Clinicoradiological correlation of infarct patterns on diffusion-weighted magnetic resonance imaging in stroke

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Purpose

Stroke is one of the major causes of disability and death worldwide. Sadly it is reported in higher proportions in the developing countries such as China, Philippines, India and Iran (1). The risk factors for stroke are reported to be in even higher numbers. Pakistan is predicted to be the 4th most populous country in Diabetes Mellitus by 2020. Every third person will also be diagnosed with hypertension. Due to lack of sufficient economic resources and health awareness, despite timely diagnosis of hypertension uncontrolled disease is prevalent. The Pakistan Stroke Society gives an estimated incidence of 250 per 100,000 which means that there are 350,000 new stroke cases per year (2).

The mainstay for the diagnosis in stroke has been conventional CT scan and MRI (3). However with advances in Radiology diffusion weighted MRI, has emerged as the "gold standard" for stroke diagnosis. DW images are very sensitive and specific for the detection of hyperacute and acute infarctions, with a sensitivity of 88%-100% and a specificity of 86%-100% detecting infarcted tissue as early as 1-2 hours after onset (4). Another new concept is the identification of various infarct patterns which are based on the involvement of brain parenchyma and are broadly classified as cortical, subcortical and territorial (5). Multiple studies have depicted a relationship between the etiology and infarct pattern. Therefore its association with the clinical outcome is also of significant value in clinical studies (6).

Many scales have been devised for the evaluation of clinical outcome in stroke patients (7). The National Institute Health Sciences Scale is a validated tool for evaluation however due to its technicality it is difficult to implement and therefore scales assessing the functional outcome of patients such as Modified Rankin score and Barthel Index (BI) are used which are easier to implement and provide knowledge regarding the daily activity and functional ability of the patient (8).

Thus the objective of the study was to determine the frequency of various infarct patterns and their relationship with functional outcome of the patient according to the Barthel index.
Methods and Materials

The study was conducted in Department of Radiology, Aga Khan University Hospital Karachi

Data was collected from Sept. 2009 till Feb.2010

Inclusion criteria:

- All inpatients with age above 18 years
- Patients with the clinical diagnosis of stroke assessed by the attending physician as weakness or inability to move the limbs, loss of speech, loss of vision or walking disturbances and confirmed by MRI scan as ischemic stroke.

Exclusion criteria:

- Strokes due to intracranial hemorrhage
- Patients who were lost to follow up.
- Patients whose imaging findings reveal no imaging diagnosis of stroke were also excluded

Study Design:

Cross sectional Survey

Data Collection Procedure:

Informed consent was obtained from the patients on the consent form. The data was collected in a structured questionnaire.

The independent variables consisted of age, gender, diabetes, hypertension, hyperlipidemia, smoking and infarct pattern that was seen and included in the report on MRI images.

The dependant variables consisted of functional outcomes of stroke assessed by the Barthel index (BI) at the time of admission (5,6))
The scale was be categorized in 2 categories as good outcome (score of # 60) and bad outcomes (score of < 60) on the Barthel Index.

**Sample Size**: The sample size has been calculated on WHO software version of sample size determination in health studies. The prevalence of good outcome in sub cortical strokes as assessed by another scale is reported to be 59.6%. (5) The prevalence of sub cortical strokes as determined in another study was found to be 12.7% (6). The Barthel index has not been used previously for assessing outcome of patients. Thus at a confidence interval of 95% and a p value of 0.05 with absolute precision of 0.05 and the prevalence of good outcome using BI taken as 0.5 the sample size calculated to detect a good outcome in sub cortical strokes is 108 patients.

The data for the Barthel index scale was collected by an intern of the neurology ward to prevent bias.

All images were interpreted on picture archiving computer systems (PACS) by the primary investigator.

Imaging protocols were as follows:

Axial T1W, Axial T2 W, Sagittal T2 W, Coronal Flair as well diffusion weighted imaging using b values of b0, b500 and b1000. Apparent diffusion coefficient images were also evaluated for confirmation of acute stroke.

**Data Analysis**

Data analysis was performed using SPSS 16. Descriptive statistics of all the variables were calculated. The mean was calculated for continuous variables such as age. Proportions and frequency were calculated of categorical variables such as gender, diabetes, hypertension, hyperlipidemia, smoking, infarct pattern and functional outcomes by Barthel index. Chi-square test was used to analyze the difference in outcomes assessed on the Barthel index for the various infarct patterns. Subset analysis was performed for one to one comparison of the cortical versus subcortical, cortical versus territorial and subcortical versus territorial infarct patterns to assess association with outcomes. A p value of 0.05 and confidence interval of 95% was considered significant. The association of confounding effects of variables such as age, diabetes, hypertension, hyperlipidemia and smoking was also assessed with respect to infarct pattern and functional outcome.
**Results**

**Demography:**

A total of 108 patients were included in the study. The age ranged from 33 to 101 with mean age of patients at 63.8 ± 13.9 years. There were 70 males and 38 females included in the study. The frequency of the infarct patterns calculated was 14 cortical infarcts, 67 subcortical and 27 territorial infarcts confirmed on MRI.

The outcome of patients was evaluated on the barthel index and categorized into favorable and poor outcome with score of 0-59 as poor and 60-100 as favorable. In the total number of patients 56 patients had a poor outcome while 52 had favorable scores.

The presence of risk factors was also accounted for to control the effect of confounding variables. Hypertension was the most prevalent risk factor with 74 patients as hypertensive. This was followed by diabetes mellitus which was present in 52 patients and hyperlipidemia which was seen in 51 patients. Coronary artery disease was seen in 23 patients and 23 patients gave a history of smoking.
Table 1

<table>
<thead>
<tr>
<th>Infarct pattern</th>
<th>Male (70)</th>
<th>Female (38)</th>
<th>Total (108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical</td>
<td>9</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Subcortical</td>
<td>41</td>
<td>26</td>
<td>67</td>
</tr>
<tr>
<td>Territorial</td>
<td>19</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td><strong>Total number of infarcts</strong></td>
<td></td>
<td></td>
<td><strong>108</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Male (70)</th>
<th>Female (38)</th>
<th>Total (108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>40</td>
<td>34</td>
<td>74</td>
</tr>
<tr>
<td>DM</td>
<td>31</td>
<td>21</td>
<td>52</td>
</tr>
<tr>
<td>CAD</td>
<td>15</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>DLD</td>
<td>29</td>
<td>22</td>
<td>51</td>
</tr>
<tr>
<td>SM</td>
<td>22</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>Poor outcome (BI &lt; 60)</td>
<td>34</td>
<td>22</td>
<td>56</td>
</tr>
<tr>
<td>Favorable outcome (BI ≥60)</td>
<td>35</td>
<td>17</td>
<td>52</td>
</tr>
</tbody>
</table>

Fig. 1: Data demographics according to gender

**References:** diagnostic radiology, Aga Khan University Hospital - Karachi/PK

**Infarct patterns and outcome analysis:**

**Patient with poor outcome**

Amongst the three infarct patterns there was a significant difference in the outcome with a p-value of 0.004. out of 28 territorial infarcts 22 (78.6%) were associated with a poor outcome. This was followed by subcortical infarcts which constituted 43.3% (29/67)
of poor outcome patients. Only 38.5% of patients with cortical infarcts (5/8) had a poor outcome.

In subset analysis no significant difference was seen in the proportions of bad outcome in comparison of cortical versus subcortical infarct pattern [43.3% vs. 38.5% (p-value 0.5)].

However, significant difference between the proportions of territorial vs. cortical infarct pattern and territorial versus subcortical infarct pattern was seen with adverse outcomes (p-values 0.008 and 0.002) respectively.

**Patients with favorable outcomes:**

The highest number of patient with favorable outcomes was seen with cortical infarcts in which 61.5% of the infarcts were associated with favorable outcomes. This was followed by patients with subcortical infarcts which 56.7% of subcortical infarcts were associated with favorable outcomes. The least number of patients with good outcomes was seen with territorial infarcts in which only 21.4% of the territorial infarcts were associated with a poor outcome. In comparison of cortical versus subcortical infarct pattern no significant difference was seen in patients with favorable outcomes (p-value 0.5). However, there was redemonstration of significant difference between the outcomes in patients with cortical versus territorial and subcortical versus territorial infarct (p-values 0.008 and 0.002) respectively. Figure 2 shows the distribution of infarct patterns with functional outcomes.

**Assessment of effect modifiers on outcome variables:**

The effect of hypertension, diabetes mellitus, coronary artery disease, hyperlipidemia and coronary artery disease was evaluated with functional outcome. Amongst all these variables the presence of hypertension was seen in 74 patients and was associated with poor outcome in 54 patients which was found to be significant with a p-value of 0.02.

Although only 23 patients had CAD significant association with poor outcome was seen in 11 of these with p-value 0.02. However in the large number of patients who did not have CAD, poor outcome was seen in 39 patients which were also clinically significant (p-value 0.019).

The presence of diabetes mellitus was seen in 52 patients and did not show significant association with the outcome (p-value 0.106). However the absence of DM was significantly associated with good outcome with p-value of 0.02.
Smoking and hyperlipidemia were not found to have significant association with adverse outcome. They were present in only 23 patients and 51 patients respectively with p-values of 0.32 and 0.19 respectively. Figure 3 shows the distribution of risk factors with different infarct patterns.
Fig. 2: gender distribution

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Fig. 3: distribution of infarct patterns according to outcome

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Fig. 4: distribution of various risk factors

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Conclusion

In this study prospective evaluation has been performed to identify the proportions of topographical appearances of infarct in the brain parenchyma and their association with functional outcome of the patients. Furthermore the association of known risk factors of stroke in these patients with different infarct patterns and functional outcome has also been evaluated.

Frequency of infarct patterns

In this study it was found that the highest frequency of infarct patterns was the subcortical type occurring in 62.6% of the patients. This was followed by territorial infarct which were seen in 24.3% of the patients and then cortical infarcts seen in 13.1% of the patients. The proportion of infarcts that were seen in subcortical group was significantly higher than that reported in another study conducted in south Korea where a total of 12.1% infarct were subcortical which were further divided in cortical border zone and subcortical border zone (6). For the sake of achieving a manageable sample size this division was not adopted for the current study. In another study the proportion of cortical and subcortical infarcts was 83.7% while territorial infarcts accounted for 17.3%. In this study another different classification was used for cortical and subcortical infarcts (9). However the proportion of subcortical infarcts is somewhat closer to what is seen in our sample. The classification that was used in the current study was used in a study also conducted in Korea in 2003 where 67.7% of the infarcts were subcortical and 12% were territorial (5). This again shows a similarity to the prevalent proportions in our study suggesting that subcortical patterns are the most prevalent patterns seen. The proportion of cortical infarcts mentioned was 6.5%.

In all of the above mentioned studies infarct patterns and their associations with stroke subtypes and etiologies have been attempted. However we did not carry out evaluation of the MRA and other TOAST criteria for the diagnosis as we were only evaluating outcomes of the infarct patterns. Another aspect that was not evaluated in their studies was the gender difference between different infarct patterns. Overall we had an abundance of male patients with stroke with 70 (64.5%) males and 38 females (35.5%). Despite this no significant statistical difference was seen amongst the prevalence of any one infarct pattern over the other in either gender. This is indicative of the fact that stroke appears to be more of a disease afflicting the male gender irrespective of infarct pattern and etiology.

Evaluation of outcome:
The outcome of this study has been evaluated with the Barthel index. Various studies in the literature have used this index as well as many others for the evaluation of stroke outcome such as the NIHSS and modified Rankin Scale (7,8). The NIHSS has been used for evaluation of a neurological deficit and has been reported to be sensitive in assessing treatment effect. However a ceiling effect of falsely poor outcomes is noted as many commands cannot be followed by stroke patients (10). Various studies have now advocated the use of functional scales for assessing patient disability. This has been further assessed with comparison of BI with MRS where very good internal consistency of the BI was noted (11).

In this study significant difference between the outcomes were evaluated between the cortical and territorial infarcts as well as the subcortical and territorial subgroup with significant association of territorial infarcts with poor outcome. In the study by Lee et al correlation of neurological outcome by NIHSS was seen with etiology of stroke and the outcome was seen to be worse in patients with internal carotid artery atherosclerosis as seen on MRA images (5). Yong et al made a comparison between subtypes of subcortical infarct internal border zone and cortical border zone infarcts with worsening outcome seen in internal border zone infarcts (12). In another study by Lee et al comparison of infarct patterns was made in MCA disease which revealed that poor neurological outcome with NIHSS was seen in patients with cardiogenic source of embolism rather than atherosclerotic disease and the infarct pattern seen with the embolism group was of the cortical and territorial type (6). These results are somewhat similar to ours in which 77.3% of territorial infarcts are associated with BI score < 59 indicating adverse outcome with the territorial pattern.

**Evaluation OF CONFOUNDING by risk factors**

There are multiple risk factors that have been described with stroke in literature. In a local study conducted by Syed et al in which frequency of ischemic stroke subtypes are described. They found hypertension as the most prevalent risk factor 66.2% followed by diabetes in 41.5% patients. This was matched by what we saw in our study with highest proportion of hypertensives as 68.5% in our patients. In the study conducted by Lee in 2004 for determining etiology of MCA stroke it was seen that significant association between Diabetes and hypertension was noted in the group with atherosclerotic MCA disease (5). In our study we could not establish a significant association of diabetes with outcomes. Subcortical infarct pattern had the highest proportion of all risk factors. However significant association with adverse outcome was only seen with hypertension and coronary artery disease.

Multiple studies have shown that hypertension is the single most important risk factor for stroke and trials have reported that significant reduction in stroke cases have occurred with effective antihypertensive treatment.
Diabetes is another important risk factor that has shown independent risk of atherosclerosis with brain infarctions. Case-control studies of stroke patients and prospective epidemiological studies have confirmed an independent effect of diabetes with a relative risk of ischemic stroke in persons with diabetes from 1.8 to 3.0. In the Honolulu Heart Program, those with diabetes had twice the risk of thromboembolic stroke of persons without diabetes that was independent of other risk factors (13). Our results can possibly be explained by inadequate number of diabetics to yield significant results. Furthermore the duration of diabetes was not accounted for which lends an idea to the onset of complications.

In our study coronary artery disease was found to be significantly associated with poor outcomes. Myocardial disease has long been recognized as a risk factor for stroke. In the Framingham Study, when multivariate analysis was used, risk of stroke was increased twofold by coronary heart disease, threefold by electrocardiographic left ventricular hypertrophy, and threefold to fourfold by cardiac failure (14). In a separate analysis at Framingham, left ventricular mass assessed by echocardiography was also predictive of stroke in follow-up.

The other risk factors of hyperlipidemia and smoking were not found to be significantly associated with any particular infarct pattern or the adverse outcome. However their potential as effect modifiers has been established in multiple trials. While hypercholesterolemia is an important modifiable risk factor for coronary heart disease, the link to ischemic stroke is still uncertain. Cigarette smoking increases risk (RR) of ischemic stroke nearly two times, with a clear dose-response relation. In both the Framingham Study and the Nurses' Health Study cessation of smoking led to a prompt reduction in stroke risk-major risk was reduced within 2 to 4 years. This reduction in risk occurred throughout the age spans of these studies and in heavy as well as moderate smokers (15,16).

**Conclusion:**

Diffusion weighted MRI is a non invasive modality that is used for diagnosis of acute stroke. Infarct patterns can be reliably used to predict functional outcomes in patients. In this study we found the highest frequency of subcortical infarcts followed by territorial and cortical infarct patterns. The highest proportion of infarct pattern with good outcomes was seen with cortical infarcts followed by subcortical and then territorial infarct pattern. Hypertension and coronary artery disease were the effect modifiers showing significant association with poor outcomes.
**Fig. 6:** no significant abnormality on conventional MR imaging. Patient presented with loss of consciousness

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Fig. 5: subcortical infarct pattern. Patient had poor outcome risk factors of htn, coronary artery disease and dyslipidemia were present

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Fig. 7: Corresponding image of fig 6 with bright DWI and Low ADc images showing a small cortical stroke. The patient was hypertensive and had a score of more than 60 on the barthel index

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Fig. 9: Corresponding DWI image of fig 8 shows bright DWI and low ADC indicating acute territorial infarct. Patient had a significantly poor outcome and had Diabetes as well as hypertension.

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**Fig. 8:** Patient with sudden onset right hemiplegia. Asymmetry of left ventricle seen on conventional imaging

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References

