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RESEACH ARTICLE

DETECTION AND RISK STRATIFICATION OF CEREBRAL MICROBLEEDS BY SUSCEPTIBILITY WEIGHTED IMAGING

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ABSTRACT

Background and Purpose: Cerebral microbleeds have important clinical implications in Stroke and dementia. We investigated the role of SWI in detection and risk stratification of chronic microbleeds. **Materials and Methods**: Hospital based , prospective, case-control study was performed in Department of Radiodiagnosis and Imaging , ASCOMS , Jammu using 1.5 Tesla Siemens Magnetom Essenza. Our study comprised of 30 subjects (n = 30, M = 21, F=9, mean age 68 y) with an equal number of age and sex matched controls. Cases were divided on basis of number (> or < 5) and size (> or < 5mm) of microbleeds on reverse phase SWI and T2*GRE imaging. **Results:** The distinct advantage of SWI sequence was noted in detecting and evaluating CMBs compared to the T2*GRE sequence which demonstrated only 70.5% of the microbleeds seen on SWI. Most patients in the present study exhibited multiple CMBs, which were noted simultaneously in various parts of the brain. A substantially higher number of patients had mixed CMBs (n=21, 70%) than in isolated deep or lobar locations. Majority of the subjects (n=21; 70%) had more than 5 CMBs. Larger sized CMBs i.e. CMBs ≥5mm had a strong correlation with both hypertension and diabetes as compared to CMBs < 5mm. There was a higher frequency of patients with lobar CMBs (n=27, 90%) followed by the deep location (n=21, 70.%). In deep grey nuclei, majority of CMBs were seen in thalamic region (n=234; Mean ± SD = 3.49 ± 6.18) and in infratentorial location, more CMBs were seen in cerebellum (n=192; Mean ± SD = 2.87 ± 6.18). Hypertension and diabetes had a moderate correlation with CMBs in the deep grey nuclei location as well as infratentorial location. **Conclusion**: Due to increased detection of microbleeds we strongly recommend use of SWI as sequence of choice in microbleed detection. SWI offered greater reliability and sensitivity for CMB detection as compared to the T2*GRE sequence and is presently the gold standard modality for quantifying CMBs. CMBs may further indicate inappropriately treated hypertension and diabetes.

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INTRODUCTION

Cerebral microbleeds (CMBs) are small, round or ovoid foci of signal loss (hypointensity) on MR sequences sensitive to paramagnetic iron. Pathologically, they represent small areas of hemosiderin deposition adjacent to small arteries (Albertson, 2014)**.** CMBs were first described after the clinical use of Gradient (GR) MRI and are typically demonstrated on T2* weighted Gradient-Recalled Echo Imaging (GRE) and Susceptibility Weighted Imaging (SWI) that are sensitive to the susceptibility effects of iron atoms contained within hemosiderin (Akter, 2007). SWI is a high-resolution 3D GRE magnetic resonance imaging (MRI) technique which uses a flow compensated (usually applied along all axes), long echo, gradient recalled echo pulse sequence that uses these magnitude and filtered-phase information, both separately and in combination with each other to acquire images (Bansal, 2002).

On sequences sensitive to the susceptibility effect, CMBs are represented by round hypointense dots (Chan *et al*., 1996). On SWI, CMBs have a higher contrast-to-noise ratio. Additionally, SWI is typically acquired at higher spatial resolution than GRE. Several authors have reported that CMBs can be more conspicuous on SWI than GRE, based mostly on case examples from small series of patients (Charidimou, 2013; Fazekas, 1999). Both the higher signal and higher spatial resolution have been implicated as the reason for the increased conspicuity (Greenberg, 2009). Correct and validated detection is essential to determine and understand CMBs and their associated clinical implications. CMBs are, due to their microscopic appearance, not visualized on CT or conventional MR imaging (Albertson, 2014)

Objectives: Detection and risk stratification of chronic micro bleeds using SWI and T2* imaging.

MATERIALS AND METHOD

The study designed as a hospital based, prospective case-control study was conducted in the Department of Radiodiagnosis and Imaging, Acharya Shri Chander College of Medical Sciences and Hospital (ASCOMS), Sidhra Jammu. Thirty subjects with an equal number of age- and sex-matched controls were studied. The mean age (±SD) of our study population was 66.16 ± 9.38 years, which ranged from 50 to 86 years. The study group comprised of two sets of patients: 1. Cases 2 . Controls

Cases: Those patients who were > 50 years of age having cerebral microbleeds (CMBs) on MRI and included both inpatients and outpatients.

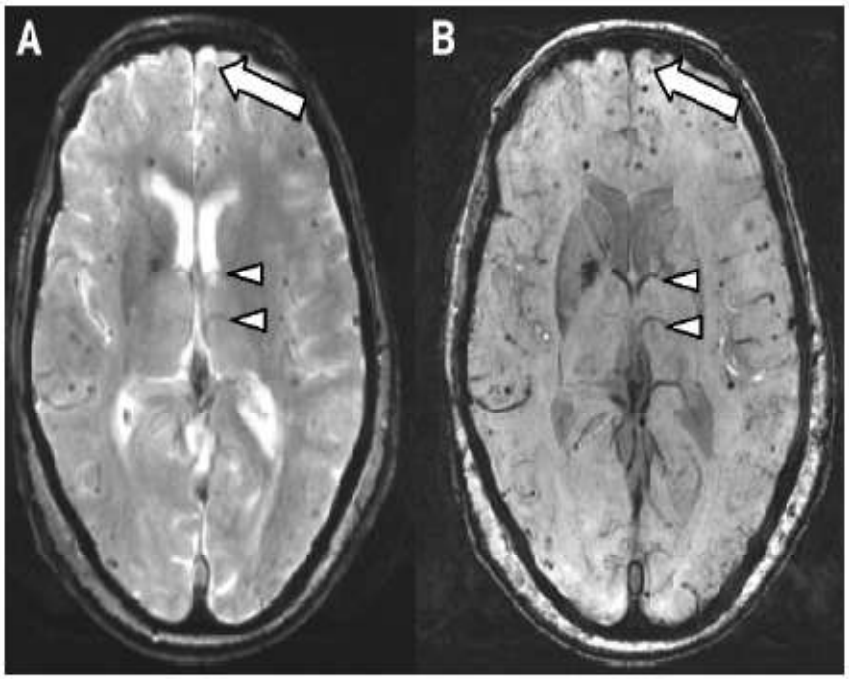
Cases were divided into the following possible groups:

According to the number of cerebral microbleeds**:**

- Patients with Microbleeds <5
- Patients with Microbleeds >5

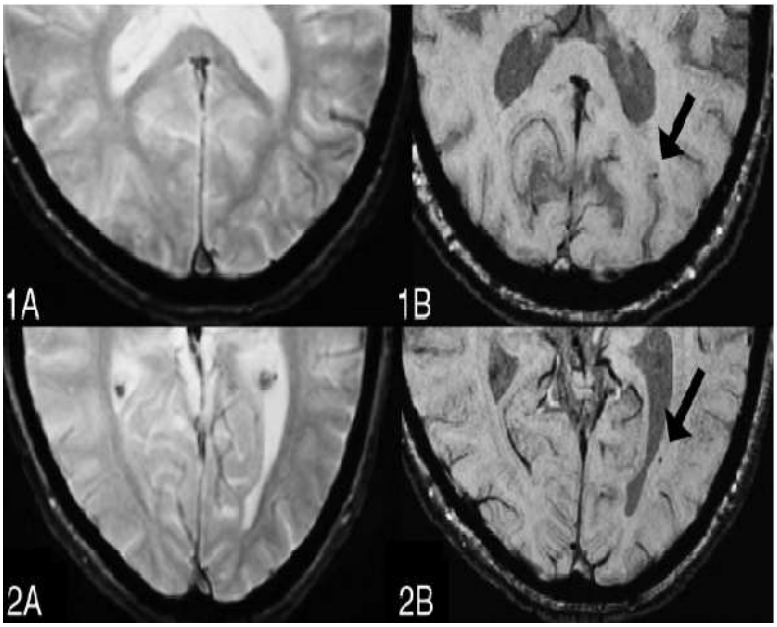
According to the size of cerebral microbleeds:

- Microbleeds <5 mm in diameter.
- Microbleeds >5 mm in diameter.



A . T2* **B . SWI**

Image 1



A*. T2 ***B*. SWI**

Image 2. CMBs on SWI but not T2*

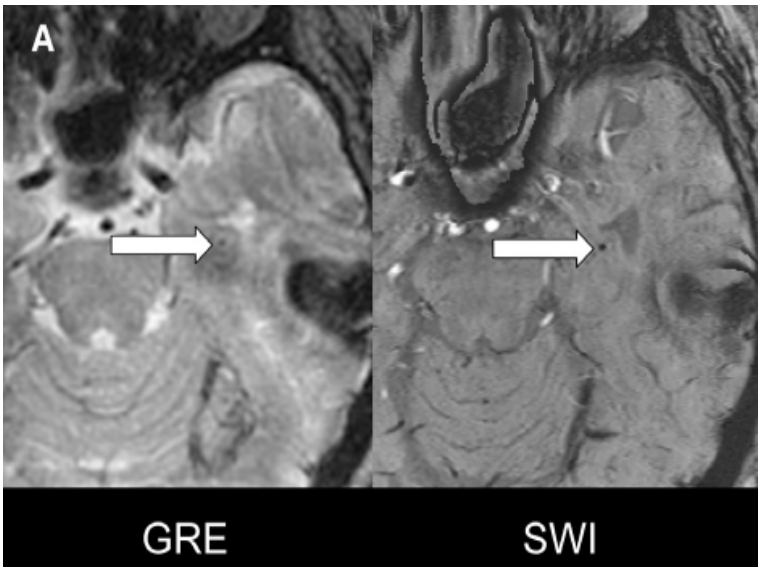


Image 3 . GRE SWI

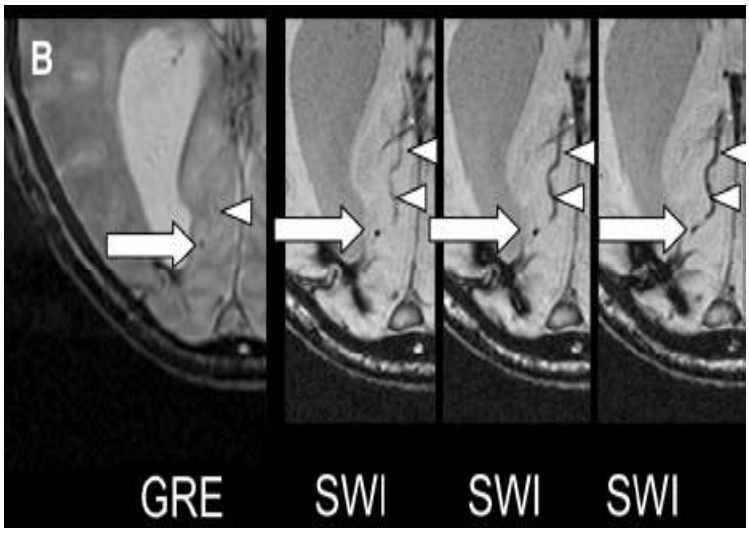


Image 3 and 4 .Comparison between GRE and SWI in detecting microbleed

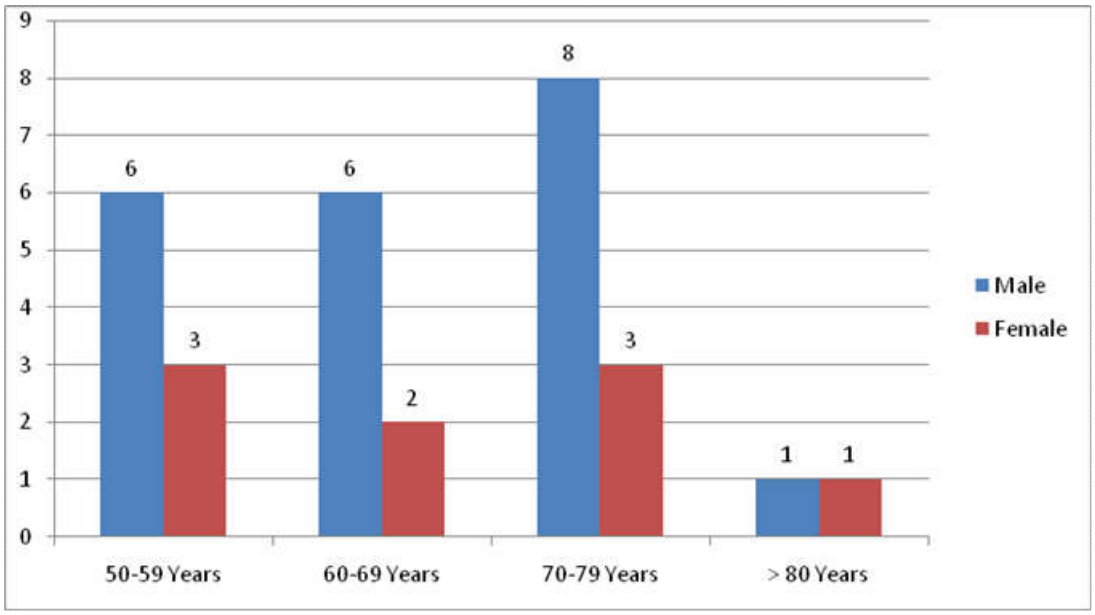
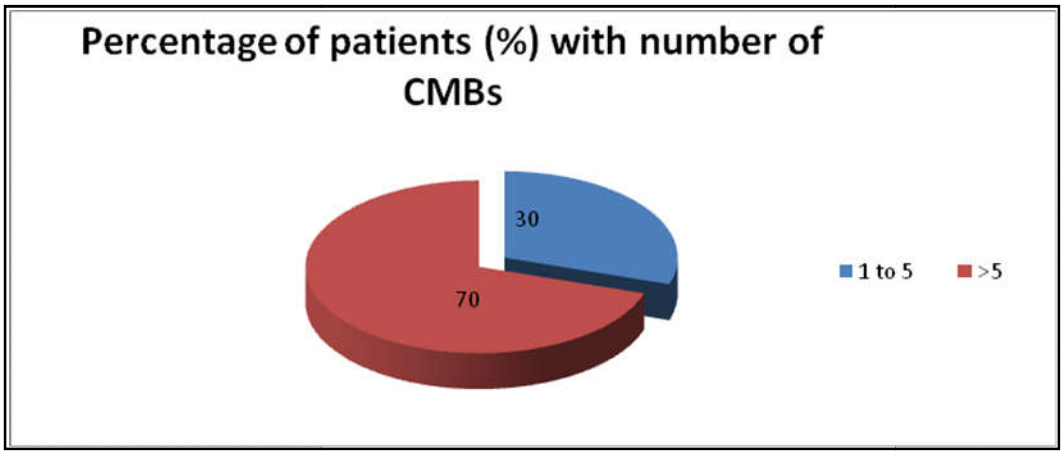
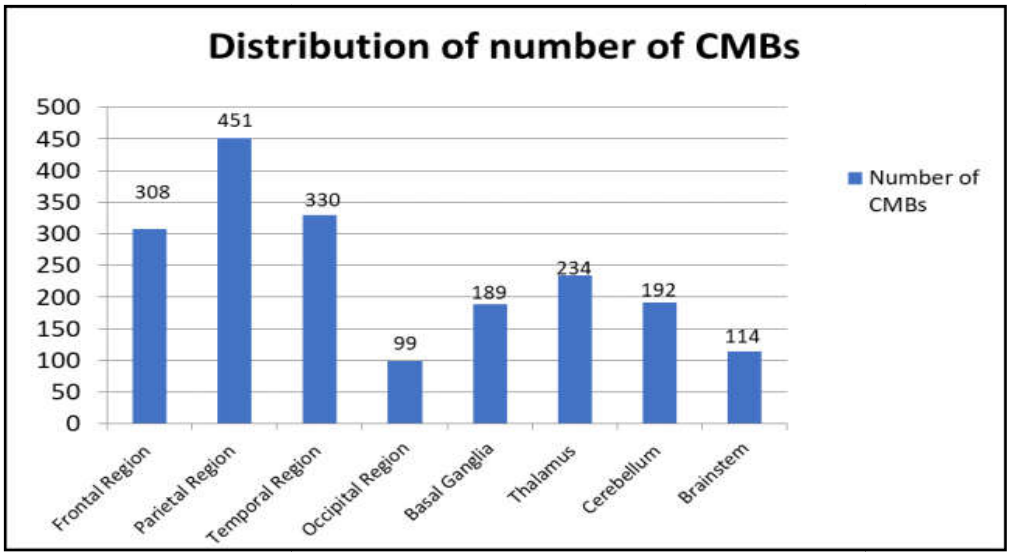


Fig. 1. Bar graph depicting age distribution of the study group with CMBs





Controls: Age and sex matched controls were recruited and we selected only those subjects who were > 50 years of age, without cerebral microbleeds (CMBs) on MRI .

Exclusion Criteria

- Diffuse Axonal Injury secondary to trauma.
- Coexistent brain tumors.
- Patients with prior brain surgery.
- Any contraindication to MR Imaging

Equipment: All the MRI scans in this study were performed using 1.5 Tesla Siemens Magnetom Essenza MR Machine. For each patient, axial SWI and T2* sequences and conventional MR Imaging sequences, such as T1, T2, and FLAIR, were performed. In a left-handed MRI system, like the one used in the present study, brain iron deposition and CMBs (paramagnetic) appeared dark (hypointense) on magnitude SWI images with a hyperintense (Bright/Positive or predominantly positive signal) on the reverse phase (RP) images. On the contrary, calcium (diamagnetic) appeared hypointense (dark/negative or predominantly negative signal) on both magnitude and RP SWI. The SWI sequence parameters were as follows: repetition time 49 ms, echo time 40 ms, field of view 24 cm, matrix 256×256, slice thickness 2 mm, reconstructed to a matrix of 512×512 with slice thickness 1 mm. Phase images were unwrapped and filtered using an 80×80-pixel low-pass filter to remove the low-spatial frequency components of the background to generate a negative phase mask.

The susceptibility images were generated by applying the phase mask, exponentiated by a factor of 3, to the magnitude images (Images 1,2,3,4)

RESULTS AND DISCUSSION

In our study out of 30 patients 21 were male and 9 were female. Majority of subjects n = 11 (36.6%) were in the age range of 70-79 years and least in the age range above 80 years i.e. 2 (6.6 %).(Table 1 and Fig 1). Equal number of age and sex matched controls were used in our study. Out of 30 patients , 11 cases (36.6%) had weakness or paralysis of either limbs as presenting complaint , followed by numbness / weakness / deviation of face in 7 cases (n=7; 23.3%) while the least common was headache / dizziness (n=1; 3.3%) as shown in Table 2 .

Table 1. Age group and gender distribution of subjects with Cerebral Microbleeds (CMBs)

Age Group	Number of subjects (%)	Male	Female
50-59Years	9 (30%)	6	3
60-69Years	8 (26.6%)	6	2
70-79Years	11(36.6%) ((36.6%)	8	3
>80Years	2 (6.6%)	1	1
Total	30	21	9

Table 2. Presenting complains of cases Risk factors and their correlation with CMBs

Symptoms	Number and %
Weakness or paralysis of limbs	11(36.6%)
Numbness/Weakness	7(23.3%)
Slurred speech/ inability to speak	5(16.6%)
Numbness or a "pins and needles" sensation anywhere in the body (Paresthesia).	4(13.3%)
Loss of balance	2(6.6%)
Headache/Dizziness	1(3.3%)

Table 3. Risk factors in the study population with CMBs

Major Risk Factors	Number of patients
Hypertension	22 (73.3%)
Diabetes	20 (66.6%)
Smoking	15 (50%)
Hypertension and Diabetes	19 (63.3%)
Hypertension and Smoking	13 (43.3%)
Hypertension, Diabetes and Smokers	12(40%)

Table 4. Number of CMBs on Magnitude and RP T2*GRE and SW by both observers

	Mag Imaging	On RP T2*GRE	Magnitude SWI	RP SWI
Observer 1	1749	1202	1964	1917
Observer 2	1671	1002	1894	1841
Average	1710	1102	1929	1879

Table 5. CMBs based on Number

Number of CMBs	Number of subjects	Percentage (%)
1 to 5	9	30
>5	21	70

Table 6. Pearson's correlation coefficient (*r*) for the major risk factors with the size of CMBs

Major risk factors	CMBs <5 mm	CMBs ≥5mm	p-value
Hypertension	0.62	0.72	0.0001
Diabetes	0.61	0.68	0.0001
Smoking	0.342	0.344	0.0001

Table 7. Number of patients in respective location of CMBs

Location	Number of Patients (n, %)
Lobar	27(90 %)
Deep Grey Nuclei location	21(70 %)
Infratentorial location	18 (60 %)

Risk factors and their correlation with CMBs: Hypertension (n=22,73.3%) and diabetes (n= 20 ,66.6%) were major risk factors followed by smoking (n=15 , 50 %) , hyperlipidemia (n=7 ,23.3%) as shown in Table 3. In our study, two observers (labelled O1 and O2) blinded to clinical information, independently interpreted the T2*GRE and SWI sequences. CMBs were only visible on T2*GRE and SWI sequences. Neither of the conventional T1, T2 or FLAIR MRI sequences demonstrated CMBs.

NUMBER OF CMBs: Reverse phase of SW imaging detected more CMB than T2*GRE as shown in Table 4. Based on number of CMBs, the study group was subdivided into CMBs less than 5 in number (1-5 CMBs) & CMBs more than 5 in number.

Majority of the subjects (n=21; 70%) had more than 5 CMBs as shown in Table 5 and Fig 2. Size of CMBs was categorized into less than 5mm (<5mm) and more than 5mm (≥5mm). Both observers measured the size of CMBs. Larger sized CMBs i.e. CMBs ≥5mm had a strong correlation with both hypertension and diabetes as compared to CMBs < 5mm. However, smoking and hyperlipidaemia had a weak correlationas shown in Table 6. There was a higher frequency of patients with lobar CMBs (n=27, 90%) followed by the deep location (n=21, 70.%) as depicted below in Table 7 and Fig 3.

In the lobar location, maximum number of CMBs were seen in the parietal region (n=451; Mean ± SD = 6.73 ± 11.40) with least in occipital region (n=99; Mean ± SD = 1.48 ± 3.80).In deep grey nuclei, majority of CMBs were seen in thalamic region (n=234; Mean ± SD = 3.49 ± 6.18) and in Infratentorial location, more CMBs were seen in cerebellum (n=192; Mean ± SD = 2.87 ± 6.18).Hypertension and diabetes had a moderate correlation with CMBs in the deep grey nuclei location as well as infratentorial CMBs. However, correlation of hyperlipidaemia and smoking was not found to be statistically significant.

Conclusion

The T2*GRE sequence, which was previously considered to be the gold standard for detection of microbleeds, detected only 70.5% microbleeds as compared to SWI (p=0.0001). This implies that the reliability of CMB count was better on SWI than on GRE. The present study demonstrated a strong correlation between total number of CMBs and hypertension (r=0.734; p<0.0001) as well as diabetes (r=0.711; p<0.0001). Therefore, we believe that SWI, with its phase component, is the modality of choice for accurate detection and interpretation of CMBs. This is more or less in concordance with other studies published in literature.

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