

Use of Hachinski Ischemic Score in the Memory Clinic: Thai Experience

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Background: The validity of Hachinski Ischemic Score (HIS) in differentiating between Alzheimer's disease (AD) and Vascular dementia (VaD) has been questioned and compared with the gold standard autopsy.

Objective: To confirm that the HIS can be used to differentiate related VaD from AD in a Thai population.

Material and Method: A prospective study of 398 patients who were attending the Memory Clinic, at Siriraj Hospital between January 2001 and October 2003.

Results: The 214 patients, with a mean age of 71.15 ± 10.20 years, were classified as AD, VaD or mixed dementia (AD with cerebrovascular disease) in proportion of 60.2%, 30.4%, and 9.3% respectively. The authors propose HIS at 5 as a cut off point to differentiate patients with AD and those with VaD or AD with cerebrovascular disease with sensitivity of 85.3% and specificity of 72.9%.

Conclusion: The HIS can be applied to differentiate dementia related vascular etiology from AD in a Thai population.

Keywords: Hachinski Ischemic score, Alzheimer disease, Vascular dementia, Mixed dementia, Thai

J Med Assoc Thai 2006; 89 (11): 1822-8

Full text. e-Journal: <http://www.medassocthai.org/journal>

Dementia is common in elderly persons with a prevalence of 25% in those 65 years of age or older and 65% in those 85 years of age or older⁽¹⁻³⁾. Vascular dementia (VaD) is the second most common cause of dementia after Alzheimer's disease (AD) and may be the most common in Asian countries⁽¹⁻⁴⁾. The diagnosis of VaD is difficult due to various clinical presentations in different types of arterial disease⁽³⁻¹¹⁾. Depending on the criteria selected, the reported prevalence of VaD varied significantly^(1-3,9,10). Furthermore, the neuropathology of AD and VaD can show some degree of overlap⁽¹²⁻¹⁴⁾. Neuropathological study of AD and multi-infarct dementia revealed a fair accuracy of clinical diagnosis with sensitivity and specificity exceeding 70%^(12,14,15). Whereas mixed dementia of AD and cere-

brovascular disease as a separate group was relatively unreliably diagnosed^(16,17). The value of Hachinski Ischemic Score (HIS) in differentiating between AD and VaD was demonstrated in many studies^(12,14,15,18). However, recent researchers have shown that the HIS has no predictive value when using autopsy as the gold standard of diagnostic tool⁽¹²⁻¹⁴⁾.

The objective of the present study was to confirm that the HIS could be used to differentiate patients with clinical diagnosed dementia related to vascular etiology from AD in a Thai population.

Material and Method

This is a prospective study in analysis of data from 398 patients who came to the Memory Clinic, at the Division of Neurology, Department of Medicine Siriraj Hospital, Mahidol University between January 2001 and October 2003. All patients had symptoms of memory impairment or behavioral changes reported by

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relatives. Baseline data included demographic data, education, history of presenting symptoms and signs were recorded. The investigations of demented patients included complete blood count, blood chemistry profile including thyroid function tests, folate and B12 level, liver function tests, renal function, blood sugar, lipids, and syphilis serology study. Patients underwent neuroimaging either computerized tomography (CT) or standard magnetic resonance imaging (MRI) and single photon emission tomography (SPECT) if necessary. Data regarding HIS, activity of daily living (ADL)⁽¹⁹⁾, Thai Mental Status Examination (TMSE)⁽²⁰⁾ were also collected. Diagnoses of dementia were classified as VaD^(9,10), AD⁽²¹⁾, mixed dementia (AD and cerebrovascular disease), and other related diseases⁽¹⁷⁾. The institutional review boards of the participating centers approved the present study, and all patients provided written informed consent. Staging of dementia severity

was assessed by using the clinical dementia rating scale (CDR)⁽²²⁾.

Statistical analysis

Descriptive analysis was the main statistical method. Parameters among each group were computerized by using Chi-square test, ANOVA and T-test. P-value < 0.05 defined as having statistical significance. Receiver Operating Characteristic Curve (ROC)⁽²³⁾ was used to find the cut off diagnostic point of the HIS to identify vascular related dementia from AD. SPSS version 10.0 software was used to perform the statistical analysis.

Results

Three hundred and ninety eight patients attended the Memory Clinic at Siriraj Hospital, Mahidol University between January 2001 and October 2003.

Table 1. Demographic data between possible or probable AD, VaD and mixed dementia (n = 214)

Type of dementia/ characteristics	Possible or probable AD (n = 129)	VaD (n = 65)	Mixed dementia (n = 20)	p-value
Sex Female (%)	95 (73.6%)	36 (55.4%)	16 (80%)	0.018*
Mean age (yrs)	73.36±8.92	70.85±10.04	73.95±8.21	0.178
Education: none	34 (26.6%)	15 (23.8%)	7 (35.0%)	
1-4 yrs	50 (39.1%)	24 (38.1%)	5 (25.0%)	0.559
5-6 yrs	3 (2.3%)	5 (7.9%)	1 (5.0%)	
> 6 yrs	41 (32.0%)	19 (30.2%)	7 (35%)	
Alcohol 16 (12.6%)	9 (13.8%)	2 (10.0%)		0.979
Dyslipidemia	29 (22.8%)	26 (40.0%)	9 (45%)	0.016*
Diabetes mellitus	16 (12.6%)	27 (41.5%)	6 (30%)	<0.0001*
Ischemic Heart Disease	13 (10.2%)	13 (20.0%)	4 (20%)	0.145
History of hypertension	42 (33.1%)	41 (63.1%)	14 (70%)	<0.0001*
History of stroke	6 (4.7%)	45 (69.2%)	8 (40%)	<0.0001*
Mean TMSE	17.01	16.73	17.07	0.961
CDR : 0-1	79 (64.8%)	30 (57.7%)	12 (60%)	0.661
: 2-3	43 (35.2%)	22 (42.3%)	8 (40%)	
Mean ADL Score	10.39	11.60	12.40	0.380
Imaging : CT	88 (86.3%)	54 (88.5%)	18 (90.0%)	0.075
: MRI	8 (6.3%)	3 (9%)	1 (5%)	
: CT+MRI	6 (5.9%)	4 (6%)	1 (5%)	

AD: Alzheimer's disease; VaD: vascular dementia; mixed dementia: AD and cerebrovascular disease; TMSE: Thai Mental Status Examination; CDR: Clinical Dementia Rating Scale; ADL: Activity of Daily Living; CT: Computerised Tomography

* The Chi-square statistic is significant at the 0.05 level

Post-hoc analysis: Results are based on two-sided tests with significance level 0.05. For each significant pair, the key of the category with the smaller column proportion appears under the category with the larger column proportion
Tests are adjusted for all pairwise comparisons within a row of each innermost subtable using the Bonferroni correction

Twenty-eight (7.0%) were classified as normal subjects, 55 (13.8%) as patients with cognitive impairment, and 315 (79.1%) as patients with dementia. Two hundred and forty-nine individuals (62.6%) were women and 149 (47.4%) were men. There were 60.7% in the normal group, 60% in the cognitively impaired group, and 63.1% in the dementia group. The mean age of the patients was 71.15 ± 10.20 years.

Only 324 patients had been evaluated with HIS. Another one hundred and forty-eight patients were excluded from the analysis due to other diagnoses than AD, VaD, or mixed dementia (AD with cerebrovascular disease). The remaining 214 patients who met the criteria for dementia were recruited in the present study using DSM-IV⁽²⁴⁾. There were 129 patients in the possible or probable AD group (60.2%), 65 patients in VaD (30.4%), and 20 patients (9.3%) in mixed dementia (AD with cerebrovascular disease) with a mean age of 73.36, 70.85, and 73.95 years respectively. The baseline characteristics showed a higher percentage of women in possible or probable AD and mixed dementia in the present study (Table 1). Risk factors for cerebrovascular disease such as hypertension and history of stroke

were demonstrated significantly different among patients with AD, VaD, and mixed dementia (AD with cerebrovascular disease) and remained different in post-hoc analysis. On the other hand, in post-hoc analysis, risk factors like dyslipidemia and diabetes mellitus showed a difference only between patients with AD and VaD but cannot differentiate patients with AD from mixed dementia (AD with cerebrovascular disease). There was no statistically significant difference of the mean TMSE among these three groups. The TMSE were 17.02, 16.73, 17.08 for AD, VaD and mixed dementia (AD with cerebrovascular disease) respectively. There was also the same prevalence in CDR staging (0-1, 2-3) and level of education among patients with AD, VaD and mixed dementia (AD with cerebrovascular disease). Among individuals, items of HIS; abrupt onset, stepwise deterioration, fluctuating of symptoms, history of the presence of hypertension, history of stroke, evidence of associated atherosclerosis, focal neurological symptoms, and signs were found significantly in the majority of patients with VaD and mixed dementia (AD with cerebrovascular disease) compared with AD patients (Table 2). In post-hoc analysis, how-

Table 2. Variable items used based on Hachinski Ischemic Score to three groups; AD, VaD and mixed dementia (n = 214)

Type of dementia/ characteristics	Possible or probable AD (n = 129)	VaD (n = 65)	Mixed dementia (n = 20)	p-value
Abrupt onset	23 (17.8%)	39 (60.0%)	7 (35%)	<0.0001*
Stepwise deterioration	12 (9.3%)	24 (36.9%)	7 (35%)	<0.0001*
Fluctuating course	20 (15.5%)	21 (32.3%)	6 (30.0%)	0.019
Nocturnal confusion	45 (34.9%)	22 (33.8%)	6 (30%)	0.911
Perservation of personality	39 (30.2%)	22 (33.8%)	11 (55%)	0.093
depression	31 (24.0%)	13 (20%)	5 (25%)	0.797
Somatic complaint	52 (40.3%)	18 (27.7%)	9 (45%)	0.167
Emotional incontinence	11 (8.5%)	13 (20%)	2 (10%)	0.066
hypertension	27 (20.91%)	42 (64.6%)	14 (70%)	<0.0001*
History of stroke	6 (4.7%)	45 (69.2%)	8 (40%)	<0.0001*
Evidence of associated atherosclerosis	12 (9.3%)	20 (30.8%)	7 (35%)	<0.0001*
Focal neurological symptoms	20 (15.5%)	43 (66.2%)	9 (45%)	<0.0001*
Focal neurological sign	25 (19.4%)	47 (72.3%)	12 (60%)	<0.0001*

AD: Alzheimer's disease; VaD: vascular dementia; mixed dementia: AD and cerebrovascular disease; Bold for HIS items score 2, regular for HIS items score 1

* The Chi-square statistic is significant at the 0.05 level

Post-hoc analysis: Results are based on two-sided tests with significance level 0.05. For each significant pair, the key of the category with the smaller column proportion appears under the category with the larger column proportion
Tests are adjusted for all pairwise comparisons within a row of each innermost subtable using the Bonferroni correction

ever, items of abrupt onset, fluctuating of symptoms remained significantly different only for differentiation between AD from VaD but cannot be used to differentiate between AD and mixed dementia (AD with cerebrovascular disease). Interestingly, emotional incontinence, nocturnal confusion, depression, perseveration of personality, and somatic complaints cannot be differentiated among these three types of dementia.

The authors grouped the patients into two groups, AD in one group and VaD and mixed dementia (AD with cerebrovascular disease) in the other group. The authors found that prevalence of items in HIS like abrupt onset, stepwise deterioration, fluctuating of symptoms, history of the presence of hypertension, history of stroke, evidence of associated atherosclerosis, focal neurological symptoms and signs showed significant difference between the two groups. The ROC of the HIS demonstrated area under the curve of 0.839 ± 0.030 (SE) (95% CI; 0.783-0.886) (Fig. 1). At the score of 5 offered the best cut off diagnostic point of HIS to differentiate patients with dementia related to vascular etiology; VaD and mixed dementia, from the

patients with AD, with the sensitivity of 85.3% (95% CI; 78.0-90.9), specificity of 72.9% (95% CI; 62.2-82.0), positive predictive value of 82.7% and negative predictive value of 76.5%; respectively (Fig. 2).

Discussion

In the present study, the authors report HIS of 5 as the best cut off diagnostic point to differentiate between AD and dementia related vascular causes (VaD and mixed dementia (AD with cerebrovascular disease)).

Despite new developments in the concept of vascular dementia, the HIS and its modified version continued to be widely used in the clinical differentiation of AD and ischemic vascular dementia^(6,14,18). The two cutoff points of HIS were used, the score of equal or less than 4 is more likely to have neurodegenerative disease like AD and the score of equal or more than 7 to have VaD. However, many questions remained for patients who have intermediate scores and in those who were expected to have mixed dementia (AD with cerebrovascular disease). Furthermore, recent studies showed that vascular risk factors may play important

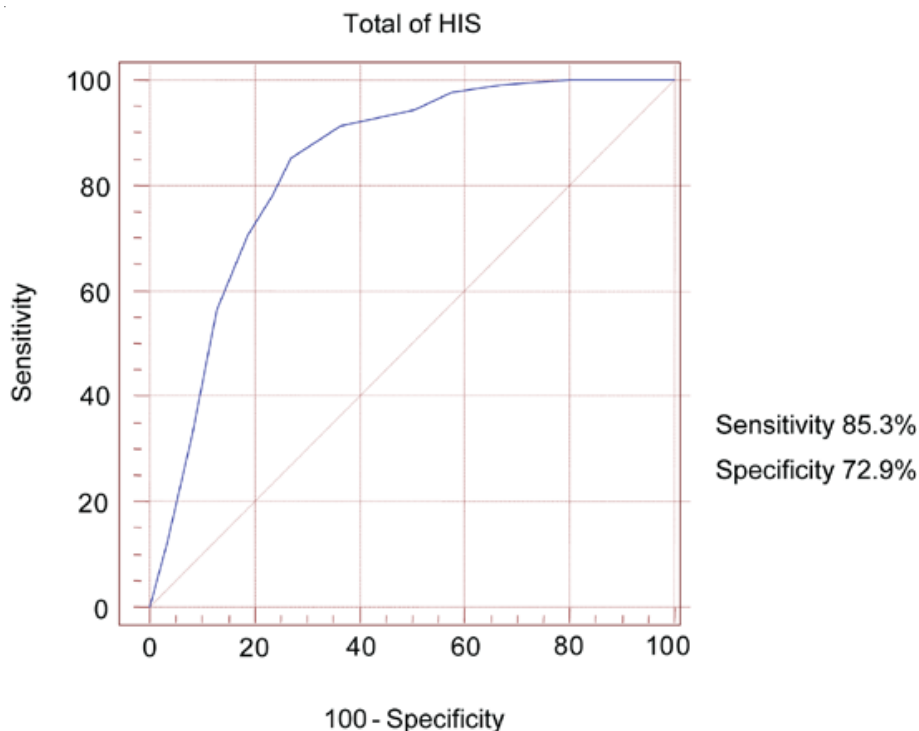
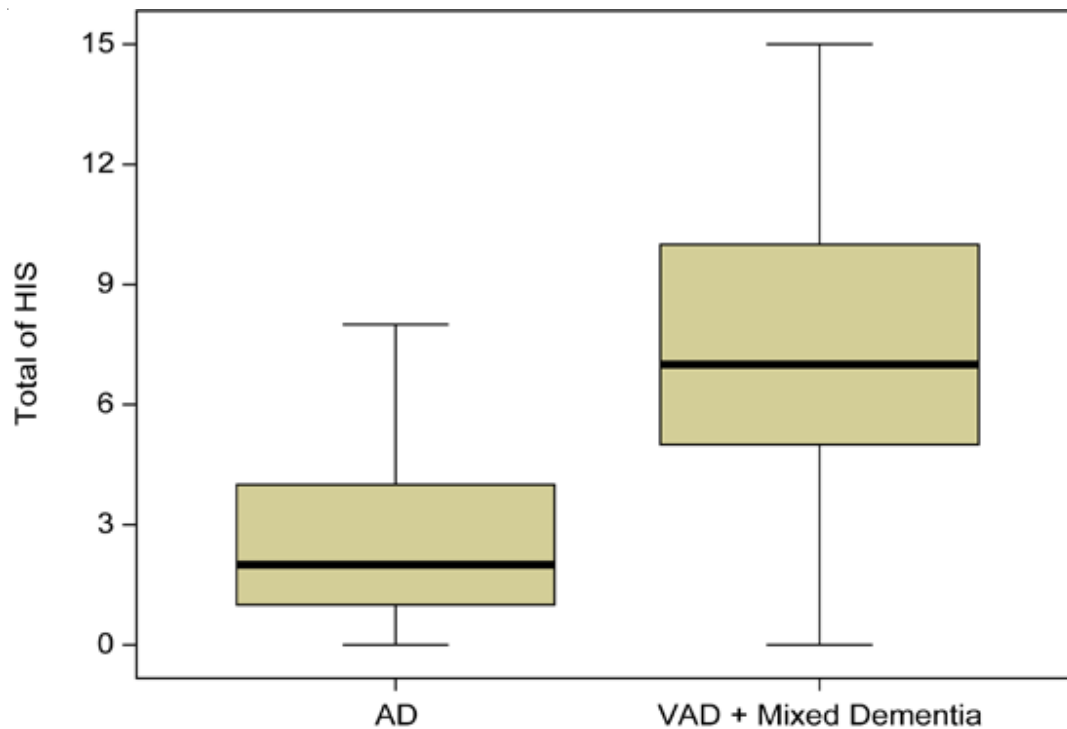


Fig. 1 Graph of VaD combined with mixed dementia patients (AD with cerebrovascular disease) showed Receiving Operating Characteristic Curve (ROC) = 0.839 by using Hachinski Ischemic Score at "5"



AD: Alzheimer's disease; VaD: vascular dementia; mixed dementia: AD and cerebrovascular disease

Fig. 2 Graph shows the Hachinski Ischemic Score at "5" was the best to differentiate AD from VaD and mixed dementia

roles in the pathogenesis of neurodegenerative disease and dementia related vascular etiology. The authors demonstrated that HIS of equal or more than 5 is important to alert clinicians to underlying dementia related vascular etiology (VaD, mixed dementia of AD with cerebrovascular disease and mixed AD and VaD) from neurodegenerative disease such as AD group, with the sensitivity of 85.3% and specificity of 72.9%.

To date many authorities suggest using neuroimaging as a diagnostic tool for vascular dementia^(9,10,18). Nevertheless, in developing countries, imaging techniques such as CT or MRI are not widely available. The HIS is significantly clinically useful and gives a reasonable sensitivity and specificity for clinical diagnosis of VaD⁽⁶⁾. In particular, it gives more accuracy in those who have more prominent cortical lesions than just subcortical infarction^(11,12,14).

The present study showed that items in HIS like stepwise deterioration, history of the presence of hypertension, history of stroke, evidence of associated atherosclerosis, focal neurological symptoms and signs can be used to differentiate neurodegenerative disease

such as AD from dementia related to vascular etiologies either VaD or mixed dementia but can not separate VaD from mixed dementia. Furthermore, items like abrupt onset and fluctuating of symptoms were more suggestive to differentiate VaD from AD rather than mixed dementia from AD. Moreover, emotional incontinence, nocturnal confusion, depression, perseveration of personality and somatic complaints were poorly differentiated vascular etiology from degenerative causes.

There are several points of attention. Firstly, in Thailand, the authors have usually not obtained pathological proof for definite diagnosis in the clinical practice. Because of cultural and traditional beliefs, the authors rarely have an autopsy done in patients with dementia. All of the patients in the present study were diagnosed with possible or probable AD, but none definite AD. Great care was taken to exclude other causes of dementia by clinical and ancillary investigations^(8,13).

Secondly, patients in the present study were found to have multiple risk factors for atherosclerosis. It is also true among dementia persons in Asia. Pre-

vious reports have suggested that the HIS was correlated well with degree of cerebral infarction. This may explain why HIS in the present study had a reasonable large area under the ROC curve.

Thirdly, the authors utilized MRI much less often than CT in patients at the authors' memory clinic because of socioeconomic reasons. Nevertheless, MRI can offer a higher yield in detecting vascular etiologies especially white matter changes. Therefore, in the present study, the authors may have under diagnosed cerebrovascular disease and the cut off diagnostic point may be less than in the present studies. For that reason, CT may not be an appropriate technique approach to discriminate demented patients from the others.

In conclusion, the present study showed the validity of HIS in differentiating dementia related vascular etiology from neurodegenerative disease like AD at the cut off point of "5" with the sensitivity of 85.3% and specificity of 72.9% in a Thai population.

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ประโยชน์ของการใช้ Hachinski Score ในคลินิกโรคความจำ

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ข้อมูลพื้นฐาน: การใช้ Hachinski Ischemic Score (HIS) ในการวินิจฉัยภาวะสมองเสื่อมที่มีสาเหตุจากหลอดเลือดสมอง (VaD) แยกออกจากโรคอัลไซเมอร์ (AD) ยังคงเป็นปัญหาเรื่องความถูกต้องแม่นยำเมื่อเทียบกับการตรวจศพ ซึ่งเป็นวิธีมาตรฐาน

วัตถุประสงค์: ยืนยันว่า HIS ใช้วินิจฉัยแยก VaD จาก AD ในผู้ป่วยชาวไทยได้

วัสดุและวิธีการ: ศึกษาแบบไปข้างหน้าในผู้ป่วย 398 คนในคลินิกความจำของโรงพยาบาลศิริราชระหว่าง มกราคม พ.ศ. 2544 ถึง ตุลาคม พ.ศ. 2546

ผลการศึกษา: ผู้ป่วย 214 คน มีอายุเฉลี่ย 71.15 ± 10.20 ปี เป็น VaD 60.2%, AD 30.4% และ mixed dementia 9.3%. ค่า HIS ที่ 5 เป็นจุดที่ใช้วินิจฉัยแยก VaD และ mixed dementia ออกจาก AD โดยมีความไวเท่ากับ 85.3% และความจำเพาะเท่ากับ 72.9%

สรุป: HIS สามารถใช้ในการวินิจฉัยแยกโรค VaD และ mixed dementia ออกจาก AD ในผู้ป่วยชาวไทยได้