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Cross-sectional Evaluation of Cognitive Impairment in Elderly Regular Hemodialysis Outpatients: A Preliminary Study

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In order to establish the etiology of cognitive impairment, this study examined the contribution of mood states, quality of life, activities of daily living, physical condition, sociodemographic factors, and brain magnetic resonance imaging (MRI) findings in 33 elderly regular hemodialysis outpatients. The patients' mean (±SD) Mini Mental States Examination score was 26.06±4.13. Of the entire cohort, 18% could potentially be diagnosed with dementia. Abnormal features and vascular damage in particular, were observed in the brain MRI of 81% of our subjects. Self-evaluation using the World Health Organization Quality of Life assessment appeared to be unaffected by cognitive impairment. However, the group with suspected dementia exhibited a significantly lower hematocrit and a significantly higher Profile of Mood States score than the non-dementia group. With the aid of discriminant function analysis, the mean hematocrit value was identified as the best predictor variables for cognitive impairment. Our findings suggest that the etiology of cognitive impairment in a lot of elderly hemodialysis patient is treatable. The most likely causative or aggravating factors appear to be anemia, pseudodementia of depressive patients, and decreased reactivity in an isolated environment. In addition, it may be that the influence of anemia on cognitive dysfunction is more serious in elderly patients than in the younger population. We propose that it is very important to impose a multidimensional approach on the diagnosis of the etiology of cognitive impairment.

Key words: cognitive impairment, elderly patient, hemodialysis, anemia, mood states

Introduction

The number of patients in Japan who require regular hemodialysis as a result of chronic renal failure, currently around 220,000, is considerably higher than in the USA and Europe. Aging represents one of the biggest factors affecting hemodialysis patients, so it is important that this process be studied in detail. It has been reported that the rate of development of dementia over the first year of hemodialysis in aged patients is higher than in the normal population[1]. Therefore, screening for dementia in the early stages of hemodialysis is especially important if we are to prevent not only worsening of the dementia itself, but also the development of some of the behavioral and psychological symptoms of dementia, such as delirium. On the other hand, it is also known that cognitive impairment in hemodialysis patients is correlated with various factors such as the effects of anemia[2], protein nutritional status, staff time, and hospitalization[3], as well as the patient's personality[4].

To diagnose correctly the etiology of cognitive impairment in elderly hemodialysis patients, this study examined the contribution of mood states, quality of life (QOL), activities of daily living, physical condition, sociodemographic factors, and brain magnetic resonance imaging (MRI) findings.

Table 1 List of psychometric measurements

Cognitive function	Mini-mental States Examination (MMSE)
Emotional state	Profile of Mood Status (POMS)
Quality of life	WHOQOL-BRIEF
Activities of daily living	Performance status
Physical condition	Electrolytes, total protein, hematocrit, hemoglobin, total cholesterol, weight gain between each HD, Blood pressure before/after HD
Socio-demographic factor	Familial state, job, education

HD: hemodialysis session

Instrument and Methods

Instruments

A list of psychometric measurements and another indexes used in this study are shown in Table 1. The Mini Mental State Examination (MMSE) is a widely used standardized measure for assessing cognitive mental status[5]. When a score of 23 points or less is achieved using MMSE, it can be assumed that cognitive function is impaired, and dementia is suspected. The Profile of Mood States (POMS) is standardized self-rating test consisting of 65 items, which identifies and assesses transient, fluctuating affective mood states in patients[6]. In particular, POMS examines the mood states of tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment. POMS has been proven to be particularly useful in measuring changes in mood states over time. The World Health Organization QOL (WHOQOL) Brief is an abbreviated, 26-item version of the WHOQOL-100, which is used to evaluate general QOL[7]. It is divided into five subscales; a physical domain, a psychological domain, social relationship, environment, and total evaluation of the overall QOL. The Eastern Cooperative Oncology Group (ECOG) performance status is an evaluation scale that grades objectively, according to six ranks (0–5), the ability of a patient to perform the normal activities of daily living[8].

Methods

The psychometric evaluation was carried out over a 2-months period, from March to April, 2001. MMSE were assessed for each patient by three well-trained psychologists. POMS and the WHOQOL-BRIEF were administered on the same day. While most of the patients could complete the questionnaires by themselves, some patients, such as the physically handicapped, were helped by a psychologist. ECOG performance status was also evaluated on the same day by a staff-nurse.

During the month preceding the initial evaluations, the physical condition and sociodemographic factors relating to each patient were also examined; namely, serum concentration levels of electrolyte, total protein, hemoglobin, hematocrit, and total cholesterol, weight gain between each hemodialysis session, blood pressure before and after hemodialysis, familial state, job, and education. In addition, a brain MRI was performed for each subject within the same period.

Subjects

Of the 36 patients studied, who were 55 years old and over and were treated in an outpatient hemodialysis clinic, 33 agreed to participate in this study. The psychiatrist and psychologist interviewed the patients after the dialysis attending physician explained the outline of this research and obtained orally their consents. This research was planned as a systematized routine inspection for general complications of regular hemodialysis patients. Because of the high risk of arteriosclerosis in hemodialysis patients, patients who had passed middle age were included in the subject cohorts.

All of the subjects (14 male, 19 female) were Japanese. Their mean ± SD age was 65.5 ± 6.6 years and they had been undergoing hemodialysis for 105 ± 68 months. Diabetes mellitus was responsible for chronic renal failure in 21% of the cohort. The level of education achieved by the subjects is as follows: primary school graduation 24%, junior high school graduation 18%, high school graduation 45%, and university graduation 12%.

Statistics

Our results were analyzed statistically. The results of those patients with suspected dementia because of existence of cognitive impairment (MMSE score of 23 or less, suspected-dementia group) were compared with those of the non-dementia group (MMSE score of over 23). The following aspects were evaluated and compared between those two

Table 2 ECOG performance status related to activities of daily living

Grade		Subjects (%)
0	Fully active, able to carry on all pre-disease performance without restriction	30
1	Restricted in physically strenuous activities, but ambulatory and able to carry out work of a light or sedentary nature (eg, light house work, office work)	40
2	Ambulatory and capable of all self-care, but unable to carry out any work activities Up and about more than 50% of waking hours	15
3	Capable of only limited self care Confined to bed or chair more than 50% of waking hours	9
4	Completely disabled, cannot carry on any self-care Totally confined to bed or chair	6
5	Dead	0

groups: mood states, QOL, ability to perform the normalof daily activities, physiological condition and sociodemographic factors.

They were analyzed by the chi-squared test, the Mann-Whitney U test and discriminant function analysis using SPSS version 10.1 on a Sony, Tokyo personal computer.

Results

Performance status

Seventy percent of the subjects were given a performance status of grade 0 or 1, which means that they had the ability to live without serious limitation to their daily life. Fifteen percent of the subjects had a performance status of grade 3 or 4. (Table 2), which means that they required care on a daily basis, including being taken to and from the hospital for every hemodialysis session.

Mini Mental State Examination (MMSE)

The mean (±SD) MMSE score of the entire cohort was 26.06 ± 4.13 (Fig. 1). The distribution of MMSE scores for each subject in the study is shown in Fig. 2. The score of six subjects was less than or equal to 23 (range; 10–23). The diagnosis of dementia was potentially applicable to 18% of the study cohort.

Profile of Mood States (POMS)

Fig. 3 presents the POMS scores of our subjects and the cut-off point for the Japanese male. The mean score in for each subcategory was as follows; tension-anxiety 9.7 ± 6.68, depression-dejection 11.3 ± 9.45, anger-hostility 6.4 ± 5.74, vigor-activity 10.0 ± 6.05, fatigue-inertia 8.7 ± 6.86, and confusion-bewilderment 7.1 ± 6.86. The mean POMS scores of our subjects either stayed within the normal range or were considerably lower than the cut-off points, (it should be noted that points higher than the cut-off point are regarded as being within the normal range for vigor-activity).

WHOQOL-BRIEF

The score for overall QOL was slightly lower, at 2.79 ± 0.63, than for the individual categories, the mean scores for which were almost always over 3.0 (physical domain 3.15 ± 0.63, psychological domain 3.10 ± 0.62, social relationships 3.17 ± 0.75, and environment 3.31 ± 0.57; the mean score of all of these items was 3.18 ± 0.48) (Fig. 4).

Comparison between the suspected dementia group and the non-dementia group

The subjects could be divided into two groups according to their MMSE score: a suspected-dementia group (n = 6, mean age 68.3 ± 6.2 years) and a non-dementia group (n = 27, mean age 64.9 ± 6.7 years). A comparison of each subcategory of the MMSE between the two groups revealed that the mean scores for attention and calculation, and recall and repetition in the suspected-dementia group were significantly lower than in the non-dementia group (Fig. 5; Mann-Whitney U test − $p < 0.001$, $p < 0.001$, and $p = 0.015$, respectively).

1) Brain MRI findings

Only one subject had a previous history of vascular infarction before becoming involved in this research project. Eighteen percent of all subjects exhibited some abnormality in their brain MRI. Table 3 gives a comparison between the brain MRI findings of the suspected-dementia and non-dementia groups. There were no significant differences between the two groups with regard to either the extent of abnormality that appeared on the brain MRI or to each finding relating to vascular damage, such

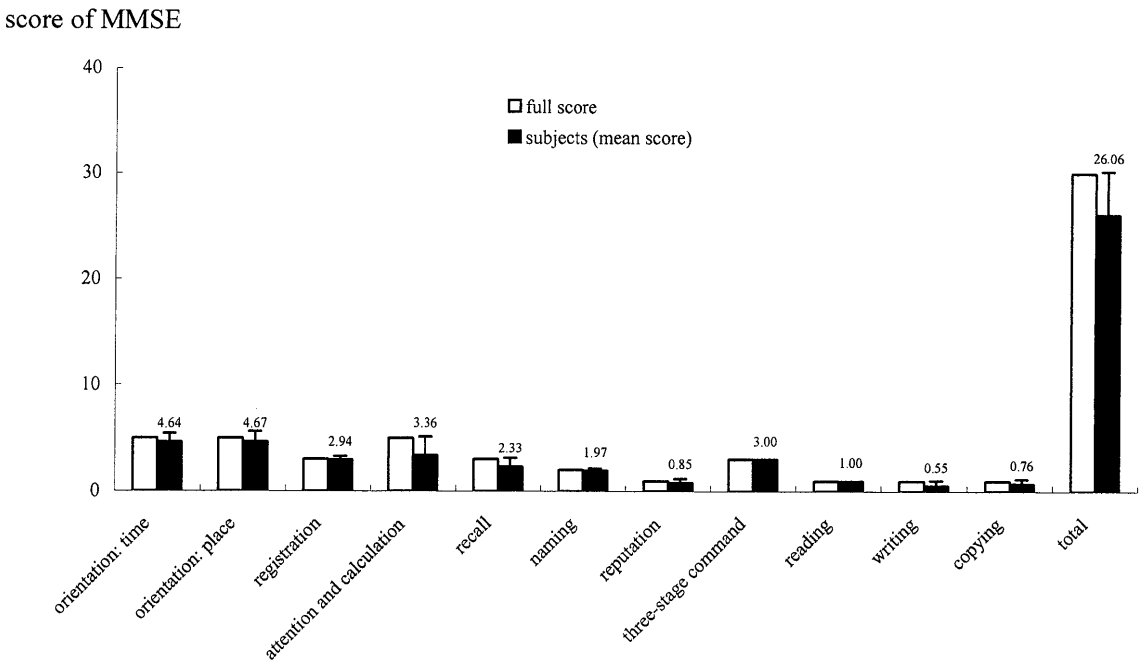

Fig. 1 Mean MMSE sores of the entire cohort of subjects

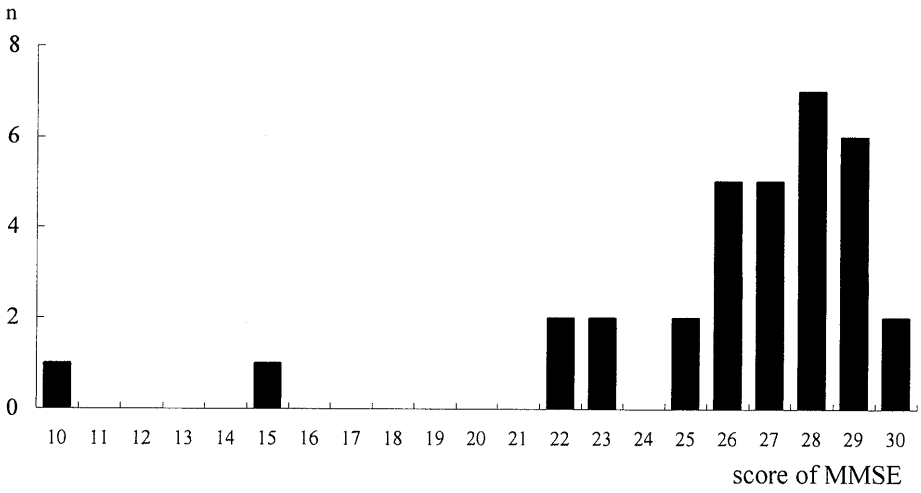

Fig. 2 The distribution of the MMSE scores of the entire cohort of subjects

as multiple vascular infarction, lacunae, and ischemic change.

2) Physical condition and sociodemographic factors

A comparison of the physical condition and sociodemographic factors between the suspected-dementia group and the non-dementia group is given in Table 4. The mean hematocrit value in the suspected-dementia group was significantly lower than in the non-dementia group (Mann-Whitney U test, $p = 0.038$). In addition, total protein, hemoglobin, and total cholesterol in the suspected-dementia group were lower than in the non-dementia group, although these differences did not reach statistical significance. The ratio of subjects living alone tended toward being higher in the suspected-dementia group than in the non-dementia group, although again, the difference was not statistically significant (chi-squared test, $p = 0.078$).

3) POMS

Fig. 6 shows the mean POMS scores of the suspected-dementia group and the non-dementia

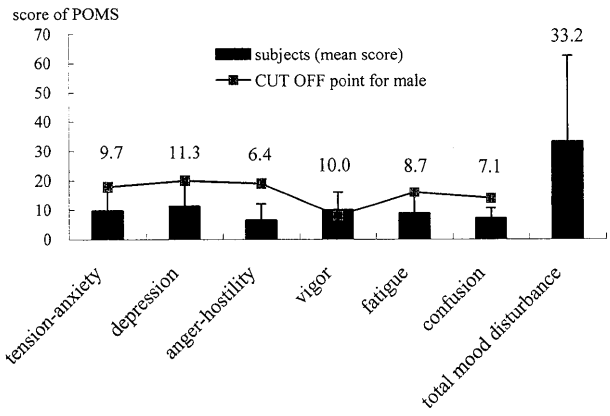

Fig. 3 Mean POMS scores of the entire cohort of subjects

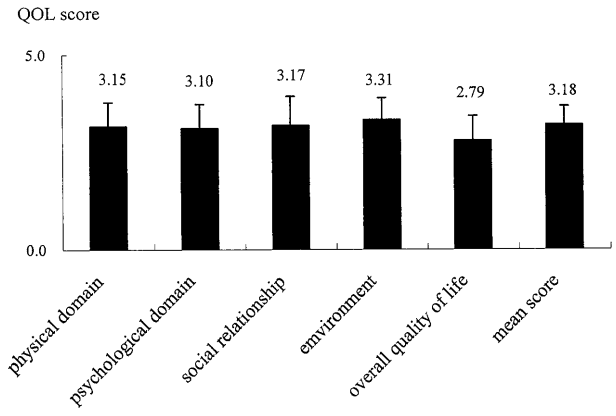

Fig. 4 Mean WHOQOL-BRIEF scores of the entire cohort of subjects

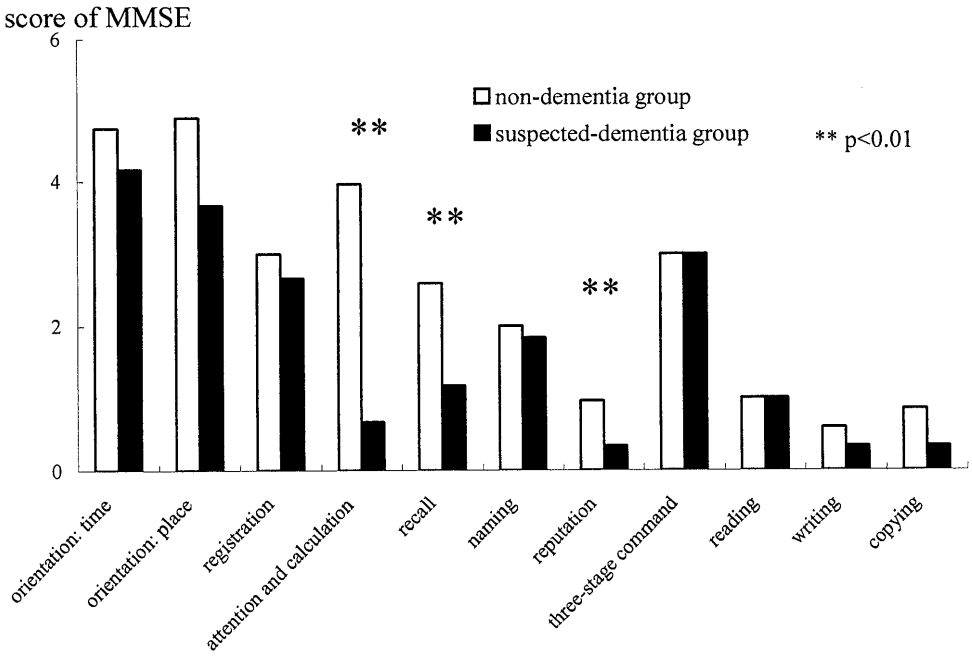

Fig. 5 Mean MMSE scores of the suspected-dementia and non-dementia group (Mann-Whitney U test)

group. Among the six subcategories of POMS, the mean scores of for fatigue-inertia and confusion-bewilderment in the suspected-dementia group were significantly higher than in the non-dementia group (Mann-Whitney U test; $p = 0.002$ and $p = 0.045$, respectively). The mean score for total mood disturbance, (ie, the sum total of all subcategories) was lower in the suspected-dementia group than in the non-dementia group (Mann-Whitney U test; $p = 0.024$).

4) WHOQOL-BRIEF

There was no significant deference between experimental groups in either the mean scores for each subcategory or the mean total score (Fig. 7).

5) Discriminant function analysis

Discriminant function analysis was performed to determine which variables can be used to discriminate between the suspected-dementia group and the non-dementia group. The dependent variable was "suspected dementia". The independent variables were mean hematocrit value, living alone, and POMS total mood disturbance.

Table 3 Brain MRI finding of the suspected-dementia and non-dementia groups

	All subjects (%)	Non-dementia group (%)	Suspected-dementia group (%)	p
Brain MRI abnormality	81	82	80	0.674
Multiple vascular infarction	59	59	60	0.970
Lacunae	48	45	60	0.462
Ischemic change	26	27	20	0.612

Table 4 Physical condition and sociodemographic factors of the suspected-dementia and non-dementia groups

	Group		p
	Non-dementia	Suspected-dementia	
n	27	6	
Age (y)	64.9 ± 6.7	68.3 ± 6.2	0.260
Sex (% male)	40.7	50.0	0.678
Duration of HD (day)	3,338 ± 2,182	2,542 ± 1,478	0.479
CRF responsible disease (%DM)	18.5	33.3	0.422
Education (% guraduation of hign school)	33.3	48.1	0.370
Job +	22.2	16.7	0.494
Living alone *	7.4	33.3	0.078
PS (% "3 + 4")	11.1	33.3	0.170
K (mEq/dl)	5.1 ± 0.7	4.8 ± 0.8	0.398
P (mEq/dl)	6.4 ± 1.6	5.9 ± 1.9	0.733
Weight gain between each HD (% DW)	4.7 ± 1.4	4.9 ± 2.6	0.874
TP (g/dl)	6.7 ± 0.33	6.0 ± 1.3	0.132
Ht (%)**	32.3 ± 2.8	27.0 ± 7.3	0.038
Hb (g/dl)	10.3 ± 1.0	9.5 ± 1.2	0.120
T-chole	186 ± 40	160 ± 38	0.145
Blood pressure systol before HD (mmHg)	144 ± 15	146 ± 11	0.838
Blood pressure asystol before HD (mmHg)	78 ± 10	78 ± 7.4	0.838

*$p < 0.1$, **$p < 0.05$, Mann-Whitney U test and chi-squared test.

This analysis revealed a significant difference between the two groups (canonical correlation = 0.599, Wilks' lambda = 0.641, chi-square = 13.138, df = 3, p = 0.004). The standardized discriminant function coefficients of the mean hematocrit value, living alone, and POMS total mood disturbance were 0.854, 0.470, and −0.395, respectively. Classification statistics showed that 81.8% of the cases had been classified correctly.

Discussion

Using MMSE scores, we found that 18% of our subjects could be functionally cognitively impaired. These subjects should be investigated further in an attempt to predict whether dementia is likely to develop. Fukunishi et al reported that the 1-year incidence rate of dementia in aged hemodialysis patients was 4.2% (for comparison, the same figure for dementia of Alzheimer's disease, is 0.5%, and that for multi-infarct dementia is 3.7%)[9]. The authors wrote also that the 1-year incidence rate of multi-infarct dementia in aged hemodialysis patients was 7.4 times large aslarger than that in the elderly general populations.

While in general the mood states in our subjects stayed within the normal range, the self-evaluation quality of QOL in our elderly hemodialysis patients seemed to be lower than that of the normal Japanese population or that of Japanese patients with other chronic physical diseases. According to Nakane et al, the mean WHOQOL-BRIEF score in 1,410 members of the general population of Japan was 3.29 ± 0.46, but that persons over 60 years of age had higher QOL scores (3.35 ± 0.49) than those in their 30s[10]. In a Japanese study of 197 cancer patients of average age 55 years, the mean QOL score was 3.30[11]. In that study, the average QOL score of a healthy object was 3.75; by comparison, the QOL scores of our subjects were slightly lower.

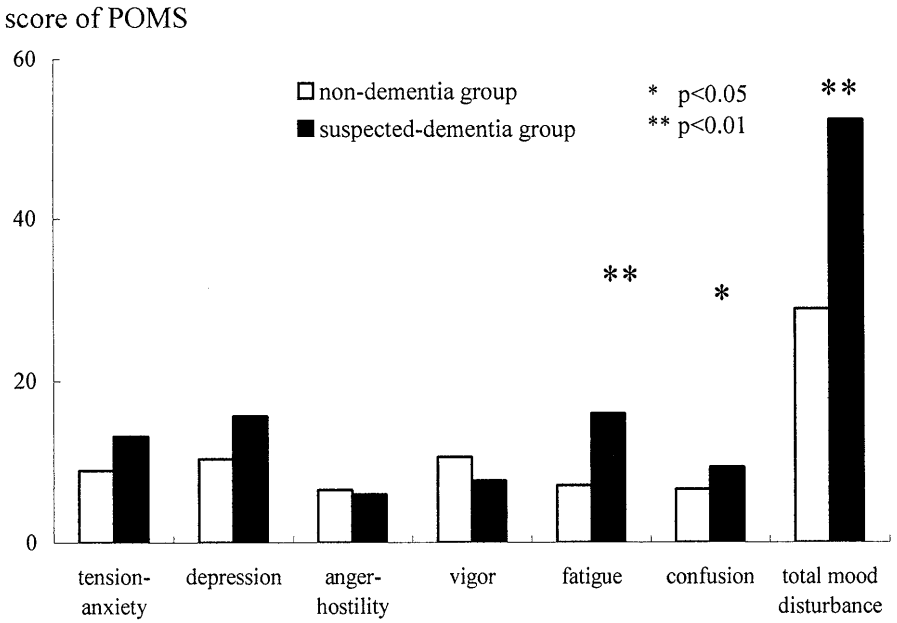

Fig. 6 Mean POMS scores of the suspected-dementia and non-dementia group (Mann-Whitney U test)

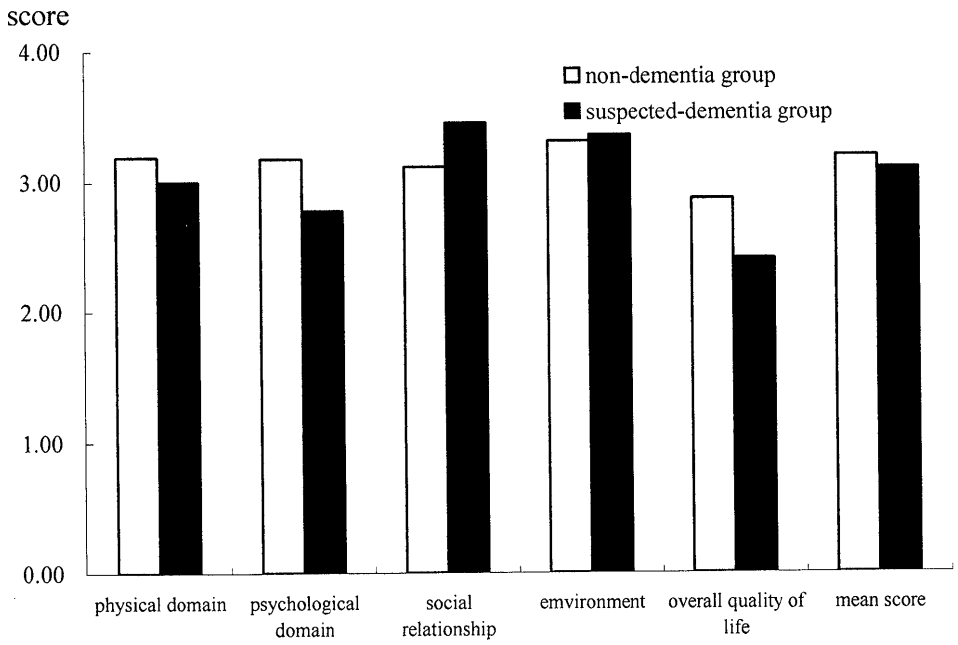

Fig. 7 Mean WHOQOL-BRIEF scores of the suspected-dementia and non-dementia groups (Mann-Whitney U test)

The different MMSE scores of the suspected-dementia group and the non-dementia group reflect mainly a disturbance of short-term memory and of attention and calculation in the suspected-dementia group. Fazekas et al reported that the brain of hemodialysis patients exhibits significantly more atrophy, and that multiple lacunas or confluent white matter hyperintensities predominate in 33% of 30 hemodialysis patients; 80% of those were demented[12]. Abnormalities in brain MRIs, especially those related to vascular damages, were also observed in 81% of our subjects.

However, MRI abnormalities were seen in both the non-dementia group and the suspected-

dementia group. In addition, it appears that in the present study at least, cognitive impairment is not reflected in the self-evaluation of QOL. Significant differences between the two groups were found in the lower hematocrit and higher POMS score in the suspected-dementia group. With regard to sociodemographic factors, living alone might also be a determinant of cognitive impairment. From these results, we have found that the etiology of cognitive impairment in elderly hemodialysis patients may be treatable, for example, impairment due to anemia, pseudodementia of depressive patients, and decreased reactivity in an isolated environment. It is also possible that some causes are not mutually exclusive, and that together their effects on cognitive dysfunction are amplified.

Discriminant function analysis of the results revealed that the mean hematocrit value is the best predictor variable for the suspected-dementia group; this was followed by living alone and then POMS total mood disturbance. The influence of anemia to on cognitive function might be more serious in elderly than in younger patients, because there is higher incidence of vulnerability due to vascular damage in these patients. It is suggested that anemia should be paid more attention as an etiological factor underlying cognitive impairment, which can sometimes be misdiagnosed as dementia, in elderly hemodialysis patients.

Our findings need to be confirmed in further well-controlled trials with larger sample sizes.

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高齢外来維持血液透析患者における認知障害に対する横断面的評価—その予備的研究

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認知機能低下の原因検索のために，高齢維持血液透析患者33人における気分の状態，生活の質，日常生活の活動性，身体的状態，社会動態学的因子，脳磁気共鳴映像法所見の関与について調査した．Mini Mental States Examinationの平均得点は26.06±4.13点であり，対象の18%に痴呆の可能性が示唆された．脳MRIにおいて，脳血管障害に関連した異常所見は対象の81%に認められた．World Health Organization Quality of Life assessmentにおける自己評価は認知機能低下に影響を受けていなかったが，痴呆が疑われる群は，非痴呆群に比べ，統計学的に明らかにヘマトクリット値が低く，Profile of Mood States得点が高かった．判別分析を用いたところ，ヘマトクリット平均値は認知障害の第一の予測因子であった．我々の所見から，多くの高齢透析患者における認知障害は治療可能であることが示唆される．原因ないし増悪因子となりうる要因は，貧血，抑うつ患者の偽性痴呆，孤立的環境における反応性の低下である．認知機能障害への貧血の影響は若い患者よりも高齢患者においてより深刻であると考えられる．本研究から高齢外来継持血液透析患者における認知機能低下については，その原因検索と診断に対し，多次元的なアプローチ施行の重要性が提案される．