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Original Article

Radiology Section

# Correlation of Neurocortical Atrophy Scores on Imaging with Mini-Mental Status Examination

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## ABSTRACT

**Introduction:** The term "Cognitive impairment" is used for decline of memory and behaviour, depicting its progressive nature, of which the most common cause is Alzheimer's followed by vascular injury. Magnetic Resonance Imaging (MRI) and Mini-Mental State Examination (MMSE) together have an established role to identify aetiology and also to distinguish normal ageing from demented patients. Final diagnosis by brain biopsy is an invasive method, hence structural MRI scores are used to differentiate and characterise the course and prognosis of disease.

**Aim:** This study was done to correlate the various imaging scores of dementia like Schelten's, Davies-Mattis-Kipps, Fazekas, Pasquier and Koedam scores with the severity of cognitive impairment on MMSE scores.

**Materials and Methods:** It was a cross-sectional study done on 100 patients based on purposive sampling techniques of exclusion and inclusion criteria. All patients above 18 years of age referred for the evaluation of cognitive impairment were included after taking informed and written consent. Magnetic Resonance Imaging (MRI) Brain was performed using a 1.5 T MRI scanner (PHILIPS ACHIEVA 16 channel system) as per the department protocol. The axis was taken perpendicular to long axis of hippocampus on sagittal, and perpendicular to the commissures intersecting the mamillary bodies on coronal. The MMSE and lobar cortical atrophy scores (Schelten's, Davies-Mattis-Kipps, Fazekas, Pasquier and Koedam) were recorded for each patient and imaging diagnosis was made. The data was then analysed for statistics. Frequency percentage distribution of range of MMSE, Pearson Coefficient of Correlation and Fisher's exact test, Chi-squared Test and Sig. (2-tailed) correlation were used. Statistical measurement was done using Statistical Package for Social Sciences (SPSS), version 21.

**Results:** There was statistically significant association ($p<0.05$) between Schelten's and Mattis imaging scores with MMSE. This determines that there exists relationship between degree of cognitive impairment and neurodegeneration predominantly temporal lobe. However, linear coefficient of correlation ($r>0.3$) was noted between MMSE severity and Schelten's, Davies-Mattis-Kipps and Fazekas grading. This determines that there is a moderately positive linear relationship between the two variables.

**Conclusion:** MRI Brain is the investigation of choice in patients with cognitive impairment to categorise the patients based on aetiology and stage the disease that could be misdiagnosed on clinical assessment alone. MRI also diagnoses stage of dementia that affects the prognosis and outcome of the patient. Patients with cognitive impairment irrespective of MMSE score severity need to undergo neuroimaging that helps in improvising patient management at the earliest.


**Keywords:** Atrophy grade, Cognitive impairment, Dementia, Memory and behaviour

## INTRODUCTION

Worldwide, there are approximately 50 million people suffering from dementia with approximately 10 million new cases every year. The prevalence rate of dementia above 60 years is about 5-8% [1]. Dementia is an epidemic of elderly with progressive neurological morbidity affecting patient and family life. There are mainly four domains of dementia namely Alzheimer's Dementia (AD), Vascular Dementia (VD), Lewy body dementia (DLB) and Fronto-Temporal Dementia (FTD) [2]. Thus, methods are needed to identify individuals at risk, to stage their disease, and to track progression with sensitive and appropriate measures [2]. Although dementia is clinically diagnosed or suspected, it can only be confirmed by postmortem examination or by brain biopsy [3]. As this gold standard cannot be achieved in every case, diagnosis, staging and prognostication is challenging [3]. A strong association exists between cognitive decline and severity of atrophy at autopsy [4]. The best way of maintaining brain function may be to offer therapies as early as possible, before irreversible neuronal loss, and when there is potential to prevent or delay the onset of cognitive impairment.

Here, comes the role of structural MR neuroimaging that determines whether a mild or moderate degree of vascular changes is sufficient to explain the cognitive impairment in cases of mixed dementias [5]. Early diagnosis of AD allows early treatment with cholinesterase inhibitors, which have been shown to delay institutionalisation and improve or stabilise cognition as well as behavioural symptoms [6]. VD is unique in that its course is not always progressive; there is potential for stabilisation of disease course and partial recovery [3]. Early MRI in dementia is helpful to diagnose, categorise, prognosticate and evaluate treatment effect [7]. Sensitivity of MRI is 68% and that of MMSE is 53% in diagnosis of AD [8]. Thus, a combination of two achieves better accuracy. Imaging significantly improves the lower bounds of diagnostic accuracy [8]. The aim of this study was to establish correlation between imaging dementia scores and severity of cognitive impairment on MMSE scoring system. It also aims to depict the diagnostic role of MRI in evaluation of cognitive impairment to detect possible aetiology and stage of disease, thereby necessitating imaging in all cases irrespective of MMSE scores.

## MATERIALS AND METHODS

It was an observational, descriptive cross-sectional study done on 100 patients selected by purposive sampling techniques based on inclusion and exclusion criteria. Ethical clearance was taken from the institute. (FMMC/FMIEC/2473). The study was done over a period of one year from March 2019 to March 2020.

## Sample Size Calculation

Hundred patients (wherein the sample size was determined based on the prevalence rate of dementia above 40 years of age being 0.43%[9])- using SPSS, version 21.

$n=Z\alpha^2p\ (1-p)\ /e^2$, where n=sample size

$Z\alpha=1.96$ at 95% confidence interval

e=allowable error. Using the formula with error of 1%, the minimum sample size required was 83 and the study included 100 patients.

**Inclusion criteria:** All patients above 18 years of age referred to the Department of Radiodiagnosis at Father Muller Medical College Hospital for MRI of Brain for the evaluation of cognitive impairment were included in study after obtaining informed consent.

**Exclusion criteria:** Patients whose MRI was not technically adequate or, those with history of trauma, alcohol abuse and psychiatric illness were excluded from the study.

**Plan of study:** MRI was performed using a 1.5 T MRI scanner (PHILIPS ACHIEVA 16 channel system) as per the department protocol. The axis was taken perpendicular to long axis of hippocampus on sagittal, and perpendicular to the commissures intersecting the mamillary bodies on coronal. MRI of the brain consisting of 3D T1, T2 FLAIR Axial was performed and appropriate quantitative data acquired from the required sequences.

Lobar atrophy score of every patient was documented in this study using standardised scores established from other sources as reference that includes: Schelten's for medial temporal lobe [10], Davies-Mattis-Kipps for frontal and temporal lobes (anterior and posterior) [11-13], Koedam for parietal lobe [12], Pasquier for global cortex and Fazekas for white matter hyperintensities [Table/Fig-1a,b].

Davies-Mattis-Kipps score involves assessing three lobes in each hemisphere for every individual, thereby making it difficult to have a validated grading system of findings unlike other scores. Thus, an array of standard reference images [Table/Fig-1a] was used to maximise consistency with a 5 point scale (0 being normal and 4 being most severely abnormal) to assess this score [11,14].

MMSE scores were also documented simultaneously from the clinical details of patient assessed by the referring doctor [Table/Fig-2] [15].

Schelten's score has a high diagnostic accuracy for autopsy confirmed Alzheimer's Disease (AD) [16]. Global Cortical Atrophy scores were found to be significantly higher in patients with AD and DLB. Early parietal atrophy is emerging as an important aspect of AD, being a particular feature of early-onset (<65 years) AD when compared to controls and other dementias. The subjects with relatively less severe neurodegenerative pathology have relatively more severe cerebrovascular disease in cases of mixed dementia [10] where white matter hyperintensities were graded on Fazekas score.

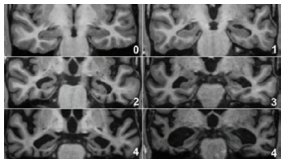
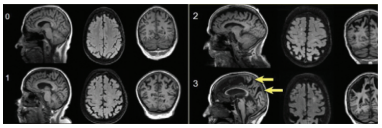
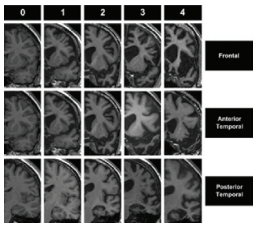
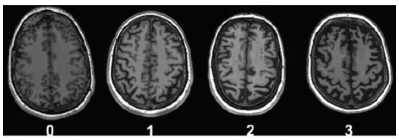
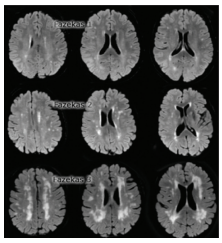
As certain stage and aetiology is regressable on medication, neuroimaging plays a major role in evaluation. The above standardised interpretation was applied for the study [Table/Fig-3] and categorised patients accordingly based on subtypes of dementia, severity of atrophy based on cortical scores [Table/Fig 1a,b].

## STATISTICAL ANALYSIS

Frequency percentage distribution of range of MMSE scores was assessed. Pearson Coefficient of Correlation and Chi-square test was used to assess correlation with clinical and imaging findings. Sig. (2-tailed) correlation was used with correlation significant at the 0.01 level (2-tailed) where $p<0.05$ was considered significant and $r>0.3$ was considered to have linear association.

## RESULTS

There were 100 patients of cognitive impairment referred for MRI Brain with their respective MMSE scorings of which majority were males in range of 60-75 years [Table/Fig-4].

| No. | Score | Visual rating score | Sequence |
|---|---|---|---|
| 1. | Schelten's |  | 3DT1 |
| 2. | Koedam |  | 3DT1 |
| 3. | Davies-mattis-kipps |  | 3DT1 |
| 4. | Pasquier |  | 3DT1 |
| 5. | Fazeka |  | T2-FLAIR |

**[Table/Fig-1a]:** Standardised lobe atrophy scores [14].

| Schelten's score for medial temporal lobe atrophy | | | | |
|---|---|---|---|---|
| Score | Width of choroid fissure | Width of temporal horn | Height of hippocampal formation | Features |
| 0 | Normal | Normal | Normal | No atrophy |
| 1 | > | Normal | Normal | Only widening of choroid fissure |
| 2 | >> | >> | < | Also, widening of temporal horn of lateral ventricle |
| 3 | >>> | >>> | << | Moderate loss of hippocampal volume (decrease in height) |
| 4 | >>> | >>> | <<< | Severe volume loss of hippocampus |
| **Koedam score for pareital lobe atrophy** | | | | |
| Score | | | | Widening of pareito-occipital sulci |
| 0 | | | | No (closed sulci) |
| 1 | | | | Mild |
| 2 | | | | Moderate |
| 3 | | | | End stage knife blade |
| **Pasquier score for global cortical atrophy** | | | | |
| Score | | | | Global atrophy |
| 0 | | | | No cortical atrophy |
| 1 | | | | Opening of sulci |
| 2 | | | | Volume loss of gyri |
| 3 | | | | 'Knife blade' atrophy. |
| **Fazekas scale for white matter hyperintensities** | | | | |
| Score | | | | White matter hyperintensities |
| 0 | | | | None or a single punctate lesion |
| 1 | | | | Multiple punctate lesions |
| 2 | | | | Beginning confluency of lesions (bridging) |
| 3 | | | | Large confluent lesions |

**[Table/Fig-1b]:** Standardised lobe atrophy scores [14].

| Clinical inference on dementia | Scores of MMSE (Out of 30) | Interpretation in this study (%) |
|---|---|---|
| Probable | 26-29 | 13 |
| Mild | 21-25 | 25 |
| Moderate | 11-20 | 38 |
| Severe | 0-10 | 24 |
| Total | | 100 |

**[Table/Fig-2]:** Distribution of Mini-Mental State Examination (MMSE) interpretation in study [15].

| Lobes assessed (Scores) | Frequency | Interpretation | Interpretation of dementia |
|---|---|---|---|
| Medial temporal (Schelten's) | 36 | Yes | Alzheimer's |
| | 64 | No | |
| Anterior temporal (Mattis) | 69 | Yes | Fronto-temporal |
| | 31 | No | |
| Posterior temporal (Kipps) | 78 | Yes | Fronto-temporal |
| | 22 | No | |
| Frontal (Davies) | 58 | Yes | Fronto-temporal |
| | 42 | No | |
| Parietal (Koedam) | 60 | Yes | Early Alzheimer's |
| | 40 | No | |
| Global (Pasquier) | 53 | Yes | Alzheimer's |
| | 47 | No | |
| White matter lesions (Fazekas) | 51 | Yes | Vascular |
| | 49 | No | |

**[Table/Fig-3]:** Pattern of dementia on MRI.

| Age (Year) | Less than 45 | 45-60 | 60-75 | More than 75 |
|---|---|---|---|---|
| Percentage distribution | 9 | 20 | 44 | 27 |
| Gender | Male | | Female | |
| Percentage distribution | 58 | | 42 | |

**[Table/Fig-4]:** Demographic data.

Most cases of clinically assessed dementia showed MMSE score indicating moderate dementia (38%) followed by mild dementia (25%) [Table/Fig-2].

In this study, lobar atrophy was graded based on scores where a score 'Yes' included grade 2 and above [Table/Fig-1b].

Based on these, a radiological interpretation on type was made with severity. This score severity was analysed with MMSE severity mentioned in the case sheet.

Of all 100 patients assessed, all had at least one lobar atrophy indicating that even high scores of MMSE need to be evaluated by MRI Brain with cortical scores aiding in closest diagnosis and patient management.

In this study, there was significant correlation between cognitive impairment severity with medial and anterior temporal lobe atrophy ($p<0.05$) [Table/Fig-5]. Moderate linear association was found between severity of cognitive impairment with atrophy of medial, anterior, posterior temporal and frontal lobes. It was also associated linearly with Fazekas scores [Table/Fig-5].

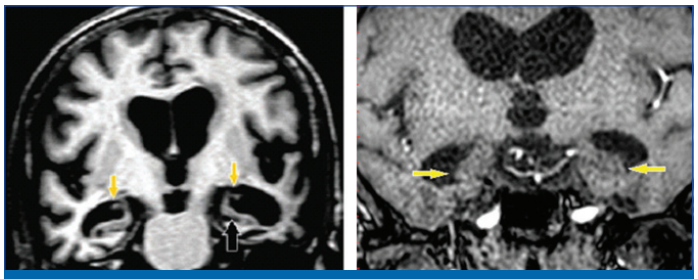
Few representative cases in the present study is as follows with [Table/Fig-6] being AD, [Table/Fig-7] being VD, [Table/Fig-8] being Frontotemporal dementia, [Table/Fig-9] being early AD and [Table/Fig-10] being mixed dementia on imaging. Arrows in all the images represents atrophy assessed based on [Table/Fig-1a,b] of medial temporal lobe.

## DISCUSSION

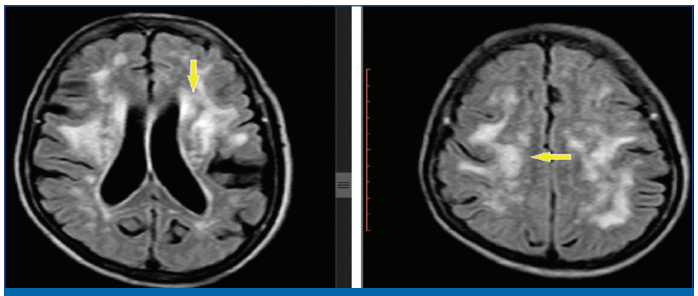
Similar to studies conducted by European federation of neurological societies 2012, Scottish intercollegiate guidelines network 2005

| Score vs MMSE | Fischer's exact test value | p-value | Correlation coefficient (r) |
|---|---|---|---|
| Schelton's | 24.392 | 0.003 | 0.53 |
| Koedam | 6.894 | 0.734 | 0.05 |
| Davies | 13.426 | 0.079 | 0.4 |
| Mattis | 23.250 | 0.004 | 0.6 |
| Kipps | 6.550 | 0.084 | 0.6 |
| Pasquier | 6.709 | 691 | 0.24 |
| Fazekas | 9.849 | 0.314 | 0.31 |

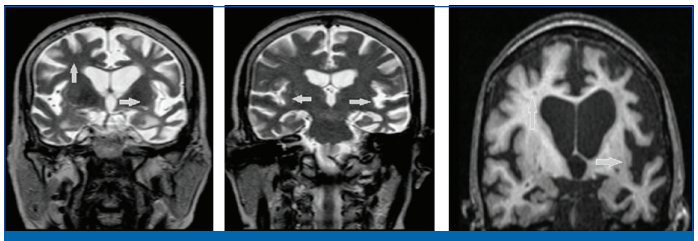
**[Table/Fig-5]:** Correlation between severity of lobar atrophy using various scores with severity of Mini-Mental State Examination (MMSE).



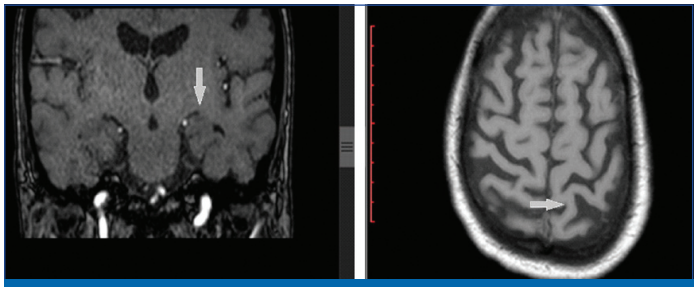
**[Table/Fig-6]:** Two cases of MMSE <10 (severe dementia) show Score 4 and Score 3 Schelten's score-diagnosis of Alzheimer's Dementia (AD).



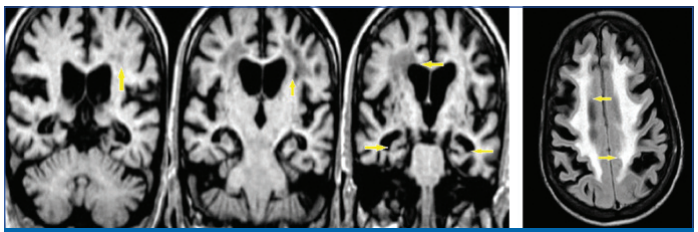
**[Table/Fig-7]:** Case of MMSE of 20 (moderate dementia) shows Score 3 Fazekas and diagnosis of Vascular Dementia (VD).



**[Table/Fig-8]:** Case of MMSE of 10 (severe dementia), shows Score 4 score on Davies-Mattis-Kipps scale with asymmetry- consistent with Fronto-temporal Dementia (FTD).



**[Table/Fig-9]:** Case with MMSE of 25 (mild dementia). On imaging, there was only Score 2 Koedam score-suggestive of early Alzheimer's Dementia (AD).



**[Table/Fig-10]:** Case of MMSE of 15 (moderate dementia). On imaging, Score 3 Fazekas with Score 3 MTA is seen consistent with mixed dementia (Alzheimer's and Vascular).

and National institute for health and clinical excellence 2018, this study also agrees that MRI of brain is investigation of choice for all patients in evaluation of dementia with a major role of MRI in determining the cause of dementia [Table/Fig-11] [18-21]. In present study, subtype was determined based on VD (using Fazekas score) and Neurodegenerative Dementia (other scores) [Table/Fig-1a,b,4]. Vascular infarcts show the strongest correlation with cognitive impairment (ROS: Religious Orders study; CFAS: Cognitive Function and Ageing Study; BLSA: Baltimore Longitudinal Study of Aging) on neuropathology findings [7]. But in this study, we lack the gold standard of brain biopsy and Fazekas score was considered for VD and its prognosis [Table/Fig-12] [22-25].

| Study | Image all | Determine subtype |
|---|---|---|
| 4th CCCDTD, 2012 [17] | No | Yes |
| EFNS task on dementia imaging, 2012 [18] | Yes | Yes |
| NICE, 2018 [19] | Yes | Yes |
| SIGN, 2006 [20] | Yes | Yes |
| AAN, 2004 [21] | Yes | No |
| This study | Yes | Yes |

**[Table/Fig-11]:** Purpose of MR imaging in cognitive impairment.
4th CCCDTD, 2012: 4th Canadian consensus conference on the diagnosis and treatment of dementia [17]; EFNS: The European federation of the neurological societies task on dementia imaging, 2012 [18]; NICE: National institute for health and care excellence-2018 NG97 [19]; SIGN: Scottish intercollegiate guidelines network 2006 [20]; AAN: American academy of neurology, 2004 [21]

| Study | Cases | Age range (Years) | VD Diagnosis | Test |
|---|---|---|---|---|
| Nun [22] | 102 | 76-100 | Number of infarcts > or <15 cm | MMSE |
| ROS [23] | 550 | 87 | Numb of infarcts | MMSE |
| BLSA [24] | 180 | 80-94 | Numb of infarcts | MMSE |
| MRC CFAS [25] | 243 | 66-100 | Regional infarcts >1 cm | MMSE |
| This study | 100 | 60-75 | Fazekas grade | MMSE |

**[Table/Fig-12]:** Variables used for evaluation of cognitive impairement in various studies.
Nun study: [22]; ROS: Religious orders study, 1993 [23]; BLSA- Baltimore longitudinal study of aging [24]; MRC CFAS: Medical research council cognitive function and ageing study [25]

MRI has been used as a diagnostic tool in evaluating the patients having moderate to severe cognitive impairment. In patients with MMSE score of less than 20, MRI was done to diagnose, classify and prognosticate cognitive impairment. This however does not provide much value as the neural damage is permanent and progressive. It is seen that in cases of early cognitive impairment, wherein patient presents with probable to mild dementia, MR imaging can be helpful to rule out VD as depicted in present study [Table/Fig-3]. It can be used as a prognostic tool, so that the type of impairment and its course can be predicted. Thus, if diagnosed early in course, appropriate treatment is started that can improve the quality of life of the patient.

Many such studies [3,5,10] showed promising results regarding discrimination between different dementias, detection of demented patients in the early stage or in the pre-symptomatic stage, follow-up of disease progression, and evaluation of cerebral condition before and after treatment. Present study could establish similar role of MRI except that follow-up was not feasible. MRI assessed lobe atrophy grade using scores and categorised severity and probable aetiology. Clinical MMSE and atrophy score grading were correlated and association was established in this study. The study aim for early inclusion of MRI Brain in all cases of cognitive impairment due to its prognostic and diagnostic role.

### Limitation(s)

Final diagnosis could not be established as brain biopsy being an invasive procedure could not be incorporated. Follow-up of patients to observe outcome, establish therapeutic role, assess reversible cause was not available as study was for one year.

## CONCLUSION(S)

MRI should be recommended in evaluation of every case of suspected or newly diagnosed dementia for the better outcome of the patient. AD, early neurodegenerative dementia are the ones where MR imaging plays a supportive role to the clinical diagnosis as treatment could be started at earliest based on aetiology. MRI plays a diagnostic role in VD where the disease progression can be haltered and if possible regressed.

Taken together, recent advancement in MRI and extensive application of these techniques in the field of dementia research certainly increase knowledge of dementia diseases and improve the management of demented patients.

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