequences. A follow-up CT was done after 48 hours. For NECT study, CT PHILIPS INGENUITY- 128 SLICE machine was used. For MRI study, 1.5 Tesla SIGNA GE HDxt MRI scanner was used to scan all patients with a eight channel NV (NAVIGATOR) radiofrequency coil. HT, as assessed by follow-up CT was considered as primary outcome variable. HT as assessed by initial CT, SWI and GRE were considered as screening tests. Areas of bleed were measured from the slices. The images obtained were cropped and converted into the binary image and then threshold image to measure the area and the measurements were calibrated with MRI work station and converted to square centimetre (sq cm) [Table/Fig-1].



[Table/Fig-1]: GRE-process of areas measurement.

STATISTICAL ANALYSIS

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Categorical variables were compared with each other, using Chi-square test/Fisher's-Exact test (If the overall sample size was <20 or if the expected number in any one of the cells is <5, Fisher's-exact test was used). The p-value <0.05 to be considered significant. Surface area of bleed in MR SWI and MR GRE sequences were calculated using image J software.

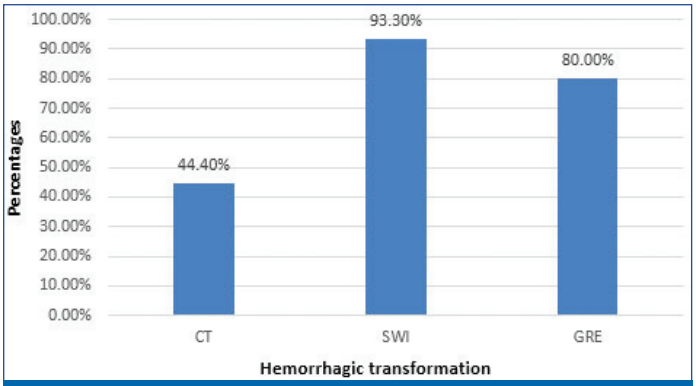
RESULTS

Out of total 45 patients, 10 patients (22.2%) were between 40-49 years, 18 patients (40%) were between 50-59 years and 17 patients (37.8%) were above 60 years. Mean age was found to be 56.73±7.26 years. A total of 31 patients (68.9%) were male and 14 patients (31.1%) were female. In this study, Middle Cerebral Artery territory (MCA) was the most commonly involved territory. A total of 22 patients (48.9%) had MCA territory infarct. Anterior Cerebral Artery (ACA) infarct was the next with 8 patients (17.8%) giving the presentation. Total 5 patients (11.1%) had Posterior Cerebral Artery (PCA) infarct. These formed the majority of infarcts of the complete study sample.

The authors assessed the various lobes involved in ischaemic infarct and found out that 9 patients (20%) had infarcts in the fronto-parietal lobe and it was the most commonly affected lobe. Frontal lobe and temporal lobe were affected in 8 patients (17.7%) and 5 patients (11.1%), respectively.

In the present study, the authors assessed early HT with a baseline CT, MR SWI and MR GRE sequences. In the baseline CT taken immediately after the patient presented to the hospital, early HT of ischaemic infarct was detected in 20 (44.4%) cases, whereas it was absent in 25 (55.5%) cases. MR SWI taken immediately following CT showed the presence of early HT in 42 (93.3 %) cases, whereas it was absent in 3 (6.7%) cases. The MR GRE sequence taken at the same time revealed early HT in 36 (80%) cases whereas it was absent in 9 (20%) cases [Table/Fig-2]. A follow-up CT was taken to confirm the presence of HT.

In the present study, we predicted the validity of baseline CT in diagnosing early HT of stroke and found the sensitivity of CT to be 46.1% and specificity to be 66.6% with diagnostic accuracy of 49%. We predicted the validity of SWI in diagnosing early HT of stroke and found the sensitivity of MR SWI to be 97.4% and specificity was 33.3% with diagnostic accuracy of 88.8% [Table/Fig-3]. The p-value obtained using Chi-square test was also significant (p-value <0.05) [Table/Fig-4].



[Table/Fig-2]: Comparison of detection of HT in various radiological modalities.
CT: Computed tomography; SWI: Susceptibity weighted imaging; GRE: Gradient recalled echo

Parameter	Value	95% CI	
		Lower	Upper
1. Baseline CT			
Sensitivity	46.15%	30.09%	62.82%
Specificity	66.67%	22.28%	95.67%
Diagnostic accuracy	48.89%	33.70%	64.23%
2. MR-SWI			
Sensitivity	97.44%	86.52%	99.94%
Specificity	33.33%	4.33%	77.72%
Diagnostic accuracy	88.89%	75.95%	96.29%
3. MR-GRE			
Sensitivity	82.05%	66.47%	92.46%
Specificity	33.33%	4.33%	77.72%
Diagnostic accuracy	75.56%	60.46%	87.12%

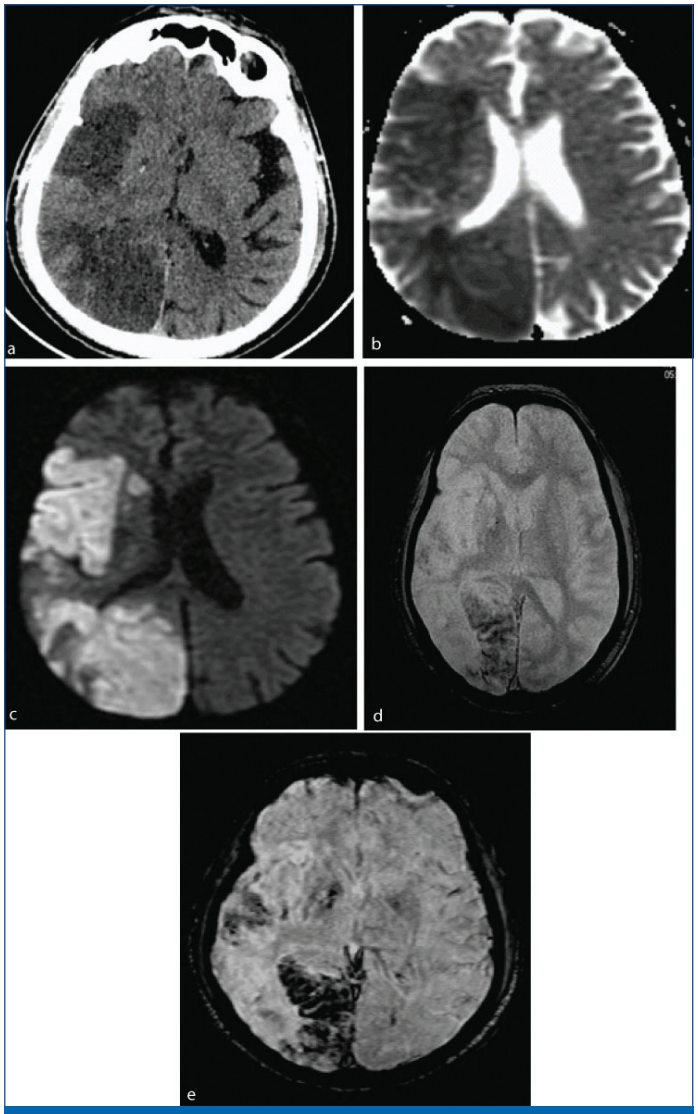
[Table/Fig-3]: Sensitivity, specificity and diagnostic accuracy of all three tests.

Haemorrhagic Transformation (HT) as per SWI	Haemorrhagic Transformation (HT) as per follow-up CT		Chi square	p-value
	Present (n=39)	Absent (n=6)		
Present	38 (97.44%)	4 (66.67%)	7.912	**0.005**
Absent	1 (2.56%)	2 (33.33%)		

[Table/Fig-4]: Comparison of early Haemorrhagic Transformation (HT) frequency between SWI and follow-up CT done after two days: p-value calculated using Chi-square test: bold p-value denotes significance.

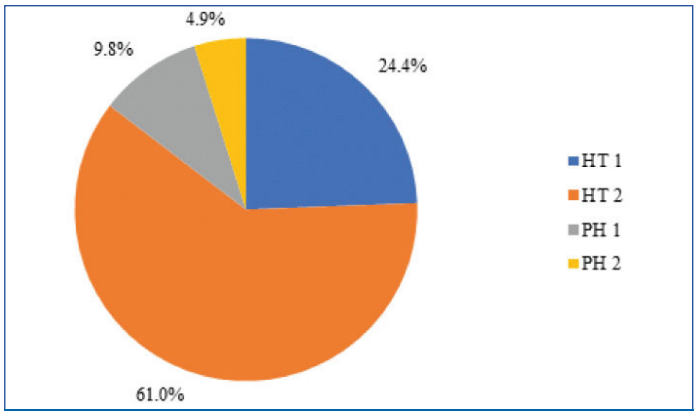
From the present study, the sensitivity and specificity of MR GRE sequence in predicting the early HT was found to be 82.05% and 33.33%, respectively. Sample case of initial CT showed infarct without any haemorrhage whereas MR GRE and SWI showed blooming suggestive of haemorrhage in the same patient are shown [Table/Fig-5].

The hypothesis in this study was that the SWI sequence was able to diagnose the HT earlier than the initial NECT, and thus it affected important decisions which predicted the prognosis of the patient, like whether antithrombotics can be administered to the patient or not. To confirm the diagnosis of early HT, for all cases a follow-up was done. Thus, the follow-up CT confirmed the presence or absence of HT and was taken as the primary outcome variable. In four cases, small areas of blooming were seen with the infarcted area in SWI and were not seen in follow-up CT and it was due to old haemosiderin deposition. SWI and GRE have this disadvantage of not being able to differentiate between acute and chronic haemorrhage. In the rest of the cases, all cases which showed blooming in SWI and GRE were confirmed by the follow-up CT. In the present study, we found out that 10 (24.4%) patients presented with type 1 HT, 25 patients (61.0%) presented with type 2 HT, 4 patients (9.8 %) had presented with type 1 PH and 2 patients (4.9%) with type 2 PH [Table/Fig-6].



[Table/Fig-5]: A 57-year-old male had come with complaints of left hemiparesis and facial weakness. Initially NECT was done followed by MRI Brain: (a) NECT brain showed large geographical hypodense area with loss of grey white matter differentiation in Right MCA and PCA territory. No evidence of haemorrhagic changes was seen within the infarct; (b) ADC; (c) DWI: both (b) and (c) showed large geographical T2 hyper-intense areas with restricted diffusion noted in right MCA and PCA territory. (d) MR GRE (e) MR SWI: both (d) and (e) sequence showed areas of blooming noted in right temporal and occipital lobes-representing haemorrhagic changes within infarct. HT within the infarct was not seen in the initial NECT.
MRI: Magnetic resonance imaging; MCA: Middle cerebral artery; PCA: Posterior cerebral artery; ADC: Apparent diffusion co-effecient; DWI: Diffusion weighted imaging

The early detection of HT by SWI sequence had an impact on the treatment plan and prognosis of the patient, as in present study, in 25 patients (55.6%), whereas there was no impact in treatment in 20 patients (44.4%). The authors found that the mean surface area of bleed calculated in SWI was 3308.86 sq mm and mean surface area of bleed calculated in GRE was 2769.05 sq mm. There was a



[Table/Fig-6]: Pie chart of type of HT in the study population (n=41).
Not applicable to 4 members; HT: Haemorrhagic transformation; PH: Parenchymal haematoma

weak positive correlation between surface area of bleed in GRE and surface area of bleed in SWI (Spearman's RHO correlation 0.324, p-value 0.030) [Table/Fig-7].

Parameter	Mean±SD	95% CI		Spearman's RHO correlation(r)	p-value
		Lower	Upper		
Surface area of bleed in GRE	2769.05±1796.61	2216.13	3321.96	0.324	**0.030**
Surface area of bleed in SWI	3308.86±2030.64	2691.49	3926.23		

[Table/Fig-7]: Descriptive analysis of surface area of bleed in GRE and SWI in study population (N=45) and their correlation by Pearson's Correlation test. Bold p-value indicates significant value.

DISCUSSION

As intracerebral haemorrhage was one of the most dreaded complications of ischaemic infarct, this early diagnosis of HT affected the treatment and thus, the prognosis of the patient. In a prospective study conducted by Elnekeidy AE et al., where out of 46 patients with cerebral infarction, 10 patients had ischaemic infarct with HT, four patients had infarction without HT but with small microbleeds, three patients with haematomas and one patient had venous infarct [8]. It was found in this study that the initial CT detected HT in 2 patients (4.3%), whereas SWI detected HT in 10 patients (21.7%). Large haematoma was seen both in CT and MR SWI. These findings are well-correlating with this study where early HT was detected by the baseline CT in 20 patients (44.4%) whereas SWI detected early HT in 42 cases (93.3%). Also, it was proved in that study that four cases with microbleeds were not seen in CT, but were detected by SWI.

In the present study, the patients were followed-up to find out whether the high diagnostic sensitivity of MR SWI in diagnosing the early HT of stroke, had an impact on treatment. It was found that in patients with early HT which was detected in SWI before NECT had an impact on treatment. In patients with type 1 HT (small tiny petechial haemorrhages), patients were safely treated with full dose antiplatelet and antithrombotic drugs. In patients with type 2 HT and with worsening clinical symptoms were managed by lowest dose antiplatelet and antithrombotic drugs. These patients were continuously monitored in ICU and their blood pressures were kept in control with close follow-up. Patients with type 2 PH were not administered any antiplatelet and antithrombotic drugs and were in intensive care units with control of high blood pressure. One of the patients had worsening symptoms and hence, the haematoma was surgically evacuated. Thus, the authors from this study concluded that early diagnosis of HT had an impact on treatment of 25 (55.6%) patients. These results were also in accordance with the study by Elnekeidy AE et al., where early diagnosis of HT of cerebral infarction by SWI before CT impacted the treatment and follow-up and in turn prognosis of the patients [8].

In a study conducted by Hermier M and Nighoghossian N, in assessing the contribution of SWI compared with stroke, it was seen that sensitivity of SWI in diagnosing HT of stroke was 100% [9]. This finding is in accordance with this study which also showed the diagnostic sensitivity of MR SWI sequence to be 97.4%. Also, in the study by Hermier M and Nighoghossian N, it was concluded that the most feared complication of ischaemic stroke which was intracerebral haemorrhage can be diagnosed earlier than CT and also with high diagnostic sensitivity [9].

In a study conducted by Truelson T et al., which was a retrospective study in assessing the reliability of SWI sequence in detection of haemorrhage in acute stroke compared with other conventional MR sequences and CT, it was found that out of the 38 patients who presented with infarct, SWI detected haemorrhages in 16 cases, compared to eight cases with Spin Echo (SE) T2, seven cases with Fluid Attenuated Inversion Recovery (FLAIR), and only five cases with CT [10]. It was concluded from the study that SWI proved to be a new powerful tool to detect haemorrhage compared with conventional MR sequences and NECT. The findings from this study correlate well with the present study where we have found the sensitivity of SWI in detecting early haemorrhagic stroke is greater than NECT.

In the study conducted by Wycliffe ND et al., it was concluded that SWI had greater sensitivity over GRE in detecting HT type 1 and HT type 2 [11]. This was in concordance with our study where, nine cases of early HT (Type 1 and Type 2) were not detected in MR GRE sequence, but were detected in MR SWI sequence. These findings are in concordance with the present study which showed that diagnostic sensitivity of MR SWI (97.5%) was greater than MR GRE (82%).

Limitation(s)

Since histopathological correlation was not available for the study, hence, the specificity and sensitivity calculated from the study is not absolute and hence, further studies on animal models is recommended. SWI and GRE cannot differentiate between acute and chronic haemorrhage.

CONCLUSION(S)

The authors concluded that the diagnostic sensitivity of SWI in diagnosing early HT was higher than the sensitivity of initial NECT and MR GRE sequence. Also it was found that the MR SWI sequence calculated the mean surface area better than MR GRE sequence. The diagnostic sensitivity of SWI in detecting HT earlier than NECT was statistically significant. However, the specificity of the initial NECT was found to be significantly higher than SWI. SWI is a very sensitive sequence in detecting early HT and hence, recommend inclusion of MR SWI sequence in routine stroke protocol. Since, the sensitivity of MR SWI sequence is higher than MR GRE, the authors concluded that MR SWI can replace MR GRE in stroke protocol. This study indicated that timely detection of HT plays a crucial role in altering the treatment and thus prognosis and quality of life of the patient improves. However, since the specificity of NECT is significantly higher than MR SWI and MR GRE, hence MR SWI sequence cannot replace NECT and we have to perform both NECT and MR SWI in evaluating HT of stroke. MR SWI sequence has the advantage of detecting HT earlier than NECT and hence alters the treatment course and improved the prognosis of the patient.

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