

Synergistic role of susceptibility-weighted imaging with diffusion-weighted imaging and magnetic resonance angiography in the evaluation of acute arterial stroke

Journal of International Medical Research

2019, Vol. 47(5) 2166–2176

© The Author(s) 2019

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/0300060519840909

journals.sagepub.com/home/imr



Santosh PV Rai¹ , Pulastya Sanyal¹,
Shivananda Pai², Basavaprabhu Achappa³,
Deepak Madi³ and Pavan MR³

Abstract

Objective: This study was performed to investigate whether diffusion-weighted imaging (DWI) and susceptibility-weighted imaging (SWI) are more effective than conventional imaging modalities for evaluation of stroke and selection of candidates for thrombolytic therapy.

Methods: Eighty patients who presented within 12 hours of onset of symptoms of brain ischemia underwent 1.5T magnetic resonance imaging. DWI and SWI were compared with conventional sequences (T1, T2, and fluid-attenuated inversion recovery [FLAIR]) and time-of-flight magnetic resonance angiography (TOF-MRA) to assess factors that affect stroke management and prognosis.

Results: The volume of brain tissue showing hyperintensity was significantly greater than that showing diffusion restriction in patients with a >6-hour symptom onset. The hypointensity sign

¹Department of Radiodiagnosis, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India

²Department of Neurology, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India

³Department of Internal Medicine, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India

Corresponding author:

Santosh Rai, Department of Radiodiagnosis, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, 203 Light House Hill Road, Manipal, Karnataka 575001, India.

Email: santosh.rai@manipal.edu



(susceptibility sign) on SWI showed a sensitivity of 66.7%, specificity of 87.5%, positive predictive value of 88.9, and negative predictive value of 63.6 compared with TOF-MRA. Micro-hemorrhagic foci were significantly associated with 27-mL infarcts on DWI (sensitivity, 71.4%; specificity, 85.0%). Patients with DWI–SWI mismatch showed better responses to thrombolytics. FLAIR–DWI mismatch helped to assess the time of stroke onset.

Conclusion: DWI and SWI should be part of the routine imaging protocol in patients with acute stroke and serve as a decision-making tool for selection of patients for thrombolytic therapy.

Keywords

Acute stroke, susceptibility-weighted imaging, diffusion-weighted imaging, magnetic resonance imaging, thrombolytic therapy, brain ischemia

Date received: 20 September 2018; accepted: 8 March 2019

Introduction

Advances in magnetic resonance imaging (MRI) neuroimaging have exponentially increased with the advent of stronger magnet systems and biomedical technology during the past two decades, leading to early detection and treatment of stroke. Stroke is emerging as a leading cause of mortality and morbidity. With the advent of newer imaging techniques such as diffusion-weighted imaging (DWI) and susceptibility-weighted imaging (SWI), management of stroke is moving toward imaging-based approaches rather than by strict time criteria. Studies have shown good results of the use of imaging criteria to select patients for thrombolytic therapy.¹ The onset of stroke symptoms is conventionally defined as the time since the patient was last known to be asymptomatic. Using this definition, many patients whose onset of symptoms was not witnessed (e.g., during sleep) would be ineligible for therapy despite the fact that their time of onset falls within the standard time criteria.² DWI can demonstrate cytotoxic edema as early as 10 minutes after onset and is more conspicuous than conventional sequences.³ DWI uses the principle of ischemia-induced restriction of water movement within the

intracellular and extracellular compartments. These ischemic areas appear bright on DWI and dark on apparent diffusion coefficient (ADC) maps.⁴ DWI has a low false-negative rate of approximately 5%.⁵ SWI takes advantage of local field inhomogeneities and the susceptibility effects of different components to produce contrast between the tissues. Deoxyhemoglobin is paramagnetic because of the presence of unpaired electrons. This causes inhomogeneity in the magnetic field and rapid dephasing of proton spins in SWI sequences.⁶ In addition to the obvious hemorrhage that is depicted on computed tomography (CT) and conventional magnetic resonance imaging (MRI) sequences, SWI can detect micro-hemorrhages, the presence of which is associated with a higher risk of post-thrombolytic hemorrhagic transformation.^{6,7} SWI can detect spontaneous and post-thrombolytic hemorrhagic transformation earlier than CT.⁸ Various factors are reportedly associated with a poor prognosis of ischemic stroke and its therapy. Apart from direct neuronal loss, most of these factors involve loss of integrity of the vascular walls because of ischemia, which causes vasogenic edema and hemorrhagic transformation. Many patients in

whom the time of symptom onset is unclear are encountered in clinical practice. In such patients, FLAIR-DWI mismatch can be used to assess the time of onset. In this study, fluid-attenuated inversion recovery (FLAIR)-DWI mismatch has been used to determine the possible time of symptom onset. Factors such as cortical venous congestion, micro-hemorrhagic foci, and SWI-DWI mismatch have been investigated as possible markers of loss of vascular integrity and thus contraindications for thrombolysis and markers of an unfavorable prognosis. This research was undertaken to study the role of advanced imaging sequences in patients with stroke and various factors that can guide institution of therapy and warn against poor prognostic factors that may portend a poor outcome following therapy.

Materials and methods

An analytical study was performed for a period of 3 years in a tertiary care hospital. The study involved patients who presented within 12 hours of onset of symptoms of brain ischemia and were advised to undergo MRI for further evaluation.

Patients with contraindications for MRI, such as the presence of intracranial aneurysm clips and cochlear implants, were excluded. Patients in whom imaging was suboptimal due to motion artifacts were also excluded. Written informed consent was obtained from the patients whenever feasible; family members provided consent for patients who were too incapacitated to provide proper consent. Approval was obtained from the institutional scientific and ethics committee before initiation of the study. Non-contrast brain MRI was performed using an 18-channel (head coil) 1.5T MRI scanner (Avanto; Siemens, Erlangen, Germany). Conventional sequences (T1, T2, and FLAIR), DWI, ADC maps, SWI (phase, minimum-intensity

projections, magnitude projections, and combined images), and time-of-flight (TOF) magnetic resonance angiography (MRA) were acquired in all patients. The DWI, ADC, and SWI findings were noted and measurements acquired. A radiologist with >10 years of experience analyzed the images, which were read primarily by the senior resident. The parameters assessed were the volume of brain tissue showing hyperintensity on FLAIR, the volume of brain tissue showing diffusion restriction, susceptibility-diffusion mismatch, a hypointensity sign on SWI with corresponding abnormality on TOF-MRA, the presence of hemorrhagic foci, venous congestion on SWI, and correlations of these parameters with the time of symptom onset. The volume of brain tissue was measured using software on the Advantage Workstation for Windows (GE Healthcare, Chicago, IL, USA). Venous congestion was visually assessed by the radiologist. Patients who underwent intravenous thrombolysis were followed up for hemorrhagic transformation or clinical improvement. The results were analyzed by the chi-square test, regression analysis, and receiver operating characteristic (ROC) analysis using SPSS version 14.0 (SPSS Inc., Chicago, IL, USA).

Results

Eighty patients who presented within 12 hours of onset of symptoms of brain ischemia were evaluated. Of these 80 patients, 42 (52.5%) presented within 6 hours of symptom onset and 38 (47.5%) presented at or after 6 hours of symptom onset. The patients ranged in age from 12 to 85 years; 24 (30%) were aged >70 years, 44 (55%) were aged 50 to 70 years, and 12 (15%) were aged <50 years.

The infarcted volume of brain tissue ranged from 6 to 88 mL as measured on FLAIR sequences. The volume of brain tissue showing hyperintensity on FLAIR

was significantly greater than the volume of brain tissue showing diffusion restriction in patients with a symptom onset of >6 hours ($p=0.001$, Fisher's test). For an infarct volume of >20 mL on DWI (34 patients), regression analysis showed the following relationship among the volume of brain tissue showing hyperintensity (F), volume of brain tissue showing diffusion restriction on DWI (D), and time since onset:

$$F - D = -13.14 + 2.731 \times \text{time since onset}$$

Forty-eight of the 80 patients (60.0%) showed TOF-MRA abnormalities indicating

occlusion. The hypointensity sign on SWI was present in 44 of the 48 patients with a sensitivity of 66.7%, specificity of 87.5%, positive predictive value of 88.9, and negative predictive value of 63.6 (Figures 1–3). The hypointensity sign on SWI was highly correlated with abnormal findings on TOF-MRA ($p=0.001$) (Figure 3). Diffusion–susceptibility mismatch was seen in 16 (20.0%) of the 80 patients (Figures 2, 4, and 5). Diffusion–susceptibility mismatch was not correlated with the volume of infarcted brain tissue or time since onset of symptoms. Micro-hemorrhagic foci on SWI (Figure 6) were seen in 28 of the 80 patients (35.0%).

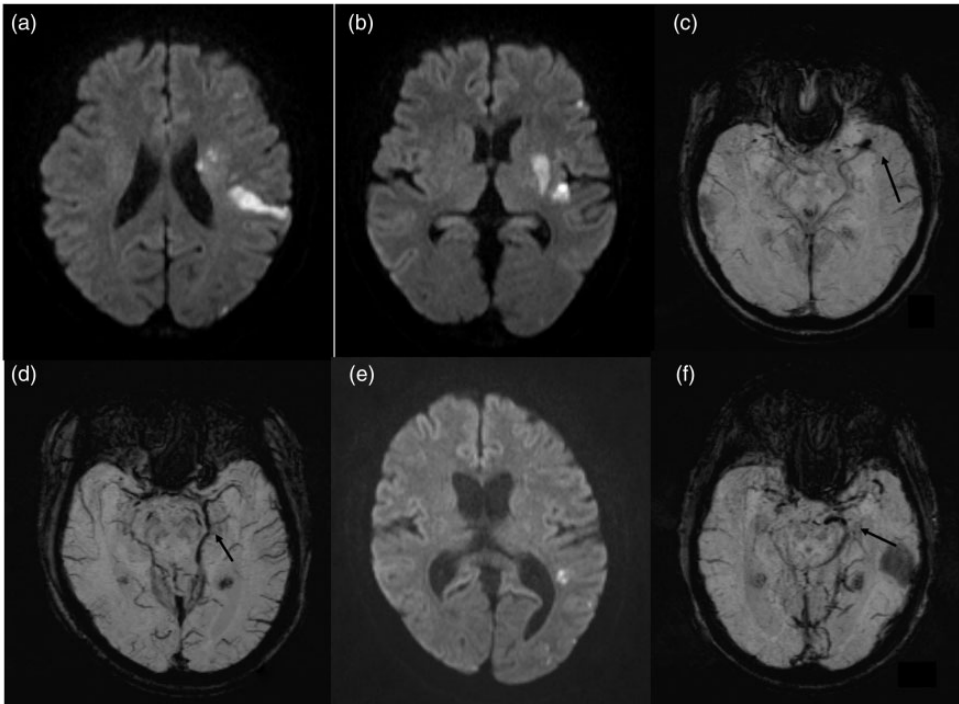


Figure 1. Axial magnetic resonance images of the brain. (a–c) Patient with left middle cerebral artery (MCA) territory infarcts. (a, b) Acute infarct showing diffusion restriction in the left MCA territory involving the left parietal cortical and subcortical regions, caudate and lentiform nuclei, and insular cortex. (c) Susceptibility sign in M1 segment of left MCA (black arrow). (d) Patient with a left posterior cerebral artery (PCA) territory infarct. The susceptibility sign is present in the P2 segment of the left PCA (black arrow). (e, f) Patient with left MCA-PCA watershed territory infarcts. (e) Acute infarcts in the left MCA-PCA watershed territory and left PCA territory (occipital cortical and subcortical regions). (f) Susceptibility sign in the P1 segment of the left PCA (black arrow).

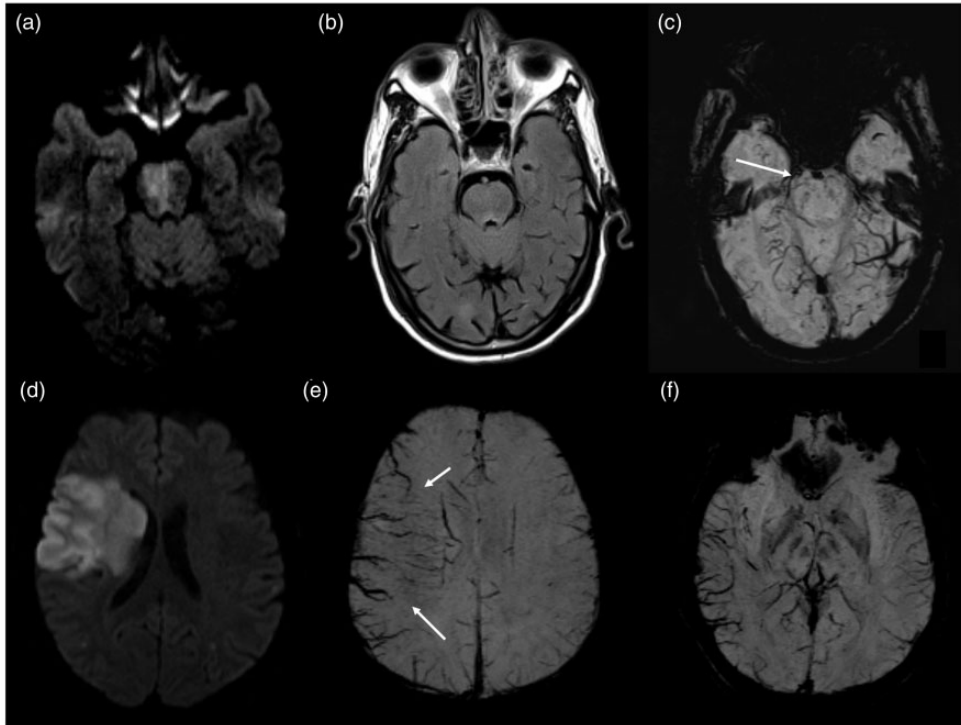


Figure 2. Axial magnetic resonance images of the brain. (a–c) Patient with an acute brain stem infarct. (a) Diffusion restriction in the right hemipons. (b) Fluid-attenuated inversion recovery image of the same patient shows no demonstrable hyperintensity. This patient presented 3 hours after onset of symptoms. (c) Susceptibility sign in the basilar artery in the same patient (white arrow). (d–f) Patient with a right middle cerebral artery (MCA) territory infarct. (d) Acute infarct in the right MCA territory. Note that the area showing cortical venous congestion is larger than the area of infarct (e, white arrows) and (f) diffusion–susceptibility mismatch.

ROC analysis showed associated micro-hemorrhagic foci in infarcts with a cut-off volume of 27 mL on DWI (sensitivity, 71.4%; specificity, 85.0%). Cortical venous congestion was seen in 16 (20.0%) patients. No statistically significant correlation was found between cortical venous congestion and either the volume of brain tissue showing diffusion restriction or the time since onset of symptoms. However, thrombolysis resulted in resolution of cortical venous congestion. Of the 80 patients, 24 underwent intravenous thrombolysis. Post-thrombolysis hemorrhagic transformation occurred in six

patients. Early spontaneous hemorrhagic transformation was seen in four patients and was depicted by SWI. T1/T2/FLAIR failed to demonstrate the hemorrhagic transformation. SWI–DWI mismatch was observed in 16 of the 80 patients (Figures 6 and 7). Of these 16 patients, 10 underwent thrombolysis, and all of them showed improvement of muscle power by 3 grades. In the 14 other patients who did not demonstrate diffusion–susceptibility mismatch, the improvement in muscle power ranged from 1 to 3 grades. Clinical assessment was performed 6 hours after instituting therapy.

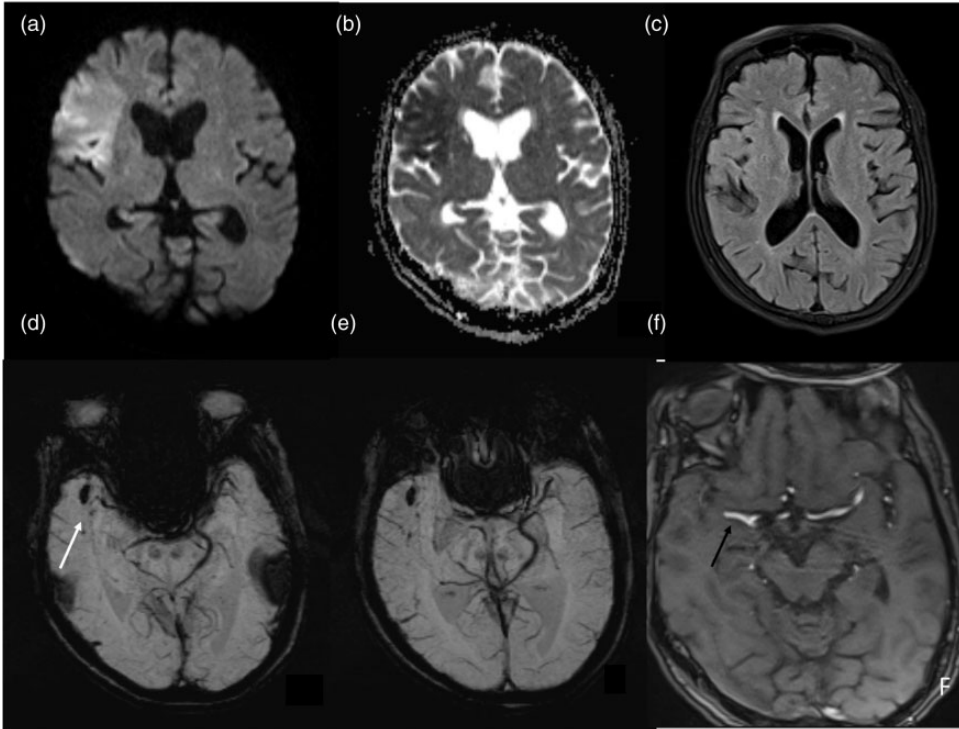


Figure 3. Patient with a right middle cerebral artery (MCA) territory stem infarct. (a, b) Acute infarct in the right MCA territory, seen as (c) areas of diffusion restriction with no demonstrable hyperintensity on fluid-attenuated inversion recovery images. (d, e) Susceptibility sign in distal M1 and proximal M2 segments of the right MCA. (f) Absence of flow-related enhancement in distal M1 and proximal M2 segments of the right MCA in the same patient, suggesting thrombus.

Discussion

SWI and DWI play an important role in imaging of patients with acute stroke. Several DWI and SWI features were examined in the present study of 80 patients with acute ischemic stroke.

Among the 80 patients who presented with stroke, the volume of brain tissue showing hyperintensity on FLAIR was greater than the volume of brain tissue showing diffusion restriction in patients with a symptom onset of >6 hours ($p=0.001$). The volume of brain tissue showing hyperintensity increased with time in this study, and this is consistent with the findings reported by other investigators.⁹

Using our formula for calculation of the time of onset based on DWI–FLAIR mismatch, thrombolysis can be offered to patients with an unknown time of symptom onset who would otherwise not receive thrombolysis if strict time criteria were followed.

The hypointense vessel sign on SWI is caused by a high concentration of deoxyhemoglobin and clot retraction in the thrombosed vessel. Deoxyhemoglobin is a paramagnetic substance that produces a blooming artifact on SWI.¹⁰ At 1.5T, the T2 relaxation time of arterial blood is higher than that of venous blood (approximately 200 vs. 100 ms, respectively).¹¹ In the present study, 48 of the 80 patients (60.0%) showed TOF-MRA abnormalities

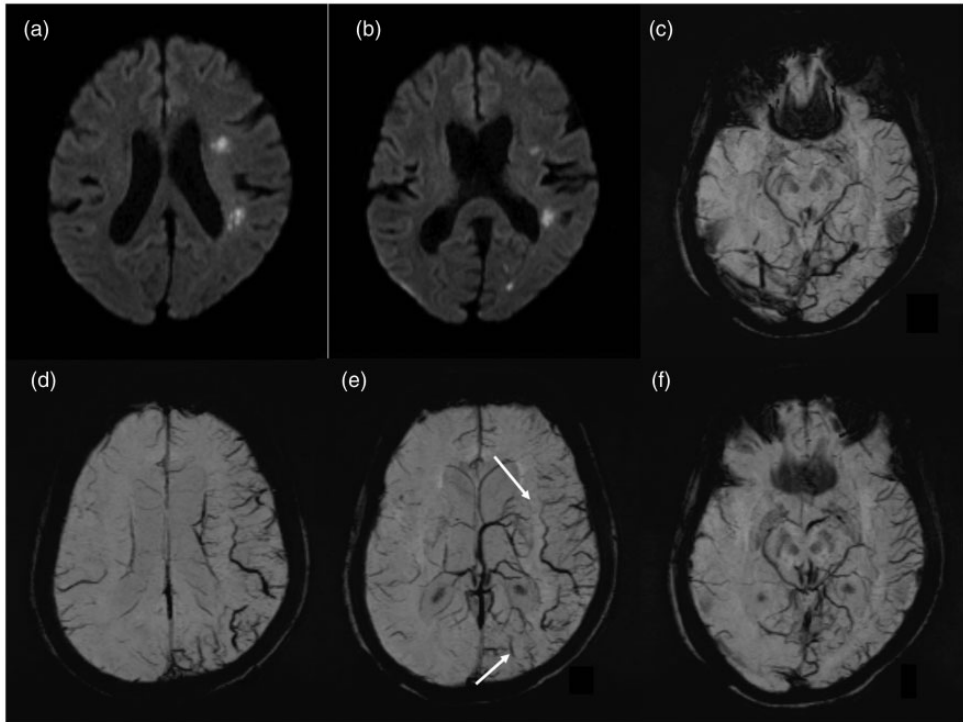


Figure 4. (a, b) Small acute infarcts in the left middle and posterior cerebral artery territories with the area of cortical venous congestion (white arrows) extending beyond the infarcted areas. (c–f) Diffusion–susceptibility mismatch is evident.

indicating occlusion of the vessels. Of these 48 patients, the hypointensity sign on SWI was present in 44 patients. The hypointense vessel sign showed a sensitivity of 66.7%, specificity of 87.5%, positive predictive value of 88.9, and negative predictive value of 63.6 for intracranial arterial occlusions. The hypointensity sign on SWI was significantly correlated with intracranial arterial occlusions on TOF-MRA ($p=0.001$). In another study, a strong correlation was found between the location of the thrombus on SWI and that on TOF-MRA (Pearson's correlation coefficient = 0.918, $p < 0.001$),¹² which is comparable with our study.

Another study showed a sensitivity of 82% and specificity of 100% of the susceptibility sign for acute intracranial arterial

occlusions.¹³ Our sensitivity and specificity for this sign were lower. However, the aforementioned study used contrast-enhanced MRA as the gold standard instead of TOF-MRA. Not all acute thrombi produce blooming. The changes in the paramagnetic effect of the thrombus compared with the rest of the flowing blood depend on the content of the clot. Clots in which white blood cells predominate show more subtle changes in the paramagnetic effect than do clots in which red blood cells predominate.¹⁴

Micro-hemorrhagic foci on SWI were seen in 28 of the 80 patients (35.0%) in the present study. Micro-hemorrhagic foci were significantly correlated with a time since symptom onset of >6 hours ($p=0.026$). Micro-hemorrhagic foci were

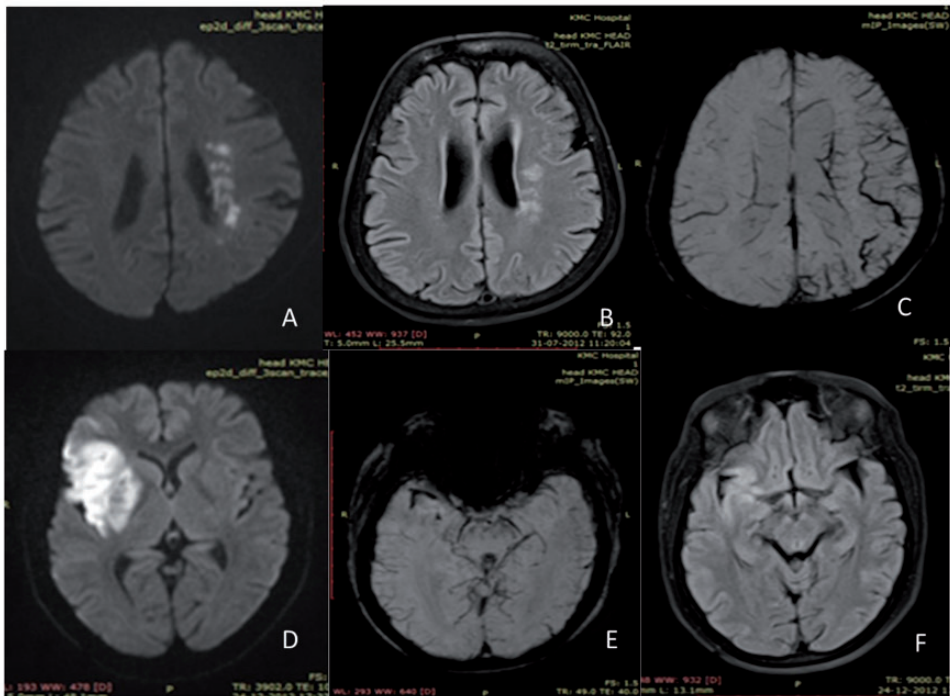


Figure 5. (a–c) Patient with right hemiparesis. (a) Acute infarct in the left corona radiata. (b) Fluid-attenuated inversion recovery (FLAIR) image showing hyperintensity in the same area. (c) Susceptibility-weighted image shows diffusion–susceptibility mismatch. (d–f) Patient with left hemiparesis. (d) Diffusion-weighted imaging showing an acute infarct in the right middle cerebral artery (MCA) territory. (e) Susceptibility sign in the distal M1 and proximal M2 segments of the right MCA. (f) Hyperintense vessel sign on FLAIR image in the distal M1 and proximal M2 segments of the right MCA.

also significantly associated with the volume of infarcted brain tissue showing diffusion restriction ($p = 0.007$). ROC analysis showed an association between micro-hemorrhagic foci and infarcts with a cut-off volume of 27 mL on DWI (sensitivity, 71.4%; specificity, 85.0%). Anticoagulant use per se should not cause intracerebral hemorrhage if the cerebral vessels are intact and therapeutic doses are adhered to. However, the presence of microangiopathy causes small vessels to become fragile. This could act as an aggravating factor for post-thrombolysis intracranial hemorrhage.¹⁵ The significant association of micro-hemorrhagic foci with a time of

symptom onset of >6 hours could be explained by vasculopathy induced by prolonged ischemia. This is further supported by the association between micro-hemorrhage and larger-volume of infarcts found in our study. More severe ischemia induces a greater increase in the fragility of small vessels. However, the literature shows conflicting results regarding the association of micro-hemorrhages with post-thrombolysis intracranial hemorrhage. A study performed by Gratz et al.¹⁶ showed no significant correlation between the presence of micro-hemorrhages and post-thrombolytic intracranial hemorrhage. In contrast, a study performed by Soo

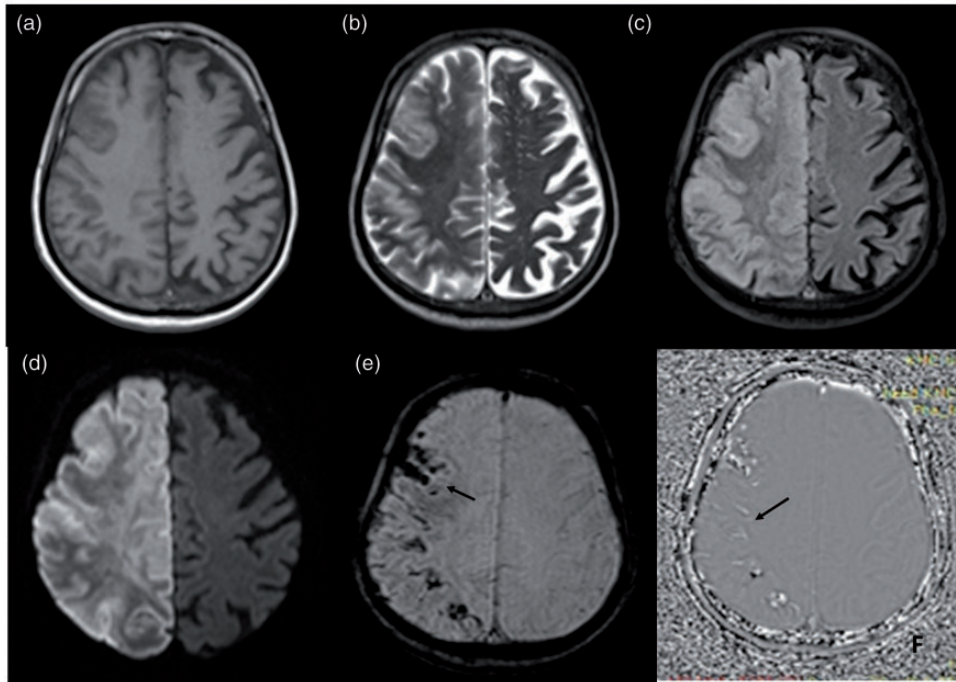


Figure 6. Patient with right middle cerebral artery territory stem infarct. (a) T1-weighted image showing no altered-intensity areas in the infarcted area to suggest hemorrhage. (b, d) Acute infarct showing diffusion restriction in the right cerebral hemisphere. (c) Hyperintensity in the same area on fluid-attenuated inversion recovery image. (e, f) However, susceptibility-weighted imaging shows multiple foci of hemorrhage within the infarcted area.

et al.¹⁷ showed that the presence of more than five microbleeds was associated with a higher risk of post-thrombolytic intracranial hemorrhage.

Venous congestion was detected in 16 (20.0%) of all 80 patients. Venous congestion was not detected in any other sequence (T1, T2, FLAIR), thus making it 100% sensitive. The thin imaging sections used in SWI and the high sensitivity of SWI to deoxyhemoglobin products are responsible for the detection of venous congestion.¹⁸

No statistically significant correlation was found between cortical venous congestion and either the volume of brain tissue showing diffusion restriction or the time since onset of symptoms in our study. This implies that venous congestion does not depend on the clot burden.

SWI–DWI mismatch was found in 16 of the 80 patients. Of these 16 patients, 10 underwent thrombolysis and all showed improvement of muscle power by 3 grades. In the 14 other patients who did not demonstrate diffusion–susceptibility mismatch, the improvement in muscle power ranged from 1 to 3 grades. There is evidence to suggest a more favorable post-thrombolysis outcome in patients with diffusion–susceptibility mismatch than in patients who do not demonstrate this sign.¹⁸

The main limitation of our study was the relatively small sample size. However, the novelty of this study is the comparison of DWI and MRA with susceptibility sequences. We did not take into account the role of CT or the Alberta Stroke Program Early CT Score (ASPECTS) scoring system. DWI and

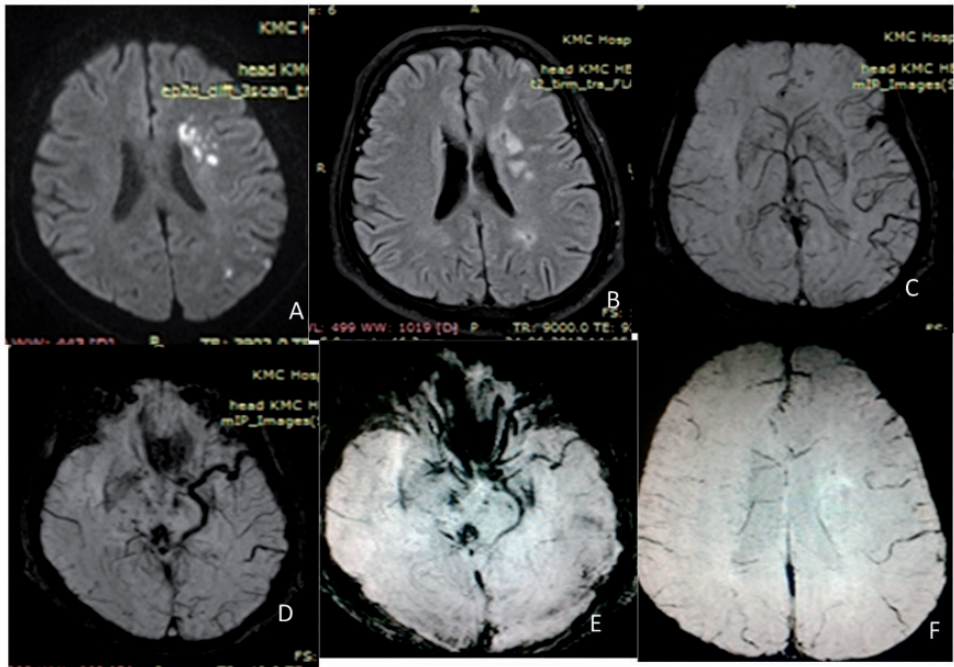


Figure 7. Patient with right hemiparesis. (a) Acute infarct in the left corona radiata. (b) Fluid-attenuated inversion recovery image showing hyperintensity in the same area. (c, d) Susceptibility-weighted image shows diffusion–susceptibility mismatch. (e, f) Resolution of the venous congestion in the same patient as seen on susceptibility-weighted images following successful thrombolysis.

SWI should be part of the routine imaging protocol for patients with acute stroke and should be used as a decision-making tool to select patients for thrombolytic therapy.

Contribution details (to be ticked marked as applicable)

	Contributor 1	Contributor 2	Contributor 3, 4, 5, 6
Concepts	*	*	*
Design	*	*	
Definition of intellectual content	*	*	*
Literature search	*	*	
Clinical studies	*	*	*
Experimental studies			

(continued)

Continued

	Contributor 1	Contributor 2	Contributor 3, 4, 5, 6
Data acquisition	*	*	*
Data analysis	*	*	
Statistical analysis	*	*	
Manuscript preparation	*	*	*
Manuscript editing	*	*	*
Manuscript review	*	*	
Guarantor	*		

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD

Santosh PV Rai  <http://orcid.org/0000-0002-7750-7147>

References

1. Yoo AJ, Verduzco LA, Schaefer PW, et al. MRI-based selection for intra-arterial stroke therapy: value of pretreatment diffusion-weighted imaging lesion volume in selecting patients with acute stroke who will benefit from early recanalization. *Stroke* 2009; 40: 2046–2054.
2. Wu O, Schwamm LH and Sorensen AG. Imaging stroke patients with unclear onset times. *Neuroimaging Clin N Am* 2011; 21: 327–344.
3. Moseley ME, Kucharczyk J, Mintorovitch J, et al. Diffusion-weighted MR imaging of acute stroke: correlation with T2-weighted and magnetic susceptibility-enhanced MR imaging in cats. *AJNR Am J Neuroradiol* 1990; 11: 423–429.
4. Birenbaum D, Bancroft LW and Felsberg GJ. Imaging in acute stroke. *West J Emerg Med* 2011; 12: 67–76.
5. Singer MB, Chong J, Lu D, et al. Diffusion-weighted MRI in acute subcortical infarction. *Stroke* 1998; 29: 133–136.
6. Hermier M and Nighoghossian N. Contribution of susceptibility-weighted imaging to acute stroke assessment. *Stroke* 2004; 35: 1989–1994.
7. Kidwell CS, Saver JL, Villablanca JP, et al. Magnetic resonance imaging detection of microbleeds before thrombolysis: an emerging application. *Stroke* 2002; 33: 95–98.
8. Chalela JA, Kang DW, Luby M, et al. Early magnetic resonance imaging findings in patients receiving tissue plasminogen activator predict outcome: insights into the pathophysiology of acute stroke in the thrombolysis era. *Ann Neurol* 2004; 55: 105–112.
9. Aoki J, Kimura K, Iguchi Y, et al. FLAIR can estimate the onset time in acute ischemic stroke patients. *J Neurol Sci* 2010; 293: 39–44.
10. Flacke S, Urbach H, Keller E, et al. Middle cerebral artery (MCA) susceptibility sign at susceptibility-based perfusion MR imaging: clinical importance and comparison with hyperdense MCA sign at CT. *Radiology* 2000; 215: 476–482.
11. Hayman LA, Ford JJ, Taber KH, et al. T2 effect of hemoglobin concentration: assessment with in vitro MR spectroscopy. *Radiology* 1988; 168: 489–491.
12. Weisstanner C, Gratz PP, Schroth G, et al. Thrombus imaging in acute stroke: correlation of thrombus length on susceptibility-weighted imaging with endovascular reperfusion success. *Eur Radiol* 2014; 24: 1735–1741.
13. Thomas B, Hingwala D, Sylaja P, et al. ‘Susceptibility sign’ on susceptibility-weighted imaging in acute ischemic stroke. *Neurol India* 2012; 60: 160.
14. Kim HS, Lee DH, Choi CG, et al. Progression of middle cerebral artery susceptibility sign on T2*-weighted images: its effect on recanalization and clinical outcome after thrombolysis. *AJR Am J Roentgenol* 2006; 187: W650–W657.
15. Charidimou A, Shakeshaft C and Werring DJ. Cerebral microbleeds on magnetic resonance imaging and anticoagulant-associated intracerebral hemorrhage risk. *Front Neurol* 2012; 3: 133.
16. Gratz PP, El-Koussy M, Hsieh K, et al. Preexisting cerebral microbleeds on susceptibility-weighted magnetic resonance imaging and post-thrombolysis bleeding risk in 392 patients. *Stroke* 2014; 45: 1684–1688.
17. Soo YOY, Yang SR, Lam WWM, et al. Risk vs benefit of anti-thrombotic therapy in ischaemic stroke patients with cerebral microbleeds. *J Neurol* 2008; 255: 1679–1686.
18. Lou M, Chen Z, Wan J, et al. Susceptibility-diffusion mismatch predicts thrombolytic outcomes: a retrospective cohort study. *AJNR Am J Neuroradiol* 2014; 35: 2061–2067.
19. Pexman JH, Barber PA, Hill MD, et al. Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. *AJNR Am J Neuroradiol* 2001; 22: 1534–1542.