**T2 gradient echo sequence versus susceptibility-weighted angiography sequence in detecting microhemorrhages in hypertensive patients.**

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**Abstract**

**INTRODUCTION:** cerebral microhemorrhages are deposits of hemosiderin in small blood vessels produced by microangiopathic processes and represent a risk for the development of strokes; in magnetic resonance they appear as rounded focal areas with lack of signal.

**OBJECTIVE:** compare T2 gradient echo and SWAN (susceptibility-weighted angiography) magnetic resonance sequences in describing cerebral microhemorrhages in hypertensive patients.

**MATERIAL AND METHODS:** a transverse, descriptive, observational study in a group of hypertensive patients admitted to Hospital Christus Muguerza Alta Especialidad de Monterrey and who underwent magnetic resonance.

**RESULTS:** fifty-seven patients were included (35 men and 22 women) with mean age of 63 years. Seventeen had microhemorrhages detected with susceptibility-weighted angiography (SWAN) sequence and 15 with T2 gradient echo sequence, the majority with lobar localization. On comparing the procedures one-to-one, the SWAN showed a larger number of microhemorrhages.

**CONCLUSION:** both sequences are useful to detect the presence, localization, and degree of cerebral microhemorrhages, but the susceptibility-weighted angiography sequence proved to be more useful in detecting the total number of microhemorrhages.

**KEYWORDS:** microhemorrhages; magnetic resonance; high blood pressure; T2 gradient echo; susceptibility-weighted angiography sequence

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INTRODUCTION

Cerebral microhemorrhages are hemosiderin deposits in the brain due to red blood cell leaks in small blood vessels without any symptoms. Cerebral microbleeds are neuroimaging findings defined as small areas with void signal on MRI imaging as a consequence of old bleeding foci. They are thought to be the result of microangiopathic processes either from atherosclerosis or fibrohyalinosis or from amyloid cerebral angiopathy. The main contributors of these lesions are cardiovascular risk factors, underlying active angiopathy disease mechanisms or perhaps changes due to aging.

Previous reports have shown that the number of microhemorrhages is associated to the severity of changes in the white matter and with the number of lacunar infarcts, believed to happen as a result of small vessel disease in the brain. Walker et al found evidence of microhemorrhages with cortical-subcortical distribution, a characteristic feature in 15.5% of patients over 70 years of age. There is substantial evidence that supports an important association between microhemorrhages and hypertensive and atherosclerotic vasculopathy. These lesions are found in more than 71% of individuals that present with intracerebral hemorrhage and in 20 to 68% of patients that are admitted with an ischemic event.

Talking specifically about cerebral hypertensive angiopathy, which is caused by intimal hyperplasia and hyalinosis in the deep cerebral arteriolar branches as a result of hypertension, it involves pathophysiologic changes that lead to cerebral microhemorrhages, mainly in the thalamus, basal ganglia, cerebellum and pons. Based on these findings, it is postulated that cerebral microhemorrhages are an important risk factor for a subsequent intracerebral hematoma. Also, microhemorrhages have been found to be associated with a greater risk of hemorrhagic transformation after an ischemic vascular event and with recurrence of spontaneous intracerebral bleeds. There are also controversial results that suggest that cerebral microhemorrhages involve an increased risk for bleeding complications from thrombolytic therapy or the use of platelet agents.

Hemosiderin deposits lead to a lack of uniformity in the areas where the lesions are found, leading to a signal breakdown in MRI (called magnetic susceptibility effect) so there is a signal loss or low intensity areas. In magnetic resonance imaging, cerebral microhemorrhages are defined as multiple oval or circular foci with a substantial loss of signal in T2 weighted images mainly in echo-gradient sequences that have proven a higher sensitivity for detection of old bleedings compared to conventional spin-echo sequences; such images should always be differentiated from bloodflow voids and calcifications in the brain.

Concerning size, the criteria have been inconsistent and most of the studies indicate that microhemorrhages tend to be smaller than 5 mm or, 10 mm as the upper limit. Traditionally, echo-gradient T2 weighted sequence has been used for detection of microhemorrhages; however, Haacke and his group presented a resonance sequence called susceptibility weighted image and called it (SWI) to further improve the effect of T2 weighted sequences using detection and measurement of iron and other substances that alter the magnetic field. This sequence provides information of any tissue that has a different susceptibility in its surrounding structures such as deoxygenated blood, hemosiderin, ferritin and calcium. There are multiple neurologic disorders in which we can dramatically benefit from this highly sensitive method to monitor the amount of iron in the brain, either as deoxyhemoglobin, ferritin or hemosiderin. Such sequence has the peculiarity of being able to present the data with maximal or minimal projection intensity.
MinIP) in a given image, to get a better assessment of the vascular tracts.

The General Electric units offer susceptibility weighted image (SWI) and call it susceptibility weighted angiography (SWAN), that helps to clearly outline the small blood vessels, microhemorrhages and large vascular structures in the brain, aside from visualizing iron and calcium deposits due to the paramagnetic properties already mentioned.¹⁵

Timely detection of microhemorrhages in hypertensive patients plays an important role in the prognosis and probability of ischemic event risk with probable hemorrhagic transformation or a new hemorrhagic vascular event in patients with previous events. We must know, detect, characterize and quantify microhemorrhages, so the echo-gradient T2 weighted images, as well as SWAN, play a crucial role in such an assessment. The objective of this study is to compare echo-gradient T2 weighted MRI sequences and susceptibility weighted angiography sequence (SWAN) in the description of cerebral microhemorrhages in hypertensive patients.

**MATERIAL AND METHODS**

An observational, descriptive and cross-sectional study was conducted in hypertensive patients who were admitted to the Hospital Christus Muguerza Alta Especialidad de Monterrey who had an MRI of the brain with a 3 Tesla unit from March, 2014 to September, 1915. Patients diagnosed with hypertension who would have an echo-gradient T2 sequence and a susceptibility weighted angiography sequence (SWAN) were included, regardless of the cause. Patients who had a history or suspicion of a vascular malformation, brain tumor on CT or MRI, or history of previous surgery, or recent trauma were excluded; as well as patients with metal objects in the brain or skull base and patients who did not cooperate and whose images were suboptimal for proper evaluation and interpretation.

The evaluation using the sequences mentioned above was done at the Hospital Christus Muguerza Alta Especialidad, with a General Electric Healthcare MRI scanner, Signa HDx model, 3 tesla, with trained radiologists having over two years experience, and obtaining the sequences according to the standardized protocols (Table 1). Echo-gradient T2 weighted sequences and susceptibility weighted angiography sequences (SWAN) were obtained from all the participants, from the skull base to the convexity of both brain hemispheres.

**Table 1. MRI sequence parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2d Echo gradient</th>
<th>SWAN 3D 3T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetition time (ms)</td>
<td>650</td>
<td>41.2</td>
</tr>
<tr>
<td>Echo time (ms)</td>
<td>15.0</td>
<td>24.7</td>
</tr>
<tr>
<td>Flip angle (grados)</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Band width (kKz)</td>
<td>20.8</td>
<td>62.5</td>
</tr>
<tr>
<td>Field of vision (cm)</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>Matrix size</td>
<td>256 x 224</td>
<td>320 x 224</td>
</tr>
<tr>
<td>Flow compensation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Section thickness (5 mm)</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Gap</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Number of sections</td>
<td>30</td>
<td>62 hasta 128</td>
</tr>
<tr>
<td>Acquisition time</td>
<td>3:42</td>
<td>3:20</td>
</tr>
</tbody>
</table>

SWAN: susceptibility-weighted angiography sequence.

**Classification of microhemorrhages**

The MRI sequences were reviewed and classified based on the presence, location, number and grade of microhemorrhages, defining microhemorrhages as focal areas of very low signal intensity under 10 mm in size. Based on previous studies²,¹⁶ the microhemorrhages were classified into one of the following locations: 1) lobar:
involvement of the cortical gray matter and the subcortical white matter; 2) deep: involvement of the deep gray matter (basal ganglia and thalamus) and the deep white matter (corpus callosum); 2) infratentorial: involvement of the cerebellum and the bulbo-medullary junction.

The signal from vessels in the sulci, symmetrical calcifications in the deep gray matter, calcified choroidal plexus, calcified pineal gland as well as signal disturbances from the bone were excluded because they appear like microhemorrhages. Finally, the grade of microhemorrhages was assessed according to the classification from Lee et al.: 17

a. Grade I: absence of microhemorrhages.

b. Grade II: mild, 1 or 2 microhemorrhages.

c. Grade III: moderate, 3-10 microhemorrhages.

d. Grade IV: severe, 10 or more microhemorrhages.

Multivariate logistic regression analysis was used to evaluate the statistical significance ($c^2$, K-S) concerning the main demographic variables, and normal distribution, respectively. Prevalence, multiplicity and grade of microhemorrhages were estimated in both sequences. The statistical significance was evaluated using the McNemar non-parametric test for matched proportions. Besides, in both sequences the rate of individuals with microhemorrhages was described per location (lobar, deep or infratentorial). For those in which both sequences showed microhemorrhages, the difference (in the number of microhemorrhages in one or the other sequence) was analyzed to see if it was statistically significant using the non-parametric Wilcoxon test.

Microsoft Excel 2012 and the statistical software of the Social Science Statistics web site were used for statistical measurements. 18

RESULTS

Fifty-seven patients with a median of 63 years were included (DE $\pm$14), 35 (61%) were males and 22 (39%) were females. A summary of the distribution of the main demographic variables in the evaluation is shown on Table 2. Out of the total number of hypertensive patients, 26 had comorbidities (Table 3), and headaches were the main reason for consultation in 40% of cases, while the rest are basically divided into hemiparesis, vertigo, amnesia, disorientation, syncope and aphasia in consecutive order of frequency (Table 4). Cerebral microhemorrhages (Figure 1) were found in 15 patients with echo-gradient T2 sequences and in 17 susceptibility weighted angiography sequence (SWAN) (Table 5).

There was not enough evidence to rule out the null hypothesis concerning the difference in microhemorrhages between the sequences, with 0.5 McNemar test result. In both sequences, echo-gradient T2 as well as susceptibility weighted angiography (SWAN), most of the subjects had microhemorrhages with lobar location; however, in the SWAN sequence more lobar and deep microhemorrhages were found, infratentorially the amount was the same. (Table 5).

Table 2. Main population in the study and their association to presence of absence of microhemorrhages

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with microhemorrhages (n=17)</th>
<th>Patients with no microhemorrhages (n=40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>68.5 ± 12.59</td>
<td>61.27 ± 14.07</td>
<td>0.918</td>
</tr>
<tr>
<td>Male gender</td>
<td>13 (37%)</td>
<td>22 (62%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Female gender</td>
<td>4 (18%)</td>
<td>18 (82%)</td>
<td></td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>17 (30%)</td>
<td>40 (70%)</td>
<td>0.08</td>
</tr>
</tbody>
</table>
One to one comparison

In the one to one comparison of sequences there were no microhemorrhages seen in echo-gradient T2 sequence that could not be shown in the susceptibility weighted angiography sequence (SWAN); but in the patients in whom microbleeds were shown (n=15) in both sequences significantly more microhemorrhages were documented, visualized with a critical W value of 8, with an average difference of around 4 and \( p < 0.05 \), in the SWAN sequence, with Wilcoxon test. Also, it must be mentioned that in two patients the SWAN sequence revealed microhemorrhages not seen with echo-gradient T2 sequence; there was also a difference in the classification of the different grades of microhemorrhage (Table 6).

DISCUSSION

The susceptibility weighted angiography sequence (SWAN) revealed more cerebral
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Microhemorrhages than the gradient-echo T2 weighted sequences in two patients, however, this difference was not statistically significant in the assessment concerning prevalence. But in the patients in whom the total amount of microhemorrhages was assessed, the SWAN sequence revealed greater amount of microbleeds. This is important because a greater number of microhemorrhages suggests that the microangiopathy has progressed and reached a stage where the blood vessels tend to bleed.

Before interpreting our data, an explanation is needed about our method and potential limitations in our trial. Both MRI sequences were used in hypertensive patients, resulting in a limited sample of only 57 patients. Also, the classification or definition of microhemorrhages with MRI might be thought to be overestimated because other brain structures (deoxygenated blood in small veins, calcification of basal ganglia, choroidal plexus and pineal gland) may appear like cerebral microhemorrhages. Nevertheless, in both investigated sequences, blood products may be clearly identified as lineal structures, where, using susceptibility weighted angiography sequence and with reformatting and Minlp and MIP post processing, they can be better depicted. On the other hand, calcifications in the brain have a typical location and when located in the basal ganglia they tend to have a symmetrical distribution. Therefore, we believe that microhemorrhages are properly characterized without overestimating their occurrence, location, number or grade.

In both sequences we might have overlooked some microhemorrhages at the skull base due to artifact susceptibility, either in echo-gradient T2 sequence as well as susceptibility weighted angiography sequence (SWAN), due to air or bone interphases.

We found microhemorrhages in 17 hypertensive patients, (30%) of the sample, a figure that agrees with the distribution rate described in previous reviews.6 We also found a high frequency compared to other morbidities, similar to the study conducted by Poels et al24 where they confirm an association between hypertension and occurrence of microhemorrhages.

Because of the increased risk of adverse neurologic events (recurrence of a previous spontaneous hemorrhagic event, hemorrhagic transformation of an ischemic vascular event) an adequate assessment of microhemorrhages is important. A larger sample must be collected in future studies, aside from trying to evaluate the inter and intraobserver reliability.

**CONCLUSION**

Both echo-gradient T2 sequence and susceptibility weighted angiography sequence are useful in the localization and determination of the grade of cerebral microhemorrhages; however, the

<table>
<thead>
<tr>
<th>Table 6. Prevalence of cerebral microbleeds on MRI</th>
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<tbody>
<tr>
<td><strong>Exact number and grade of microbleeds</strong></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td><strong>Exact number</strong></td>
</tr>
<tr>
<td><strong>Grade</strong>&lt;sup&gt;*&lt;/sup&gt; &lt;br&gt; n=57</td>
</tr>
<tr>
<td>I</td>
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<tr>
<td>II</td>
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<tr>
<td>III</td>
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<td>IV</td>
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</table>

Note. The exact number of microhemorrhages is globally described in patients.

<sup>*</sup> Wilcoxon test.

<sup>*</sup>Rates were calculated based on the total sample of patients since grade I includes patients with no microbleeds, this rate does add up to 100% in both sequences.

SWAN: susceptibility-weighted angiography sequence.

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susceptibility weighted angiography sequence (SWAN) proved to be more efficient to determine the exact number of microhemorrhages found in each patient, having an impact on the evaluation of microangiopathic diseases.

REFERENCES


