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The Utility of Subset of Subjective Memory Complaint Questionnaire and Mini-Mental State Examination for Dementia Screening

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Objective : Purpose of this study was to assess the potential added values of Subjective Memory Complaint Questionnaire (SMCQ) combined with Mini-Mental State Examination (MMSE) in developing a brief screening battery to improve the early detection rate of dementia in community setting.

Methods : Non-depressed community-dwelling Korean elderly aged 65 years and older who 945 randomly selected and 734 voluntarily involved were recruited. Dementia was diagnosed using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. Diagnostic ability of 10 point SMCQ subscale for everyday memory (SMCQ-E) for dementia was evaluated. Additive values of SMCQ-E combined with MMSE for dementia screening and the economic benefits of SMCQ-E and its combination with MMSE were also evaluated.

Results : Overall area under the curve values of SMCQ-E were 0.605 (0.565−0.646) for nonrandom sample and 0.836 (0.783−0.890) for random sample. When SMCQ-E was combined with MMSE using 'AND' rule, accuracy, specificity, positive predictive values and positive likelihood ratio were increased than those of MMSE. While SMCQ-E was combined the MMSE using 'OR' rule, sensitivity and negative predictive values were increased and negative likelihood ratio were decreased than those of SMCQ-E and MMSE. When SMCQ-E and MMSE combined with AND rule, total cost for dementia screening was reduced to about 80% compared to MMSE single use model.

Conclusion : Results of this study showed that brief SMCQ-E and its combination with MMSE could be used to dementia screening with cost effective manner.

KEY WORDS : Subjective memory complaints · Subjective memory complaints questionnaire · Reliability · Validity · Dementia.

Introduction

Dementia is one of the major public health problems in modern society with prevalence ranging from 3% to 13% among people aged 65 and over.[1)] In an effort to reduce the societal burden of dementia by vigorous researches, accumulating evidences showed that pharmacological and non-pharmacological interventions might delay the progression of disease and admission to institutional setting. Early detection and diagnosis of dementia would be fundamental to any treatment effort. However, nearly two thirds of dementia cases might remain undetected unfortunately.[2,3)] Although US Preventive Service Task Force (USPSTF) concluded that the evidence is insufficient to recommend for or against routine screening for dementia in non-symptomatic older adults,[4)] growing consensus including USPSTF recommends routinely screening subjects for cognitive decline is suspected based on direct observation, subjects reports or concerns raised by family members.[4,5)]

Subjective memory complaints (SMC) might be one of the

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first symptoms of dementia or cognitive decline. It was associated with the increased risk of dementia and changes in hippocampus and cerebral white matter.[6-8] However, association between SMC and objective cognitive function was not consistently reported in cross sectional studies.[9] Previous study showed that SMC questionnaire (SMCQ) was associated with results of objective cognitive tests and had moderate diagnostic ability for dementia.[10] But potential benefits of its combination with objective cognitive tests such as Mini-Mental State Examination (MMSE) were not evaluated in that study.

Thus, the primary purpose of this study was to assess the potential added values of SMCQ combined with MMSE in developing a brief screening battery to improve the early detection rate of dementia in community setting.

Subjects and Methods

Subjects

Non-depressed community-dwelling Korean elderly aged 65 years and older were recruited from two ways. Total 1,318 randomly selected subjects were recruited from two population-based epidemiological studies on health and aging in Korea. From the Korean Longitudinal Study on Health and Aging,[11] 692 subjects were recruited and from Jungu in Seoul study (unpublished data), 626 subjects were recruited based on elector's list. In addition, 1,181 volunteer subjects were recruited from dementia outpatient clinic in Seoul National University Bundang Hospital and National Dementia Early Detection Program (NDEDP) which was freely serviced at Community Health Center in Yongin and Seoul.

All of the subjects were subjected to a standardized clinical interview, physical and neurological examinations, which were administered by a neuropsychiatrist with advanced training in dementia research in accordance with the protocol of the Korean Version of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) clinical and neuropsychological assessment battery (CERAD-K) in which MMSE-Korean version in CERAD (MMSE-KC) is included.[12] The diagnoses of dementia and Clinical Dementia Rating (CDR)[13] were made by a panel of neuropsychiatrists with expertise in dementia research. Diagnoses of dementia were made according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria.[14]

Korean version of the Geriatric Depression Scale (GDS-K, 30 item version)[15] was also administered for the evaluation of concomitant depressive symptoms. To exclude the effect of depressive disorder, GDS score below 17 which was suggested as an optimal cut off point of major depression in Korean elderly were used.[15] Thus, data from total 1,679 non-depressed community living elderly was entered into further analysis.

All of the subjects who participated in this study were fully informed regarding study participation, and informed consent was obtained from each subject or their legal guardians. The study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB No. B-0508/023-003).

SMCQ-E

SMCQ consists of two subscales ; 4 point SMCQ subscale for general judgment of memory (SMCQ-G) and 10 point SMCQ subscale for everyday memory (SMCQ-E). To enhance the feasibility and reliability of each item in the elderly, the subject's responses to each question were restricted to either 'Yes' or 'No.' Higher SMCQ scores are indicative of more severe SMC. Detailed developmental process and description on items of SMCQ was described in previous report.[10]

Because SMCQ-E has higher correlation with results of objective cognitive tests than SMCQ-G in the developmental study,[10] it would be plausible that SMCQ-E could have more benefits when it used in combination with MMSE. Thus, in this study, we measured SMC by SMCQ-E and tested its psychometric properties for dementia screening. Reported internal consistency and Intra class coefficient of test-retest reliability for SMCQ-E were 0.827 and 0.836 ($p<0.001$), respectively.

Analysis

In the first step, diagnostic ability of SMCQ-E for dementia was evaluated. To compare the diagnostic ability of SMCQ-E to that of MMSE, receiver operator characteristic (ROC) curve analyses were performed and area under the ROC curves (AUC) were compared by calculating a critical ratio z proposed by Hanley and McNeil (1983).[16] The z was defined as :

$$z=\frac{A_1-A_2}{\sqrt{SE_1^2+SE_2^2-2rSE_1SE_2}}$$

where A_1 and SE_1 refer to the observed AUC and estimated standard error of the AUC associated with test 1, A_2 and SE_2 refer to the observed AUC and estimated standard error of the AUC associated with test 2, and r refers to the estimated correlation coefficient between A_1 and A_2. Note that z follows the standard normal distribution.

In a second step, additive values of SMCQ-E combined with MMSE for dementia screening was evaluated. Cut off point of SMCQ-E which could maximize the sensitivity of SMCQ-E was selected for this evaluation and that of MMSE was selected as z score -1.5, which was commonly used for dementia screening. Combination of SMCQ-E and MMSE were made by AND rule (screen positive when both tests were positive) and OR rule (screen positive when one of both tests were positive). Seven indices including diagnostic accuracy, sensi-

tivity, specificity, negative predictive value (NPV), positive predictive value (PPV), positive likelihood ratio (LR+), negative likelihood ratio (LR-) were calculated. To explore the difference between sampling methods, models were separately analyzed in non-random and random samples. Models were also tested after excluding moderate to severe dementia subjects.

In the third step, to evaluate the economic benefits of SMCQ-E and its combination with MMSE for dementia screening in NDEDP, total economic cost of dementia diagnosis for 10,000 community living elderly was simulated based on the results of random sample analysis. NDEDP consist of dementia screening phase with cost free and dementia diagnostic phase with fixed payment system. For screening phase, cost of MMSE and SMCQ-E were estimated based on a fee from Korean National Health Insurance and for dementia diagnostic phase, cost of dementia diagnosis was estimated based on maximum payment per capita of NDEDP. Subjects with positive result from screening tests were entered into diagnostic stage.

All statistical analyses were carried out using SPSS 11.0 (SPSS Inc., Chicago, IL, USA).

Results

Clinical characteristics of the subjects

Among total 1,679 non-depressed community living subjects, 945 subjects were randomly selected and 734 subjects were volunteers (Table 1). Randomly selected subjects were older and had less depressive symptoms, lowered MMSE score and high SMCQ-E scores than non-random sample ($p<0.01$). Total 413 subjects had dementia, of which 83.1% of the dementia subjects had mild severity (39.1% in non-random sample, 5.9% in random sample). Demented subjects were significantly older, low educated than non-demented subjects ($p<0.01$).

Table 1. Demographic and clinical characteristics of the subjects

	Non-random sample	Random sample
Number	734	945
Age (years)	73.8±6.9	74.7±8.5*
Gender (women, %)	459 (62.5)	497 (52.6)†
Education (years)	7.5±5.6	7.8±5.6
Geriatric depression scale	8.7±4.4	8.2±4.4*
SMCQ-E	3.7±2.9	2.3±2.6*
MMSE	19.9±5.9	23.5±5.0*
Dementia patients (n, % to total)	349 (47.5)	64 (6.8)†
Mild severity (n, % to total)	287 (39.1)	56 (5.9)†

* : Statistically different from non-random sample (independent t-test, $p<0.01$), † : Statistically different from non-random sample (chi-square test, $p<0.01$). SMCQ-E : everyday memory subscale of subjective memory complaints questionnaire, MMSE : Mini-Mental State Examination

Diagnostic ability of SMCQ-E

To evaluate the screening ability of SMCQ-E, ROC curve analyses were performed (Table 2). Overall AUC values of SMCQ-E were 0.605 (0.565−0.646) for nonrandom sample and 0.836 (0.783−0.890) for random sample. Those values were significantly lower than those of MMSE ($z=9.64$ in non-random sample, $z=2.53$ for random sample, all were $p<0.05$).

Combination of SMCQ-E with MMSE

Results of ROC analysis showed that sensitivity of SMCQ-E at cut off point 0/1 was comparable to that of MMSE at -1.5 standard deviation. At this point, sensitivity of SMCQ-E was 0.891 for non-random sample and 0.953 for random sample. Psychomteric properties of several models were evaluated using selected cut off points in both non-random and random sample (Table 3). When SMCQ-E was combined with MMSE using 'AND' rule, accuracy, specificity, PPVs and LR+ were increased than those of MMSE. While SMCQ-E was combined the MMSE using 'OR' rule, sensitivity and NPVs were increased and LR- were decreased than those of SMCQ-E and MMSE. When subjects with moderate to severe stages of dementia were excluded from the analysis, results were similar. When subjects with GDS score above 16 were included, results were also not changed.

Economic benefits of SMCQ combined with MMSE

Simulated economic costs of dementia examination for 10,000 subjects were presented in Table 4. Screening positive ratio was calculated from the results of analysis for random sample. When SMCQ-E and MMSE combined with AND rule, total cost for dementia screening was reduced to about 80% compared to MMSE single use model. Meanwhile, those tools were combined with OR rule, total costs increased to 120%.

Table 2. Results of dementia screening using optimal cutoff point by ROC analysis

	Nonrandom sample		Random sample	
	SN	SP	SN	SP
SMCQ-E				
AUC	0.605 (0.565−0.646)		0.836 (0.783−0.890)	
Optimal cut off points				
0/1	0.891	0.194	0.953	0.347
1/2	0.774	0.337	0.891	0.528
2/3	0.676	0.477	0.766	0.7885
MMSE				
AUC	0.867 (0.842−0.893)		0.904 (0.862−0.945)	
Optimal cut off points				
-1	0.943	0.521	0.953	0.650
-1.5	0.883	0.674	0.938	0.776
-2	0.759	0.810	0.797	0.864

ROC : receiver operator characteristic, AUC : area under the curves, SMCQ-E : everyday memory subscale of subjective memory complaints questionnaire, SN : sensitivity, SP : specificity, MMSE : Mini-Mental State Examination

Table 3. Screening properties of SMCQ, MMSE and its combinations

	Non-random sample				Random sample			
	SMCQ-E	MMSE	SMCQ-E and MMSE	SMCQ-E or MMSE	SMCQ-E	MMSE	SMCQ-E and MMSE	SMCQ-E or MMSE
Accuracy	0.525	0.761	0.755	0.532	0.388	0.776	0.837	0.321
Sensitivity	0.891	0.883	0.793	0.979	0.953	0.937	0.906	0.982
Specificity	0.195	0.651	0.720	0.503	0.347	0.766	0.834	0.279
PPV	0.500	0.697	0.719	0.504	0.095	0.225	0.284	0.009
NPV	0.663	0.860	0.794	0.875	0.990	0.994	0.991	0.996
LR+	1.11	2.53	2.83	1.12	1.46	3.97	5.38	1.36
LR-	0.56	0.18	0.29	0.16	0.154	0.093	0.128	0.006

Cut off value of SMCQ-E and MMSE were 0/1, -1.5 standard deviation from established norm, respectively. SMCQ-E : everyday memory subscale of subjective memory complaints questionnaire, MMSE : Mini-Mental State Examination, PPV : positive predictive value, NPV : negative predictive value, LR+ : positive likelihood ratio, LR- : negative likelihood ratio

Table 4. Economic cost of dementia screening using SMCQ-E and MMSE in random sample (Unit : 1,000 won)

	SMCQ only	MMSE only	Model I	Model II	Model III	Model IV
Screening cost	10,000*	70,000†	57,110‡	72,810	80,000	80,000
Screen positive (%)	67.3	28.1	21.6	21.6	21.6	32.7
Diagnostic cost§	1,110,450	463,650	356,400	356,400	356,400	539,550
Total cost	1,120,450	533,650	413,510	429,210	436,400	619,550
Cost ratio	2.09	1	0.77	0.80	0.81	1.16

* : Cost of SMCQ-E was indirectly estimated based on a fee for self questionnaire from Korean National Health Insurance (approximately 1,000 won/person), † : Cost of MMSE was estimated based on a fee from Korean National Health Insurance (approximately 7,000 won/person), ‡ : Calculated by equation of 1,000,000+10,000×0.673×5,000, § : Diagnostic cost was calculated by maximum cost of Early Detection Program in Korea (165,000 won). Model I : SMCQ-E as a first step and MMSE as a second step, Model II : MMSE as a first step and SMCQ-E as a second step, Model III : SMCQ-E and MMSE were applied simultaneously using AND rule, Model IV : SMCQ-E and MMSE were applied simultaneously using OR rule, SMCQ-E : everyday memory subscale of subjective memory complaints questionnaire, MMSE : Mini-Mental State Examination

Discussion

Results of this study showed that SMCQ-E combined with MMSE using AND rule increased specificity, PPV and LR+ than SMCQ-E or MMSE alone. In addition, this combination method could reduce the total cost for identifying dementia.

Brief cognitive screening represents the initial step in a process of further assessment of dementia. Traditionally MMSE is one of the most widely using instruments for this purpose. But one of well known weak points is the low specificity and NPV.[4] Results of this study also confirmed that sensitivity of MMSE was enough high but specificity was relatively low. This low specificity could be increased when SMCQ-E was combined with MMSE using AND rule without significant scarifying sensitivity especially in random sample. Although sensitivity and specificity were well known indices for evaluating diagnostic properties, it depends on many variables such as disease stage, age and gender.[17] In addition, sensitivity and specificity are not so helpful for clinical situation because clinician will not start from diseased or not diseased, but from a positive and negative test.[18] In this situation, predictive value could be used as an alternative. But it should be reminded that predictive value depends on the prevalence of disease in the study population.[18] If prevalence of the disease is low, the PPV will not be close to 1 even if both sensitivity and specificity are high. In this study, PPVs in random sample were much lower than those in non-random sample, which might be influenced by relatively low prevalence of dementia patients in random sample. The LR indicates the value of the test for increasing certainty about a positive diagnosis and not influenced by disease prevalence. A LR greater than 1 indicates that the test result is associated with the presence of disease, whereas a LR less than 1 indicates that the test result is associated with the absence of disease. Results of this study showed that addition of SMCQ-E to MMSE could increase LR+ of MMSE to moderate level in random sample.[19]

SMCQ-E has several advantages. Objective cognitive tests like MMSE need a certain level of training and it takes at least 10−20 min for testing. It also gave stress to elderly who was not familiar to cognitive testing. SMCQ-E is a 10 item brief scale and easily administered since it is similar to questions that clinicians commonly ask to detect dementia. In addition, it could elicit the hidden problem of memory because elderly people are not accustomed to reporting their memory problems to clinicians since they usually regard their forgetfulness as a normal part of aging.[20] Combination of SMCQ-E with MMSE could be a very simple cognitive battery and used in two different setting for dementia screening.[21] One is epidemiological setting in which dementia screening could be defined as tests done among apparently asymptomatic individu-

als and other is clinical setting in which opportunistic case finding could be done. In large epidemiological study, using SMCQ-E before objective testing using MMSE could save the cost for dementia examination about 20% without significant reducing sensitivity. In a primary clinic setting, items of SMCQ-E could be asked or self-administered before clinician's interview. Thus, SMCQ-E could be a helpful tool in busy and unskilled primary physician's clinic.

Recent evidences support the suggestion that SMC might be a first symptom of cognitive decline. It might be associated with the risk of dementia[22,23] in spite of the inconsistent results of the association between cognitive function and SMC.[24-30] In addition, subjects with SMC showed a smaller hippocampal volume and more extensive white matter hyperintensities than those without SMC.[6,8,31] Thus, testing the availability of SMC for dementia detection might be a valuable work. Although not sufficiently high, diagnostic accuracy of SMCQ-E for dementia measured by AUC value was fair and similar to previous study (0.74 in that study, 0.605 in non-random sample and 0.836 in random sample of this study).[32]

Several cautions should be kept in mind for interpreting result of this study. First, SMCQ-E could not replace MMSE because of low specificity and overall diagnostic accuracy. Cut off point was lowered to 0/1, sensitivity of it could elevated and was similar to that of MMSE especially for random sample, but specificity was much lower than that of MMSE. Results of this study showed that combined used of SMCQ-E with MMSE had several advantages. Second, results of this study could be changed if different cut off points were selected. Cut off point of MMSE in this study was selected using age- and sex- adjusted established norm to increase sensitivity and specificity of MMSE.[33] Likewise, that of SMCQ-E was selected to achieve high sensitivity of it for dementia screening. Third, although moderate to severe depression was excluded from the analysis based on the scores of GDS, mild depressive symptoms could affect the results. But, overall results were not changed when subjects with depression were included in the analysis (data was not shown). Fourth, combined use of SMCQ-E and MMSE showed superior screening function in random sample in this study. Although exact cause of this phenomenon was unclear, sample characteristics including age, sex and number of dementia patients could affect the results. Fifth, simulation of economic cost for dementia screening was based on the cost of NDEDP in Korea. Thus, total budget for dementia exam could vary in different study.

Results of this study showed that brief SMCQ-E and its combination with MMSE could be used to dementia screening with cost effective manner.

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