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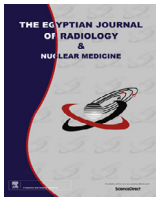

Original Article

Reliability of magnetic susceptibility weighted imaging in detection of cerebral microbleeds in stroke patients

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ABSTRACT

Objective: We investigated the reliability of susceptibility weighted imaging (SWI) in detecting cerebral microbleeds in stroke patients which predicts future recurrence and judges thrombolytic drugs.
Methods: A total of 124 patients referred from stroke unit underwent conventional MRI and SWI. Two observers reviewed twice the SWI separately to identify presence, anatomical location and count of cerebral microbleeds. Inter and intraobserver agreement were calculated using Kappa statistics.
Results: In SWI, intraobserver agreement for presence of CMBs in any brain location was almost perfect for both observers (K = 0.86, p < 0.01, 95% CI = 0.83–0.89) (K = 0.94, p < 0.01, 95% CI = 0.92–0.96), the interobserver agreement was almost perfect for first and second times (k = 0.95, p < 0.01, 95% CI = 0.94–0.96), (k = 0.84, p < 0.01, 95% CI = 0.8–0.89). Intraobserver agreement was almost perfect for the identified CMBs in each of the three main brain locations : lobar (k = 0.9, p < 0.01 95% CI = 0.8–1), deep (k = 0.81 p < 0.01, 95% CI = 0.71–0.91) and infratentorial (k = 0.95 p < 0.01, 95% CI = 0.9–1).
Conclusion: SWI is an important reliable technique allows accurate detection of CMBs occurring in association with hemorrhage in acute and chronic stroke and should be included in the protocols for assessment of stroke to help in choice of proper treatment and prediction of future attacks.

1. Introduction

Cerebral microbleeds (CMBs) are identified as rounded, small, hypointense foci seen on T2*-MRI sequences. Pathologically, CMBs are composed of hemosiderin, occurring from leakage through small cerebral vessels and surrounded by macrophages within brain parenchyma [1,2].

CMBs have great clinical implications [3,4] being linked to hypertension [5,6], small blood vessel diseases, stroke whether ischemic or hemorrhagic [7], cognitive impairment, traumatic brain injury and mortality in different populations [8,9].

In Hemorrhagic stroke patients and intracerbral Hematoma (ICH), CMBs are associated with higher risk of ICH and ischemic stroke recurrence, independent of potential confounding factors; the co-existence of CMBs and ischemic stroke specially in patients receiving antiplatelet agents is associated with an increased risk of future stroke [9,10].

Susceptibility weighted imaging (SWI) was originally called 'High-Resolution Blood oxygen level dependent (BOLD) Venography' which gives an expanded visibility of the venous vasculature in the brain. Susceptibility weighted imaging based magnetic resonance venography uses the fact that paramagnetic deoxyhemoglobin in veins causes a shift in resonance frequency between the venous vessel and the surrounding tissue [11].

The sequence of SWI is a fully flow-compensated, high-spatial-resolution conventional T2*-weighted sequence [12,13] which can detect hemorrhage as early as six hours and can reliably detect acute intracerebral parenchymal, as well as subarachnoid hemorrhage [12]. Moreover, the use of filtered phase information leads to increase the contrast in magnitude images. It provides data about the difference in susceptibility between tissues; hence used to visualize smaller veins and other sources of susceptibility effects e.g. hemosiderin, ferritin and calcium [14]. Currently, SWI is considered the most sensitive modality for detection of CMBs as it can detect more microbleeds than GRE imaging. Therefore, SWI is more sensitive than GRE sequence in CMBs detection [9,14,15].

The aim of this study was to investigate the reliability of SWI in detection of CMBs in stroke patients.

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Abbreviations:

CMBs: Cerebral microbleeds.
SWI: Susceptibility Weighted Imaging.
ICH: Intracererbal Hematoma.
GRE: Gradient Recalled Echo.

2. Patient and methods

2.1. Patients

This is a prospective study that included 124 consecutive patients with haemorrhagic brain lesions referred from stroke unit. All patients were examined by a 1.5-T MRI machine. Fourteen patients were excluded because of poor quality of scans. The total number of patients with both conventional MRI and SWI sequences of appropriate diagnostic quality was 110 (mean age, 54 years; 59% male).

2.2. MRI protocol

All patients underwent MR imaging using 1.5 T MR Unit (Philips Ingenia, Philips Medical Systems, the Netherlands) with head coil in the supine position with the head first by the following parameters: (Cranial, axial and sagittal FSE T1WI (TR: 580 ms, TE: 15 ms, Flip angle: 70°), T2WI (TR: 4000 ms, TE: 100 ms, Flip angle: 90) and FLAIR (TR: 11,000 ms, TE: 110 ms, TI: 2800 ms, Flip angle: 90), DWI: (TR: 3614 ms, TE: 160 ms, TI: 2800 ms, axial, Flip angle: 90). SWI then obtained with sequence(Ven-BOLD) [16] venography using the following parameters: (TR: 25 ms, TE: 35 ms, axial plane, Flip angle: 20°, Matrix: 256 × 256, FOV: 256 mm, Total time 11 min). SWI post-processing techniques was done using minIP reconstruction integrated in the MR imaging system.

2.3. Image analysis

Two radiologists with 25 and 15 years experience in neuroradiology reviewed SWI images separately two times with 8 weeks interval time. The observers were blinded to each other's results and to clinical data of the patients.

The images were analyzed according to the presence, localization age and size of the detected Heamorrhagic brain lesion and presence of microbleeds.

Categorization of the heamorrhagic brain lesion into primary (hypertensive hematoma) or secondary (Hemorrhagic infarcts, vascular malformations, tumors, and cerebral venous sinus thrombosis).

CMBs were diagnosed as low signal intensity homogeneous round lesions up to 10 mm in size on SWI images [4]. We excluded CMBs mimickers e.g. linear vascular flow voids representing blood vessels, mineral deposits in basal ganglia, bony or sinus artifacts, parts of large heamatomas, iron or calcium deposits in the globus pallidus [17] and calcifications within choroid plexus and pineal gland. The location of CMBs was lobar (cortical, subcortical regions), deep (basal ganglia, thalamus, internal capsule, external capsule and deep periventricular white matter) and infratentorial (cerebellum and brain stem) based on Microbleed Anatomical Rating Scale (MARS) [2].

2.4. Statistical analysis

For statistical analysis, SPSS 21.0 for Windows (SPSS, Chicago, IL) was used. The degree of agreement was defined according to the method of Landis and Koch with weighted Cohen's kappa's, as follows: for slight agreement, the kappa value ranged from 0.00 to 0.20;for fair agreement, the kappa value ranged from 0.21 to 0.40; for moderate agreement, the kappa value ranged from 0.41 to 0.60; for substantial agreement, the kappa value ranged from 0.61 to 0.80;and for almost perfect greement, the kappa value ranged from 0.81 to 0.99. A (P) value less than 0.01indicated a statistically significant difference.

3. Results

3.1. Demographic and clinical data

The study included 110 patients (46 females and 64 males), their ages ranged from 18 to 90 years with mean age of 54y at time of presentation. There was no difference in clinical presentations between patients with and without CMBs. There was no statistical significant association between sex and presence of CMBs.

3.2. The radiologic findings

In the study group, there were 78 hypertensive hematoma, 10 hemorrhagic transformation of ischemic infarction, 6 primary brain tumors and 10 metastatic tumors, vascular malformations in 2 cases and 4 cases with cerebral venous sinus thrombosis.

3.3. CMBs detection

CMBs were detected in 26 (23.6%) & 28 (25.4%) patients by observer 1 & 2 for first time, 22 (20%) & 26 (23.6%) patients by observer 1 & 2 in second time. CMBs were associated with hypertensive hematoma in 19 cases (73%) and hemorrhagic transformation of ischemic infarction in 7 cases (27%). None of these microbleeds were detected on CT examination or conventional MRI images. Eighty-four (76.3%) & 82 (74.5%) cases were negative for CMBs by observer 1 & 2 in first time, 88 (80%) & 84 (76.3%) were negative for CMBs by observer 1 & 2 in second time.

3.4. Reliability of SWI in detection of CMBs

Intraobserver agreement for CMBs presence in any brain location was almost perfect for both observers (K = 0.86, p < 0.01, 95% CI = 0.83–0.89) (K = 0.94, p < 0.01, 95% CI = 0.92–0.96), the interobserver agreement was almost perfect for first and second times (k = 0.95, p < 0.01, 95% CI = 0.94–0.96), (k = 0.84, p < 0.01, 95% CI = 0.8–0.89) as shown in Table 1.

A total number of 256 CMBs were detected by observer1 and 260 CMBs by observer 2. The most prevalent location was deep location (n = 110, 111, 43%) followed by infratentorial location (n = 93, 92, 36%) and lastly the lobar location (n = 54, 56, 21.5%) (Table 2).

Intraobserver agreement was almost perfect for identified CMBs in each of the three main brain locations: lobar (k = 0.9 p < 0.01, 95% CI = 0.8–1), deep (k = 0.81 p < 0.01, 95% CI = 0.71–0.91) and infratentorial (k = 0.95 p < 0.01, 95% CI = 0.9–1) (Table 2).

We could not calculate the interobserver agreement for identified CMBs in each of the three main brain location because of the small number of patients with microbleeds in each location.

4. Discussion

SWI is currently considered a technique of choice for CMBs detection with higher sensitivity than other imaging modalities including CT, conventional MRI [4,8,9,16] & GRE [15,18]. This was confirmed in our study because non of the CMBs detected on SWI were found on CT or conventional MRI (Figs. 1 and 2). SWI has highlighted the association between CMBs and stroke [19]. Detection of CMBs in stroke patients is extremely important

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Table 1
Reliability of SWI in detection of CMBs at any brain location in the study group.

Microbleeds At any location	Presence of CMBs			
	n (%), observer 1	n (%), observer 2	IO (95% CI)	IEO(95%CI)
First time	26 (23.6)	28 (25.4)	0.86** (0.83–0.89)	0.95** (0.94–0.96)
Second time	22 (20)	26 (23.6)	0.94** (0.92–0.96)	0.84** (0.8–0.89)

Kappa Agreement
<0 Less than chance agreement.
0.01–0.20 Slight agreement.
0.21–0.40 Fair agreement.
0.41–0.60 Moderate agreement.
0.61–0.80 Substantial agreement.
0.81–0.99 Almost perfect agreement.
** Significant at 0.01 level, IO = intraobserver, IEO = interobserver, CI = confidence interval.

Table 2
Intraobserver variability of SWI in identified CMBs in each of the three main anatomical brain locations.

Location	Identified CMBs		
	n (%), observer1	n (%), observer 2	IO (95% CI)
Lobar	54 (21.1)	56 (21.5)	0.9** (0.8–1)
Deep	110 (43)	111 (42.7)	0.81** (0.71–0.91)
Infratentorial	92 (35.9)	93 (35.8)	0.95** (0.9–1)
Total	256	260	–

Kappa Agreement
<0 Less than chance agreement.
0.01–0.20 Slight agreement.
0.21–0.40 Fair agreement.
0.41–0.60 Moderate agreement.
0.61–0.80 Substantial agreement.
0.81–0.99 Almost perfect agreement.
** Significant at 0.01 level, IO = intraobserver, CI = confidence interval.

because recent studies indicate that CMBs may lead to ICHs after using intra-arterial thrombolytics and after using antithrombotic medicines for acute stroke [8,15,16,19,20].we confirmed the reliability of SWI in detection of CMBs in stroke patients by testing the interobserver and intraobserver agreement in 110 stroke patients.

The results of this study yielded almost perfect inter and intraobserver agreement in detection of CMBs in any brain location using SWI, as well as in specific location which are comparable with the results of Gregorie et al., 2011. However, the authors were testing the reliability of MARS system in localization of CMBs utilizing SWI technique [2].

CMBs were found in about (20–25.4%) of cases presented with acute stroke, 19 cases of them with ICH (73%) while found in 7 cases with ischemic stroke (27%) parallel to the results of Lovelock et al. & Imazumi et al. [5,17].Also multiple studies showed that CMBs was detected in 33–80% of patients with primary intracerebral hemorrhages, in 21–26% of patients with ischemic stroke, and in 5–6% of asymp-tomatic or healthy elderly individuals [21–23].

The Microbleed Anatomical Rating Scale (MARS) has been introduced and validated in 2009. In MARS, CMBs are classified according to location into deep, lobar and infratentorial regions. Lobar regions included cortical and subcortical regions, while deep location included the basal ganglia, thalamus, internal capsule, external capsule, corpus callosum, and deep periventricular white matter. Brain stem and cerebellum were considered infratentorial regions [2].

The predominant deep location of CMBs (found in about 43% of total CMBs) implies the possibility of hypertensive arteriopathy which is the major cause of intracerebral hematoma [2,6] Figs. 3 and 4. This also carries the risk of recurrent future attacks of stroke [9].

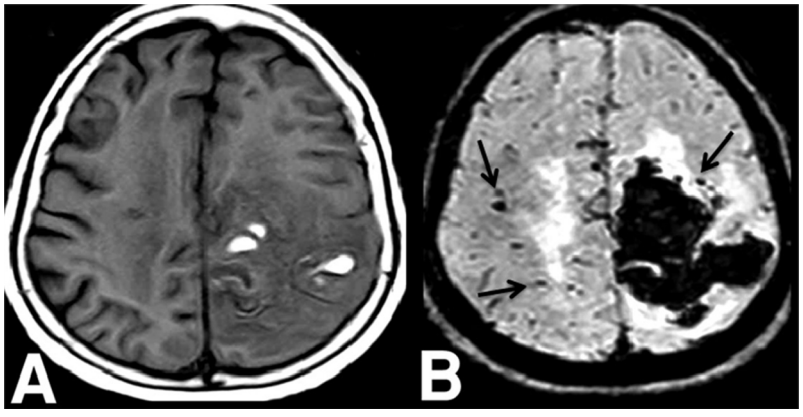

Fig. 1. Female patient 71 years old presented to the emergency hospital with loss of consciousness and right sided hemiparesis with history of hypertension. (A) T1WI shows ill defined iso intense area with blood signal inside in the left parieto-occipital region. (B) SWI shows blooming of the haemorrhagic component of the ICH, tiny CMB is detected in the left & right parietal regions (arrows).

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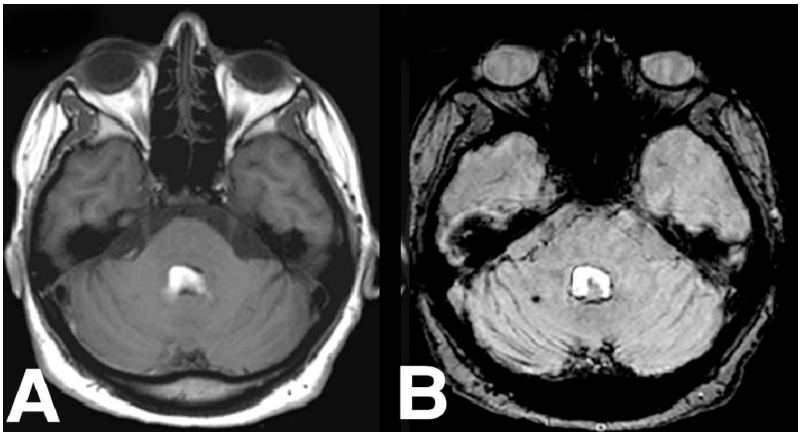

Fig. 2. Female patient 33 years old, no history of hypertension, presented to the emergency hospital with sudden attack of loss of consciousness. (A) T1WI reveals intraventricular hemorrhage. (B) SWI reveals tiny infratentorial CMB.

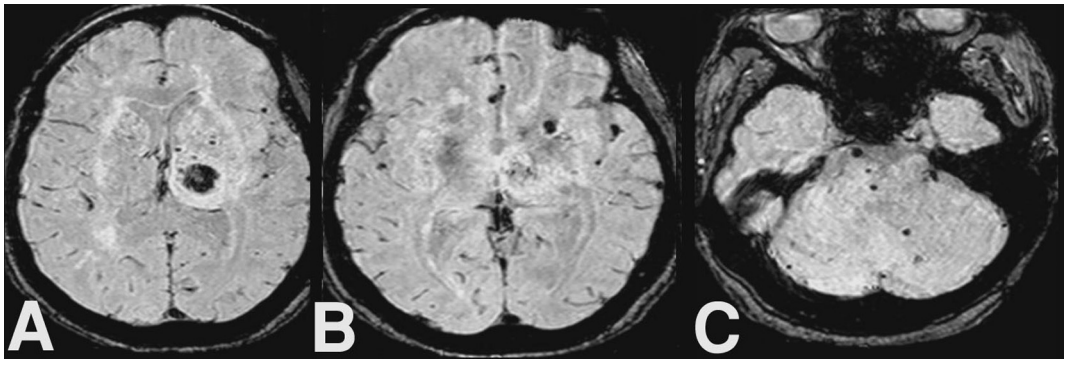

Fig. 3. (A–C) SWI shows left thalamic hematoma in 56 ys hypertensive female presented by stroke to emergency unit. Multiple CMBs are seen in lobar, deep and infratentorial locations.

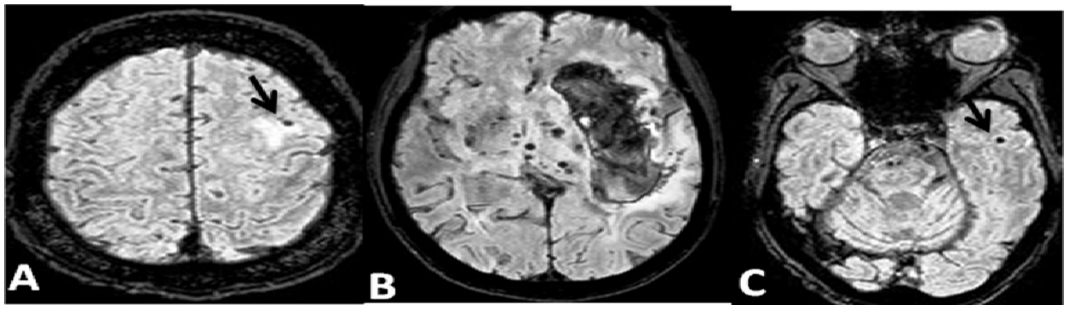

Fig. 4. (A–C): SWI in patient with left temporoparietal ICH; Lobar CMB in left frontal & temporal lobes (arrow in A, C), multiple deep CMB (B).

The difference in CMBs detection between the two reviewers was due to the cases with single CMBs which were misinterpreted as a mimicker of CMBs. Faint or indefinite Microbleeds were excluded to avoid further interobserver variations. The cause of misinterpretation was similar to MARS study [2].

Limitation of the study included small number of the patients, further studies and follow up of patients treated with anticoagulants is recommended. Further studies are better adopted to test the clinical and diagnostic significance of number of CMBs.

5. Conclusion

SWI is an important reliable technique allows accurate detection of CMBs occurring in association with hemorrhage in acute and chronic stroke and should be included in the protocols for assessment of stroke to help in choice of proper treatment and prediction of future attacks.

Conflict of interest

The authors declare that there are no conflict of interests.

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