Patterns of Single Photon Emission Tomography (SPECT) among Patients with Dementia in the Memory Clinic at Siriraj Hospital

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Objective: *The authors hypothesized that there is a pattern difference in cerebral perfusion of the 99-Technitium L, L-ethyl cysteinate dimer Single Photon Emission Computer Tomography (99-Tc ECD SPECT) between mild and moderate to severe dementia.*
Material and Method: *The authors reported a retrospective study in the Memory Clinic, Siriraj Hospital between January 2001 and October 2003 including only patients with Alzheimer's disease, vascular dementia, and mixed dementia. Clinical dementia rating (CDR) was used to document dementia severity. Patterns of hypoperfusion were classified into no definite hypoperfusion, regional hypoperfusion, and diffused hypoperfusion.*
Results: *One hundred and seven patients were included in the present study. Only mean Thai Mental State Examination (TMSE) score was different between the two groups. There was no significant correlation between pattern of hypoperfusion in brain SPECT and severity of dementia.*
Conclusion: *The authors cannot demonstrate the pattern of hypoperfusion of 99-Tc ECD SPECT among patients' difference in dementia severity.*

Keywords: *SPECT, Dementia, Thai*

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Memory clinics were introduced in the United States in the mid 1970s with the aim of identifying patients in the elderly stages of dementia and to act as a resource and database for research into memory impairments[1]. Since then, they have spread around the world and the number and range of assessments offered at such clinics has increased in the context of demographic changes, improved assessment techniques and emerging treatments for patients with dementia[2]. Neuroimaging techniques such as computer tomography (CT), magnetic resonance imaging (MRI), and single photon emission computer tomography (SPECT) imaging, have been used to evaluate a wide variety of conditions of dementia[3]. 99-Technitium L, L-ethyl cysteinate dimer SPECT (99-Tc ECD SPECT) is one of the most successful and widely used for brain perfusion imaging in various conditions including dementia[4]. Brain SPECT provides tridimentional information on the perfusion and metabolic status of brain tissue. This information is often complementary to the anatomical details provided by structural neuroimaging techniques[5]. Brain SPECT can provide substantial assistance in the initial diagnosis of dementia and in the differential diagnosis of specific dementia

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disorders[6-9]. However, the authors do not know the correlation between severity of dementia and the pattern of hypoperfusion of the brain SPECT.

The authors analyzed the clinical data on patients' characteristics of those who had brain SPECT and clinical dementia rating (CDR)[10]. The authors also looked at problems that led them to medical consultation at the memory clinic. The authors hypothesized that there is a difference in patterns of hypoperfusion in brain 99-Tc ECD SPECT between patients with mild dementia and patients with moderate to severe dementia.

Material and Method

This retrospective study identified the patients in the Memory Clinic, Siriraj Hospital between January 2001 and October 2003.Demographic data such as age, sex, education, body weights, chief complaints, duration of complaints, and Thai Mental State Examination (TMSE)[11] were collected. A physical examination was performed by doctors together with standard physical investigation as appropriate. These were performed to assess general physical health and to detect any potentially reversible causes of memory impairments[12]. Hematological investigations included a complete blood count, urea and electrolytes, fasting blood glucose, thyroid function test, and syphilis serology. Other investigations included brain imaging, even CT or MRI or both, electrocardiogram, and Tc-99m ECD SPECT. The results of these investigations were used in reaching the diagnosis, but do not form the focus of the present report. This research protocol was approved by the committee of Siriraj Hospital Research Review Board.

To document dementia severity, the clinical dementia rating scale (CDR) was completed by doctors and psychologists at the end of the assessment process. This scale examines the domains of memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Impairment in any of these areas was assigned a corresponding score: no impairment = 0; questionable impairment = 0.5; mild, moderate, and severe impairment were assigned score of 1, 2, and 3 respectively.

As a result of the assessments and investigations described above, it was possible to derive diagnosis the specific types of dementia according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[13]. The diagnosis was made at the consensus conferences. The panel consists of consultant neurologists, residents in neurology, and neuropsychologists.

Only Alzheimer's disease (AD), vascular dementia (VaD), and mixed dementia that had the result of brain SPECT were included in the present study. Severity in dementia was separated to two groups: questionable to mild (CDR 0.5-1), and moderate to severe (CDR 2-3). Patterns of hypoperfusion in brain SPECT were separated into three main groups: normal and no definite hypoperfusion, regional hypoperfusion that included parietotemporal, and frontal hypoperfusion, and diffused hypoperfusion.

Statistical analysis

Statistical analysis was done by SPSS Version 10.0. Clinical data on patients' characteristics and problems of the patients, which led them to medical consultation, were described by descriptive analysis. Differences among some demographic data of patients between mild dementia and moderate to severe dementia were compared by unpaired t-test. Analysis in association between patterns of brain SPECT hypo-perfusion and severity of dementia was done by Pearson Chi-Square test. A difference in mean TMSE in mild and moderate to severe group was done by two way ANOVA test. Statistical significance was defined by $p < 0.05$.

Results

There were 398 patients during the study period, but only 174 patients had brain SPECT performed. Data were recruited only in 107 patients who had CDR staging and diagnosis of AD (82 patients, 76.6%), VaD (15 patients, 14.0%), and mixed dementia (10 patients, 9.4%). Thirty (28%) patients were men, and 77 (72%) patients were women. The age range was 49-90 years with a mean of 71.69 ± 9.19 years. Twenty-three (21.5%) patients were considered as having no school education, 41 (38.3%) patients had 1-4 years of education, two (1.9%) patients had 4-6 years of education, and 41 (38.3%) patients had more than 6 years of education. Ninety (84.1%) patients with dementia had a chief complaint of memory problems, and seventeen (15.9%) patients had behavioral changes leading to medical consultation. The mean age was 71.95 ± 9.06 in the mild group and 71.06 ± 9.61 years in the moderate to severe group that was not different ($p = 0.996$). There were statistically significant differences in the mean TMSE score between mild (19.91) and moderate to severe (13.13) groups ($p = 0.019$). The mean length of clinical history was between 2-3 years in both mild and moderate to severe groups despite the difference in

staging (p = 0.227). There was no statistically significant difference in education between these two groups (6.63 years vs 5.29 years, p = 0.135). (Table 1). Among these 107 patients with dementia, 91 patients (85.05%) showed abnormal patterns of perfusion on brain SPECT. In both groups, the majority had regional hypoperfusion in the SPECT finding (64.5% in the mild group and 58.1% in the moderate to severe group). Among these with regional hypoperfusions, four patients had frontal hypoperfusion (3 in mild group and 1 in moderate to severe group), and 63 patients had temporoparietal hypoperfusion (46 in mild group and 17 in moderate to severe group). Those with mild dementia showed a trend to have no more definitive hypoperfusion in SPECT scan than in moderate to severe dementia (17.1% vs 9.7%). Diffused hypoperfusion in SPECT scan was found in one third of the patients with moderate to severe dementia. There was no significant statistical difference between hypoperfusion patterns of the brain SPECT and the severity of dementia (p = 0.242). (Table 2.) There were differences in the mean TMSE of patients in the mild and moderate to severe groups categorized by the pattern of the brain SPECT. However, there was no significant difference in mean TMSE among each hypoperfusion patterns of the brain SPECT (p = 0.200) (Table 3.)

Table 1. Demographic data of patients compared between mild and moderate to severe groups (n = 107)

	Mild	Moderate to severe	p-value
Number (%)	76 (71)	31 (29)	
Age (years)	71.95 ± 9.06	71.06 ± 9.61	0.996
TMSE	19.91 ± 4.81	13.13 ± 6.56	0.019*
Duration (years)	2.48 ± 1.27	2.55 ± 1.39	0.227
Education (years)	6.63 ± 4.86	5.29 ± 4.66	0.135

Values are mean ± SD* = $p < 0.05$

Table 2. The Single Photon Emission Computer Tomography patterns of patients with Alzheimer's disease, vascular dementia, and mixed dementia (n = 107)

Dementia Severity / SPECT pattern	Mild N (%)	Moderate to severe N(%)	Total N(%)	p-value
No definite hypoperfusion	13 (17.1)	3 (9.7)	16 (15.0)	-
Regional hypoperfusion	49 (64.5)	18 (58.1)	67 (62.6)	-
Diffuse hypoperfusion	14 (18.4)	10 (32.2)	24 (22.4)	-
Total	76 (100)	31 (100)	107 (100)	0.242

Table 3. Mean of TMSE in patients with AD, VaD, and mixed dementia categorized by severity of dementia and SPECT pattern

TMSE in each group	Mild Mean	Moderate to severe Mean	Total Mean	p-value
No definite hypoperfusion	19.62	13.00	18.38	-
Regional hypoperfusion	19.93	14.86	18.55	-
Diffuse hypoperfusion	20.14	10.05	15.94	-
Total	19.91	13.13	17.93	0.200

TMSE = Thai Mental State Examination
VaD = Vascular dementia
AD = Alzheimer's disease
SPECT = Single Photon Emission Computer Tomography

Discussion

The authors demonstrated that 84.1% of patients in the present study had memory problems as the chief complaint of which 15.9% had behavioral problems as the chief complaint. The SPECT study with AD, VaD, and mixed dementia did not show different patterns of hypoperfusion between the mild and moderate to severe dementia groups. The majority in both groups had regional hypoperfusion in the SPECT study.

This is the first paper among demented Thai patients that showed the results of SPECT study in a Thai experience. Previous neuropsychological and neuropathological studies in patients with AD showed that frontal involvement was more prominent among severely demented patients[14-17]. The present results did not support these findings. Some neuropathological studies also showed that there are other factors complicated with pathological changes and dementia severity such as advanced age in AD is associated with lower densities of senile plaques and neurofibrillary tangles[18], and others showed that senile plaques were only related to dementia severity in the lower range and no further increase in plaque burden was observed beyond a CDR of 2[19]. Additionally, diffused hypoperfusion of 99-Tc ECD SPECT was found in both the mild and moderate to severe groups. The majority of patients in dementia regardless of the staging showed regional hypoperfusion. The present findings suggested that differences in patterns of hypoperfusion of the brain SPECT cannot distinguish the severity of dementia. It is known that parietotemporal hypoperfusion of the brain SPECT is commonly found in patients with AD[20,21]. Recently, studies in patients with mild dementia or very early AD revealed regional hypoper-fusion in posterior cingulated cortex[22], hippocampus-amygdala complex, thalamus and anterior cingulated cortex[23,24]. They concluded that abnormal cerebral blood flow could be found even in the predemented stage. A few reports in patients with mild cognitive impairment also showed blood flow reduction in prefrontal, frontal, and parietal areas[25]. It means that frontal lobe involvement in brain SPECT is not always present only in the late state of dementia. Because SPECT patterns are not only associated with duration and severity of dementia, but also complicated by age of onset[26], and years of education[27], this reason can explain the negative result in the present study. The relationship among abnormal perfusion, metabolic changes, and pathological changes need to be investigated in the future.

In the present study, patients with mild and moderate to severe dementia had the same duration of memory complaint. This may be related to education of the patients and the families. The authors found that patients with moderate to severe dementia had lower educational levels. This may mean that caregivers of these patients did not recognize dementia symptoms at an early state. Recent scientific data showed earlier treatment of patients with dementia give better functional outcome[28]. The authors encourage medical and caregiver societies for patients with dementia to set up activities to alert high public awareness of dementia.

The strength of the present study was that the authors demonstrated that 85.05% of patients with dementia showed abnormal perfusion patterns. Since functional imaging is not available in all general hospitals, brain SPECT should be considered selectively as one of the biomarkers in patients with dementia adjunct to clinical evaluation and structural imaging in tertiary care hospitals in diagnosing and differentiating the specific types of dementia. The weakness of the present study was that the authors did not have data from brain SPECT in normal subjects that could have helped to elicit sensitivity and specificity of 99-Tc ECD brain SPECT for diagnosis in patients with dementia; larger sample size may be needed to confirm the authors' findings.

In conclusion, there are different abnormal patterns of abnormal hypoperfusion reported through brain SPECT utilized in patients with dementia. The authors found the differences in pattern of hypoperfusion in 99-Tc ECD SPECT were not related to clinical severity of dementia in the Thai population.

References

1. Lindesay J, Marudkar M, van Diepen E, Wilcock G. The second Leicester survey of memory clinics in the British Isles. Int J Geriatr Psychiatry 2002; 17: 41-7.
2. O'Brien JT, Ames D, Burns A. Dementia. 2nd ed. London: Edward Arnold; 2000.
3. Masdeu JC, Brass LM, Holman BL, Kushner MJ. Brain single-photon emission computed tomography. Neurology 1994; 44: 1970-7.
4. Camargo EE. Brain SPECT in neurology and psychiatry. J Nucl Med 2001; 42: 611-23.
5. Catafau AM. Brain SPECT in clinical practice. Part I: perfusion. J Nucl Med 2001; 42: 259-71.
6. Buttler CRE, Costa DC, Walker Z, Katona CLE. PET and SPECT imaging in the dementias. In:

Murray IPC, Ell PJ, editors. Nuclear medicine in clinical diagnosis and treatment. 2nd ed. Edinburgh: Churchill Livingstone; 1998: 713-28.
7. Ryding E. SPECT measurements of brain function in dementia; a review. Acta Neurol Scand Suppl 1996; 168: 54-8.
8. Brooks DJ. Functional imaging techniques in the diagnosis of non-Alzheimer dementias. J Neural Transm Suppl 1996; 47: 155-67.
9. Devous MD Sr. Functional brain imaging in the dementias: role in early detection, differential diagnosis, and longitudinal studies. Eur J Nucl Med Mol Imaging 2002; 29: 1685-96.
10. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. Br J Psychiatry 1982; 140: 566-72.
11. Poungvarin N. Thai mental state examination (TMSE). Train the Brain Forum Committee. Siriraj Hosp Gaz 1993; 45: 359-74.
12. Wilcock GK, Bucks RS, Rockwood K. Diagnosis and management of dementia. Oxford: Oxford University Press; 1999.
13. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: APA Press; 1994.
14. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. Br J Psychiatry 1982; 140: 566-72.
15. Braak H, Braak E. Neuropathological stageing of Alzheimer-related changes. Acta Neuropathol (Berl) 1991; 82: 239-59.
16. Grady CL, Haxby JV, Horwitz B, Sundaram M, Berg G, Schapiro M, et al. Longitudinal study of the early neuropsychological and cerebral metabolic changes in dementia of the Alzheimer type. J Clin Exp Neuropsychol 1988; 10: 576-96.
17. Locascio JJ, Growdon JH, Corkin S. Cognitive test performance in detecting, staging, and tracking Alzheimer's disease. Arch Neurol 1995; 52: 1087-99.
18. Perry RJ, Hodges JR. Attention and executive deficits in Alzheimer's disease. A critical review. Brain 1999; 122(Pt 3): 383-404.
19. Tiraboschi P, Hansen LA, Thal LJ, Corey-Bloom J. The importance of neuritic plaques and tangles to the development and evolution of AD. Neurology 2004; 62: 1984-9.
20. Prohovnik I, Perl DP, Davis KL, Libow L, Lesser G, Haroutunian V. Dissociation of neuropathology from severity of dementia in late-onset Alzheimer disease. Neurology 2006; 66: 49-55.
21. Masterman DL, Mendez MF, Fairbanks LA, Cummings JL. Sensitivity, specificity, and positive predictive value of technetium 99-HMPAO SPECT in discriminating Alzheimer's disease from other dementias. J Geriatr Psychiatry Neurol 1997; 10: 15-21.
22. Jobst KA, Barnetson LP, Shepstone BJ. Accurate prediction of histologically confirmed Alzheimer's disease and the differential diagnosis of dementia: the use of NINCDS-ADRDA and DSM-III-R criteria, SPECT, X-ray CT, and Apo E4 in medial temporal lobe dementias. Oxford Project to Investigate Memory and Aging. Int Psychogeriatr 1998; 10: 271-302.
23. Okamura N, Shinkawa M, Arai H, Matsui T, Nakajo K, Maruyama M, et al. Prediction of progression in patients with mild cognitive impairment using IMP-SPECT. Nippon Ronen Igakkai Zasshi 2000; 37: 974-8.
24. Ishiwata A, Kitamura S, Nagazumi A, Terashi A. Cerebral blood flow of patients with age-associated memory impairment and the early stage of Alzheimer's disease. A study by SPECT using the ARG method. Nippon Ika Daigaku Zasshi 1998; 65: 140-7.
25. Johnson KA, Jones K, Holman BL, Becker JA, Spiers PA, Satlin A, et al. Preclinical prediction of Alzheimer's disease using SPECT. Neurology 1998; 50: 1563-71.
26. Encinas M, De Juan R, Marcos A, Gil P, Barabash A, Fernandez C, et al. Regional cerebral blood flow assessed with 99mTc-ECD SPET as a marker of progression of mild cognitive impairment to Alzheimer's disease. Eur J Nucl Med Mol Imaging 2003; 30: 1473-80.
27. Blake SE, Caldwell CB, Leibovitch FS. SPECT imaging in Alzheimer's disease (AD): perfusion patterns, demographic variables, and correlations with the AD assessment scale. 1997; [under review].
28. Liao YC, Liu RS, Teng EL, Lee YC, Wang PN, Lin KN, et al. Cognitive reserve: a SPECT study of 132 Alzheimer's disease patients with an education range of 0-19 years. Dement Geriatr Cogn Disord 2005; 20: 8-14.
29. Doody RS, Stevens JC, Beck C, Dubinsky RM, Kaye JA, Gwyther L, et al. Practice parameter: management of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001; 56: 1154-66.

รูปแบบความผิดปกติของSPECT ของผู้ป่วยสมองเสื่อมในคลินิกความจำ โรงพยาบาลศิริราช

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วัตถุประสงค์: *คณะผู้วิจัยตั้งสมมติฐานว่ารูปแบบความผิดปกติของ 99-Tc ECD SPECT จะแตกต่างกันตามความรุนแรงของภาวะสมองเสื่อม*

วัสดุและวิธีการ: *การศึกษาแบบย้อนหลังในผู้ป่วยอัลไซเมอร์ ภาวะสมองเสื่อมจากโรคหลอดเลือดสมอง และภาวะสมองเสื่อมแบบผสม ในคลินิกความจำโรงพยาบาลศิริราช ตั้งแต่ มกราคม พ.ศ. 2544 - ตุลาคม พ.ศ. 2546 โดยใช้ clinical dementia rating ประเมินความรุนแรงของภาวะสมองเสื่อม*

ผลการศึกษา: *ข้อมูลของผู้ป่วย 107 คนที่ศึกษา พบว่ามีแค่คะแนน TMSE ที่แตกต่างกันใน 2 กลุ่มแต่ไม่พบความแตกต่างของรูปแบบความผิดปกติของ 99-Tc ECD SPECT กับความรุนแรงของ ภาวะสมองเสื่อม*

สรุป: *ไม่มีความแตกต่างในรูปแบบความผิดปกติของ 99-Tc ECD SPECT กับความรุนแรงของภาวะสมองเสื่อมในผู้ป่วยไทย*