10 Gotoda et al.

tors such as in FCHL and homozygous familial hypertriglyceridemia, strict restriction of fat intake, such as in type I hyperlipoproteinemia, may be necessary. Since acquired environmental factors are usually present in type V hyperlipoproteinemia, they must be eliminated first. Among lipid-lowering drugs, fibrates, nicotinic acid, and strong statins are indicated, but caution against possible exacerbation of the glucose tolerance is necessary in the treatment of diabetic patients with nicotinic acid. Also, as marked weight control in obese patients may induce severe hypertriglyceridemia and acute pancreatitis associated with rebound of the body weight, this risk must be considered.

Proposal of Diagnostic Criteria for Primary Hyperchylomicronemia (Draft)

Lastly, against the background described above, provisional diagnostic criteria for primary hyperchylomicronemia are presented (**Table 3**). Items related to genetic diagnosis, which has become possible, and those related to clinical symptoms and familial history have been added to the diagnostic criteria proposed by the Tarui Group⁹⁾. Since no such diagnostic criteria or management guidelines have been established anywhere in the world, further discussion and rigorous evaluation are needed.

Conflict of Interest

Dr. Oikawa has received unrestricted grants from Daiichi-Sankyo Co. Ltd. Dr. Ishibashi has received unrestricted grants from Takeda Pharmaceutical Co. Ltd. and is an advisor of Kowa Pharmaceutical Co. Ltd. Dr. Arai has received unrestricted grants from Otsuka Pharmaceutical Co., Ltd., received honoraria from MSD, and is an advisor of Kowa Pharmaceutical Co. Ltd. Dr. Yamashita has received unrestricted grants from MSD, Otsuka Pharmaceutical Co., Ltd., Astellas Pharma Inc., and JT, collaborative research grants from Shionogi & Co., Ltd., Otsuka Pharmaceutical Co., Ltd., and National Institute of of Biomedical Innovation, honoraria for lectures from MSD, Bayer Yakuhin, Ltd., and Kowa Pharmaceutical Co.,Ltd., and is an advisory of Skylight Biotech Co. Dr. Harada-Shiba has received unrestricted grants from MSD. Dr. Eto is an advisor of MSD. The other authors declare that they have no conflict of interest.

Acknowledgements

This study was supported by research grants for health sciences from the Japanese Ministry of Health,

Labour and Welfare.

- 1) Fredrickson DS, Lees RS: Familial hyperlipoproteinemia. in The Metabolic Basis of Inherited Disease (ed. by Stanbury JB, Wyngaarden JB, and Fredrickson DS), 2nd ed., New York, McGraw-Hill, 1966, pp429
- 2) Brunzell JD, Deeb SS: Familial lipoprotein lipase deficiency, apoC-II deficiency and hepatic lipase deficiency in The Metabolic and Molecular Bases of Inherited Disease (ed. by Scriver CR, Beaudet AL, Sly WS, Valle D, Childs B, Kinzler KW, and Vogelstein B), 8th ed., New York, McGraw-Hill, 2000, pp2789-2816
- 3) Brunzell JD, Miller NE, Alaupovic P, St Hilaire RJ, Wang CS, Sarson DL, Bloom SR, Lewis B: Familial chylomicronemia due to a circulating inhibitor of lipoprotein lipase activity. J Lipid Res, 1983; 24: 12-19
- 4) Kihara S, Matsuzawa Y, Kubo M, Nozaki S, Funahashi T, Yamashita S, Sho N, Tarui S: Autoimmune hyperchylomicronemia. N Engl J Med, 1989: 320; 1255-1259
- 5) Beigneux AP, Davies BSJ, Gin P, Weinstein MM, Farber E, Qiao X, Peale F, Bunting S, Walzem RL, Wong JS, Blaner WS, Ding Z-M, Melford K, Wongsiriroj N, Shu X, de Sauvage F, Ryan RO, Fong LG, Bensadoun A, Young SG: Glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 plays a critical role in the lipolytic processing of chylomicrons. Cell Metab, 2007; 5: 279-291
- 6) Peterfy M, Ben-Zeev O, Mao HZ, Weissglas-Volkov D, Aouizerat BE, Pullinger CR, Frost PH, Kane JP, Malloy MJ, Reue K, Pajukanta P, Doolittle MH: Mutations in LMF1 cause combined lipase deficiency and severe hypertriglyceridemia. Nature Genet, 2007; 39: 1483-1487
- 7) Murase T, Ohkubo M: Investigation on the molecular basis of hyperchylomicronemia. Therapeutic Res, 2000; 21: 2347-2352 (in Japanese)
- 8) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA, 2001; 285: 2486-2497
- 9) The report by the Study Group on Primary Hyperlipidemia of the Ministry of Health and Welfare (Group leader: Tarui S), 1988 (in Japanese)
- 10) Bürger MB, Grütz O: Über hepatosplenomegale Lipoidose mit xanthomatosen Veranderungen der Haut und Schleimhaut. Arch Dermatol Syph, 1932; 166: 542-544
- 11) Havel RJ, Gordon RS Jr: Idiopathic hyperlipemia: metabolic studies in an affected family. J Clin Invest, 1960; 39: 1777-1790
- 12) Auwerx JH, Babirak SP, Fujimoto WY, Iverius PH, Brunzell JD: Defective enzyme protein in lipoprotein lipase deficiency. Eur J Clin Invest, 1989; 19: 433-437
- 13) Wion KL, Kirchgessner TG, Lusis AJ, Schotz MC, Lawn RM: Human lipoprotein lipase complementary DNA sequence. Science 1987; 235: 1638-1641

- 14) Senda M, Oka K, Brown WV, Qasba PK, Furuichi Y: Molecular cloning and sequence of a cDNA coding for bovine lipoprotein lipase. Proc Natl Acad Sci USA, 1987; 84: 4369-4373
- 15) Deeb SS, Peng RL: Structure of the human lipoprotein lipase gene. Biochemistry, 1989; 28: 4131-4135
- 16) Wilson DE, Emi M, Iverius PH, Hata A, Wu LL, Hillas E, Williams RR, Lalouel JM: Phenotypic expression of heterozygous lipoprotein lipase deficiency in the extended pedigree of a proband homozygous for a missense mutation. J Clin Invest 1990; 86: 735-750
- 17) Ma Y, Ooi TC, Liu MS, Zhang H, McPherson R, Edwards AL, Forsythe IJ, Frohlich J, Brunzell JD, Hayden MR: High frequency of mutations in the human lipoprotein lipase gene in pregnancy-induced chylomicronemia: possible association with apolipoprotein E2 isoform. J Lipid Res, 1994; 35: 1066-1075
- 18) Benlian P, De Gennes JL, Foubert L, Zhang H, Gagné SE, Hayden M: Premature atherosclerosis in patients with familial chylomicronemia caused by mutations in the lipoprotein lipase gene. N Engl J Med, 1996; 335: 848-854
- 19) Ebara T, Okubo M, Horinishi A, Adachi M, Murase T, Hirano T: No evidence of accelerated atherosclerosis in a 66-yr-old chylomicronemia patient homozygous for the nonsense mutation (Tyr61-->stop) in the lipoprotein lipase gene. Atherosclerosis, 2001; 159: 375-379
- 20) Kawashiri MA, Higashikata T, Mizuno M, Takata M, Katsuda S, Miwa K, Nozue T, Nohara A, Inazu A, Kobayashi J, Koizumi J, Mabuchi H: Long-term course of lipoprotein lipase (LPL) deficiency due to homozygous LPL(Arita) in a patient with recurrent pancreatitis, retained glucose tolerance, and atherosclerosis. J Clin Endocrinol Metab, 2005; 90: 6541-6544
- 21) Ikeda Y, Takagi A, Ohkaru Y, Nogi K, Iwanaga T, Kurooka S, Yamamoto A: A sandwich-enzyme immunoassay for the quantification of lipoprotein lipase and hepatic triglyceride lipase in human postheparin plasma using monoclonal antibodies to the corresponding enzymes. J Lipid Res, 1990; 31: 1911-1924
- 22) Kobayashi J, Hashimoto H, Fukamachi I, Tashiro J, Shirai K, Saito Y, Yoshida S: Lipoprotein lipase mass and activity in severe hypertriglyceridemia. Clin Chim Acta, 1993; 216: 113-123
- 23) Kawamura M, Gotoda T, Mori N, Shimano H, Kozaki K, Harada K, Shimada M, Inaba T, Watanabe Y, Yazaki Y, Yamada N: Establishment of enzyme-linked immunosorbent assays for lipoprotein lipase with newly developed antibodies. J Lipid Res, 1994; 35: 1688-1697
- 24) Gilbert B, Rouis M, Griglio S, de Lumley L, Laplaud P: Lipoprotein lipase (LPL) deficiency: a new patient homozygote for the preponderant mutation Gly188Glu in the human LPL gene and review of reported mutations: 75 % are clustered in exons 5 and 6. Ann Genet, 2001; 44: 25-32
- 25) http://www.ncbi.nlm.nih.gov/books/NBK1308/
- 26) Maruyama T, Yamashita S, Matsuzawa Y, Bujo H, Takahashi K, Saito Y, Ishibashi S, Ohashi K, Shionoiri F, Gotoda T, Yamada N, Kita T; Research Committee on Primary Hyperlipidemia of the Ministry of Health and Welfare of Japan: Mutations in Japanese subjects with pri-

- mary hyperlipidemia--results from the Research Committee of the Ministry of Health and Welfare of Japan since 1996--. J Atheroscler Thromb, 2004; 11: 131-145
- 27) Gotoda T, Yamada N, Kawamura M, Kozaki K, Mori N, Ishibashi S, Shimano H, Takaku F, Yazaki Y, Furuichi Y, Murase T: Heterogeneous mutations in the human lipoprotein lipase gene in patients with familial lipoprotein lipase deficiency. J Clin Invest, 1991; 88: 1856-1864
- pase deficiency. J Clin Invest, 1991; 88: 1856-1864
 28) Takagi A, Ikeda Y, Tsutsumi Z, Shoji T, Yamamoto A:
 Molecular studies on primary lipoprotein lipase (LPL) deficiency. One base deletion (G916) in exon 5 of LPL gene causes no detectable LPL protein due to the absence of LPL mRNA transcript. J Clin Invest, 1992; 89: 581-591
- 29) Kozaki K, Gotoda T, Kawamura M, Shimano H, Yazaki Y, Ouchi Y, Orimo H, Yamada N: Mutational analysis of human lipoprotein lipase by carboxy-terminal truncation. J Lipid Res, 1993; 34: 1765-1772
- 30) Takagi A, Ikeda Y: Measurements of lipoprotein lipase (LPL) activity and immunoreactive mass, and diagnosis of LPL gene. Nippon Rinsho, 2007; 65 (Suppl 7): 182-1890 (in Japanese)
- 31) Zsigmond E, Kobayashi K, Tzung KW, Li L, Fuke Y, Chan L: Adenovirus-mediated gene transfer of human lipoprotein lipase ameliorates the hyperlipidemias associated with apolipoprotein E and LDL receptor deficiencies in mice. Hum Gene Ther, 1997; 8: 1921-1933
- 32) Breckenridge WC, Little JA, Steiner G, Chow A, Poapst M: Hypertriglyceridemia associated with deficiency of apolipoprotein C-II. N Engl J Med, 1978; 298: 1265-1273
- 33) Yamamura T, Sudo H, Ishikawa K, Yamamoto A: Familial type I hyperlipoproteinemia caused by apolipoprotein C-II deficiency. Atherosclerosis, 1979; 34: 53-65
- 34) Jackson CL, Bruns GA, Breslow JL: Isolation and sequence of a human apolipoprotein CII cDNA clone and its use to isolate and map to human chromosome 19 the gene for apolipoprotein CII. Proc Natl Acad Sci USA, 1984; 81: 2945-2949
- 35) Fojo SS, Law SW, Brewer HB Jr: The human preproapolipoprotein C-II gene. Complete nucleic acid sequence and genomic organization. FEBS Lett, 1987; 213: 221-226
- 36) Fredrickson DS, Levy RI: Familial hyperlipoproteinemia, in The Metabolic Basis of Inherited Disease (ed. by Stanbury JB, Wyngaarden JB, and Fredrickson DS), 3rd ed. New York, McGraw-Hill, 1972, pp 545-614
- 37) Xiong WJ, Li WH, Posner I, Yamamura T, Yamamoto A, Gotto AM Jr, Chan L: No severe bottleneck during human evolution: evidence from two apolipoprotein C-II deficiency alleles. Am J Hum Genet, 1991; 48: 383-389
- 38) Inadera H, Hibino A, Kobayashi J, Kanzaki T, Shirai K, Yukawa S, Saito Y, Yoshida S: A missense mutation (Trp 26--->Arg) in exon 3 of the apolipoprotein CII gene in a patient with apolipoprotein CII deficiency (apo CII --Wakayama). Biochem Biophys Res Commun, 1993; 193: 1174-1183
- 39) Okubo M, Hasegawa Y, Aoyama Y, Murase T: A G+1 to C mutation in a donor splice site of intron 2 in the apolipoprotein (apo) C-II gene in a patient with apo C-II deficiency. A possible interaction between apo C-II deficiency and apo E4 in a severely hypertriglyceridemic patient.

Gotoda et al.

- Atherosclerosis, 1997; 130: 153-160
- 40) Murase T: Guidelines for the Diagnosis and Treatment of Hyperlipidemia. (Bunkodo) 2005, pp100 (in Japanese)
- 41) Marçais C, Verges B, Charrière S, Pruneta V, Merlin M, Billon S, Perrot L, Drai J, Sassolas A, Pennacchio LA, Fruchart-Najib J, Fruchart JC, Durlach V, Moulin P: Apoa5 Q139X truncation predisposes to late-onset hyper-chylomicronemia due to lipoprotein lipase impairment. J Clin Invest. 2005: 115: 2862-2869
- Clin Invest, 2005; 115: 2862-2869
 42) Zhang H, Reymer PW, Liu MS, Forsythe IJ, Groenemeyer BE, Frohlich J, Brunzell JD, Kastelein JJ, Hayden MR, Ma Y: Patients with apoE3 deficiency (E2/2, E3/2, and E4/2) who manifest with hyperlipidemia have increased frequency of an Asn 291---Ser mutation in the human LPL gene. Arterioscler Thromb Vasc Biol, 1995; 15: 1695-1703
- 43) Yang WS, Nevin DN, Iwasaki L, Peng R, Brown BG, Brunzell JD, Deeb SS: Regulatory mutations in the human lipoprotein lipase gene in patients with familial combined hyperlipidemia and coronary artery disease. J Lipid Res, 1996; 37: 2627-2637
- 44) Zhang Q, Cavallero E, Hoffmann MM, Cavanna J, Kay A, Charles A, Braschi S, Marz W, Perlemuter L, Jacotot B, Galton DJ: Mutations at the lipoprotein lipase gene locus in subjects with diabetes mellitus, obesity and lipaemia. Clin Sci (Lond), 1997; 93: 335-341
- 45) Arai T, Tsukada T, Okubo M, Murase T, Matsumoto K: Ser477Stop mutation of the lipoprotein lipase gene occurs at a higher frequency in Japanese subjects with normal triglyceride levels than in hypertriglyceridemic patients. Atherosclerosis, 1999; 147: 417-420



Contents lists available at SciVerse ScienceDirect

Journal of Clinical Gerontology & Geriatrics

journal homepage: www.e-jcgg.com



Original article

Psychosocial quality of life of elderly hemodialysis patients using visual analog scale: Comparison with healthy elderly in Japan

Hiroshi Kanamori, MD, PhD a, Motoko Yanagita, MD, PhD b, Kojiro Nagai, MD, PhD a, Takeshi Matsubara, MD, PhD b, Hajime Takechi, MD, PhD c, Keiichi Fujimaki, MD d, Akira Hra, MD, PhD d, Kazumasa Usami, MD, PhD e, Atsushi Fukatsu, MD, PhD a, Toru Kita, MD, PhD b, Kozo Matsubayashi, MD, PhD f, Hidenori Arai, MD, PhD c

ARTICLE INFO

Article history: Received 9 July 2011 Received in revised form 7 September 2011 Accepted 3 October 2011

Keywords: Elderly Hemodialysis Quality of life Visual analog scale

ABSTRACT

Background: The number of elderly hemodialysis (HD) patients is increasing in Japan, and the psychosocial impact of HD to the elderly remains unclear. The main purpose of this study was to evaluate quality of life (QOL) of elderly patients undergoing regular HD.

Methods: We examined the psychosocial status in elderly HD patients and compared it with that in healthy elderly individuals. The correlations between each item of QOL, laboratory data and comorbidities were explored. This study cohort consisted of 142 people (70 healthy elderly participants and 72 elderly HD patients). We assessed 10 items of QOL, i.e., health condition, appetite, sleep, mood, memory, family relationship, friendship, economical status, satisfaction in daily life, and happiness by visual analog scale (VAS).

Results: Overall, elderly HD patients had lower scores of VAS than healthy elderly participants, especially in sleep, mood, and happiness, but not in family relationship and friendship. Lower VAS scores for sleep were significantly correlated with the duration of HD therapy and the troubles in vascular access for HD. VAS scores for family relationship were also correlated with the duration of HD therapy.

Conclusion: The QOL of elderly HD patients was poorer than that in healthy elderly individuals, particularly in sleep, mood and happiness. Further study is needed to improve the QOL of elderly HD patients. This is of great importance, since the number of elderly HD patients is estimated to escalate in the future. Copyright © 2011, Asia Pacific League of Clinical Gerontology & Geriatrics. Published by Elsevier Taiwan LLC. All rights reserved.

1. Introduction

With the advance of dialysis technology, the number of elderly dialysis patients is increasing in Japan. According to the statistical survey by the Japanese Society for Dialysis Therapy, the mean age of the whole dialysis population was increased from 61.2 years at the end of 2000 to 65.8 years in 2009. The mean age of patients who

started dialysis was also increased from 63.8 years in 2000 to 67.3 years in 2009.¹

At the end of 2000 and 2009, there were about 200,000 and 290,000 dialysis patients in Japan, respectively. It is considered that these dialysis patients might live with more mental stress, including anxiety for comorbidities, conflicts with their family and social restrictions, than healthy individuals. It has been reported that quality of life (QOL), mental health and physical health in hemodialysis (HD) patients were poorer than those in the general population.² Depression, a key factor of QOL items to evaluate patients with end-stage renal disease,³ was an important predictor of patients' prognosis.⁴ Therefore, more attention should be paid to QOL, psychological problems and medical conditions of dialysis

2210-8335/\$ — see front matter Copyright © 2011, Asia Pacific League of Clinical Gerontology & Geriatrics. Published by Elsevier Taiwan LLC. All rights reserved. doi:10.1016/j.jcgg.2011.11.001

^a Department of Nephrology, Kyoto University Hospital, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan

Department of Cardiology, Kyoto University Graduate School of Medicine, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan

Department of Geriatric Medicine, Kyoto University Graduate School of Medicine, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan

^d Kita-Eijinkai Hospital, 1-5-21 Minamitsukaguchi-cho, Amagasaki, Hyogo, 661-0012, Japan

^e Taigenkai Hospital, 1-1 Bizen, Higashiitsushiro, Ichinomiya, Aichi 494-0008, Japan

^f Center for Southeast Asian Studies, Kyoto University, 46 Shimoadachi-cho, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan

^{*} Corresponding author. Department of Nephrology, Kyoto University Hospital, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan.

E-mail address: h-kanamori@live.jp (H. Kanamori).

^{*} Present address: Department of Nephrology, Fukuchiyama City Hospital, 231 Atsunaka-cho, Fukuchiyama, Kyoto 620-8505, Japan.

patients. With regards to QOL, assessment of HD patients' self-evaluation for psychosocial status (subjective QOL) was of great importance. Although some reports studying psychosocial QOL of HD patients have been done, little was known regarding the QOL of elderly HD patients.

Many studies examining the QOL of HD patients were performed using Kidney Disease Quality of Life (KDQOL) or Short Form 36 (SF-36) for questionnaires; however, these questionnaires are time-consuming for the elderly. Generally speaking, Japanese people, especially the elderly, are not used to selecting a single answer and have some difficulties responding to such questions. Accordingly, a visual analog scale (VAS) was a better instrument to complete questionnaires in a short period of time, and a few studies examined QOL by VAS. The main aim of this study was to evaluate the psychosocial QOL of elderly HD patients and to compare it with that of healthy elderly participants using a VAS.

2. Methods

The study was performed in 2000 at Taigenkai Hospital and Kita-Eijinkai Hospital, located in Bisai and Amagasaki cities of Japan, respectively. Among HD patients followed in the dialysis unit at these two hospitals as outpatients, 231 were given questionnaires. Patients aged \geq 65 years old were defined as "elderly", and those aged < 65 years old were defined as "non-elderly". Based on this definition, our HD patients consisted of 83 elderly and 148 nonelderly patients. The control group was composed of 70 healthy elderly people in nearby welfare facilities (places where people spend their time for their health promotion and leisure). These healthy controls were defined as community-dwelling elderly. The study was approved by each constituted Ethics Committee of the institutions where the work was undertaken and conforms to the provisions of the Declaration of Helsinki. We obtained each participant's informed consent for the study. Participants were given a brief explanation of the questionnaire by the medical technician or by the attending physician and were asked to complete the questionnaire. Assistance was given for participants who were illiterate or had poor eyesight.

QOL assessment was performed by VAS. VAS is frequently used as a subjective scale of pain in the field of anesthesiology. The VAS

questionnaire ended with a summing-up graph in the form of a 100 mm bar, graded with the subjectively worst condition on the left and the best on the right (Fig. 1). Patients were examined at the beginning of their first HD session of the week. Healthy elderly participants were examined during their regular meeting in the welfare facilities. Each participant was asked to mark, on the 100 mm bar, how his condition was. We defined the distance (mm) from the left to the marked position as the score of VAS (0-100), with high scores indicating a high QOL.5 We assessed 10 items of QOL: (1) health condition; (2) appetite; (3) sleep; (4) mood; (5) memory; (6) family relationship; (7) friendship; (8) economical status; (9) satisfaction in daily life; and (10) happiness, as described by Matsubayashi et al⁵ (Fig. 1). The VAS (10 items of QOL) has been validated for use in the Japanese population.⁶ In elderly HD patients, demographic data including age, sex, and duration of HD therapy, laboratory data [which includes cardio-thoracic ratio (CTR), plasma level of blood urea nitrogen (BUN), hemoglobin (Hb) and albumin (Alb)], and comorbidities [which includes blood access trouble, ischemic heart disease (IHD), diabetes mellitus (DM), infectious diseases, bone fracture and cerebrovascular disease (CVD)] were simultaneously collected.

Data were analyzed using JMP v. 6.0.0 (SAS Institute Inc., Cary, NC, USA). With regards to characteristics, the means were analyzed using the t-test (age) and frequencies were analyzed using the Chisquare for independence test (sex). Medians of QOL scores were calculated and analyzed using the Mann-Whitney U test, In elderly HD patients, the correlation between scores of QOL and laboratory data/personal histories was analyzed using multivariate regression analysis. Statistical significance was considered to be p < 0.05.

3. Results

Demographic characteristics are shown in Table 1. All of the 83 elderly patients were given questionnaires, and answers from 72 elderly patients (86.7%) were used for the analysis for completeness of questionnaire. By contrast, all the answers obtained from 70 healthy elderly participants (100%) were used for comparison.

The mean age of the elderly HD patients (71.8 years \pm 5.6 years) was approximately 2 years less than that of the healthy elderly participants (74.0 years \pm 6.7 years) (p = 0.0317); however, there

We would like to ask you some questions about your general daily life. On your present situation, mark a line segment with a cross "X" as showed below.



- (1) On which point is your health condition?
- (2) How about your appetite?
- (3) How is your sleep in the night?
- (4) How is your daily mood?
- (5) To what extent can you memorize something at present?
- (6) Do you get along well with your mete, your family members, your sons or daughters, and your grandchildren?
- (7) Are you satisfied with the relationships with your friends and relatives?
- (8) Is your income enough now?
- (9) Are you satisfied with your existing daily life?
- (10) Taking every factor into consideration, what extent of happiness do you have?

Fig. 1. Questionnaire form for the study. We used this form translated into Japanese.

Table 1Characteristics, laboratory data and comorbidities in HD patients

	Elderly patients $(n = 72)$
Age (y), mean ± SD	71.8 ± 5.6
Sex (M/F) (% male)	42/30 (58.3%)
Duration of hemodialysis (y), mean $\pm SD$	6.9 ± 5.0
Chronic glomerulonephritis, n (%)	38 (24.5%)
Cardio-thoracic ratio (mmHg), mean \pm SD	$\textbf{50.2} \pm \textbf{4.9}$
Blood urea nitrogen (mmol/L), mean \pm SD	26.0 ± 6.5
Hemoglobin (g/L), mean \pm SD	87.8 ± 14.4
Albumin (g/dL), mean \pm SD	38.5 ± 5.66
Blood access trouble	58.5%
Ischemic heart disease	28.6%
Diabetes mellitus	53.1%
Infectious diseases	18.4%
Bone fracture	17.1%
Cerebrovascular disease	13.3%

Data are expressed as means \pm SD or incidence of each disease (%).

was no difference in gender between the groups (58.3% males in the elderly HD patients vs. 55.7% males in the healthy elderly participants, p = 0.753). VAS scores were significantly lower in the elderly HD patients than those in the healthy elderly participants in sleep (53.0 vs. 80.5, p < 0.0001), mood (62.0 vs. 82.0, p < 0.0001), and happiness (71.0 vs. 85.5, p < 0.0001), indicating impaired general QOL in the elderly HD patients, but not family relationships and friendship (Table 2).

In the elderly HD patients, there was a significant correlation between family relationships and gender (standard $\beta=0.583$, p=0.0161), duration of HD (standard $\beta=-0.528$, p=0.0237) or CTR (standard $\beta=-0.471$, p=0.0364), between friendship and gender (standard $\beta=0.598$, p=0.0150) or CTR (standard $\beta=-0.631$, p=0.0089), between sleep and duration of HD (standard $\beta=-0.450$, p=0.0445) or blood access trouble (standard $\beta=-0.856$, p=0.0018), between memory and duration of HD (standard $\beta=-0.626$, p=0.0308), and between economical status and gender (standard $\beta=0.629$, p=0.0063) or CTR (standard $\beta=-0.701$, p=0.0024) (Table 3),

4. Discussion

In this study, we showed that elderly HD patients had lower psychosocial QOL than healthy elderly participants. We think that the response rate was high enough by using VAS in this study, despite the high age in our cohort. To compare QOL between the two groups, we analyzed the median of VAS scores using the Mann-Whitney U test, because VAS scores of some items were not

Table 2QOL scores (median) of healthy elderly and elderly HD patients

Items of QOL	Healthy elderly $(n = 70)$	Elderly patients $(n = 72)$	р
Health condition	76.5	50	< 0.0001
Appetite	88	76.5	0.031
Sleep	80.5	53	< 0.0001
Mood	82	62	< 0.0001
Memory	62.5	45	0.0005
Family relationship	90	91.5	0.5705
Friendship	90	88	0.1242
Economical status	86	70.5	0.0033
Satisfaction in daily life	92	68	0.0001
Happiness	85.5	71	< 0.0001

 $\ensuremath{\mathsf{QOL}}$ scores were compared by Mann-Whitney U test between healthy elderly and elderly HD patients in each item of QOL, respectively.

normally distributed. QOL scores were significantly lower in the elderly HD patients than those in the healthy elderly participants, except in relation to family relationships and friendship. These data indicated impaired general QOL in elderly HD patients.

By contrast, we showed that there was no difference in psychosocial QOL in these 10 items between elderly and non-elderly HD patients. Taking these results into account, our results indicate that older age by itself does not always impair QOL in HD patients. Age has been considered to be an important factor when dialysis therapy is indicated, which was not shown in this study. Therefore, as a recent report suggested, age alone should not be a barrier to initiate the dialysis therapy.

A number of studies have been reported in terms of QOL in HD patients. Most of these studies were examined using KDQOL or SF-36 for questionnaires, and have reported that the QOL of HD patients was markedly impaired in comparison to that of the general population in both physical and mental components. In Japan, a study using SF-36 reported that QOL sores of HD patients are lower than national standards in all eight dimensions, indicating impaired QOL in physical and psychosocial status. 9 However, it has been reported that QOL in both physical and mental components of older old HD patients (≥75 years old) was similar to that in the general population. 10 In our study, eight out of ten QOL items were significantly lower in the elderly HD patients than those in the healthy elderly participants, which was different from the study mentioned above. This could be related to the differences in the demographic characteristics, the age composition of HD patients, or the age with which the HD patients were classified.

Many studies concerning the QOL of HD or end stage renal disease (ESRD) patients have used KDQOL or SF-36, because these methods have high reliability and validity, and have been used internationally. With these methods, the participants need to answer no less than 36 questions, which is time-consuming and requires patience. Japanese people, especially the elderly, are not used to selecting a single answer and have some difficulties in responding to 36 questions. Therefore, we used VAS which could be completed in a short period of time, as the only requirement is to place a mark on the 100 mm bar. 11 Inter-rater reliability (r = 0.74, p < 0.05) and test-retest reliability (r = 0.82, p < 0.05) of VAS had been already confirmed.⁵ For VAS, we assessed ten items of QOL, and the rate of available answers was as much as 92.8% (= 72+70/83+70) in the elderly, including HD patients and healthy participants. A previous study reported that VAS scores of health conditions in dialysis patients were 58 [0(worst)-100(best)]. 12 As far as we know, our investigation is the first study to use VAS to assess psychosocial QOL in elderly HD patients.

Our study also revealed that the QOL of elderly HD patients was more impaired than that of healthy individuals, especially in sleep, mood, and happiness. A recent study reported that 45% of HD patients complained of insomnia compared with 4–29% in the general population.¹³ In our study, 54.5% of HD patients (56.3% in elderly) had sleep disturbance, although most patients suffering from insomnia took hypnotics (data not shown). Sleep apnea syndrome (SAS), restless leg syndrome (RLS), and skin itching may also contribute to insomnia. The relationship between these comorbidities and sleep disturbance remains to be determined in elderly HD patients.

In terms of mood, several studies found a 10–35% prevalence of depression among ESRD patients. ¹⁴ The QOL item "mood" in this study, however, does not always mean depression. In order to examine the prevalence of "real" depression, on collecting the score of "mood" 3 years later, we simultaneously examined the prevalence of depression using the Geriatric Depression Scale (GDS)-15 (Fig. 2), ¹⁵ and the incidence was estimated at 53.8% (58.3% in elderly patients) by using a cut-off of 5/6 (data not shown). This may be due to ethnic differences or the method of depression screening. Patel

Table 3Relationship between VAS scores of QOL and laboratory data/personal histories in elderly patients

	Health condition	Appetite	Sleep	Mood	Memory	Family relationship	Friendship	Economical status	Satisfaction in daily life	Happiness
R ²	0.542	0.426	0.704	0.506	0.518	0.694	0.687	0.745	0.503	0.314
Age (y)	0.049	-0.276	0.032	0.152	0.222	0.176	-0.081	0.205	0.346	0.198
Sex (female)	-0.154	0.293	-0.049	0.32	0.007	0.583*	0.598*	0.629*	0.443	0.331
Period of HD (y)	0.093	0.320	-0.450*	0.394	-0.626*	0.528*	-0.341	0.234	0.498	0.343
CTR (%)	0.126	0.371	0.058	-0.153	0.177	0.471*	-0.631*	0.701*	0.433	-0.171
BUN (mmol/L)	0.170	0,245	0.144	-0.199	0.098	-0.049	0.206	0,080	0.140	-0.044
Hb (g/L)	0.236	-0.173	-0.072	-0.397	-0.167	0.037	0.338	-0.316	-0.212	0.081
Alb (g/L)	-0.295	-0.073	0.200	0.297	0.419	-0.103	-0.421	0.150	0.072	0.009
Blood access	0.213	-0.389	-0.856*	-0.410	-0.024	-0.228	-0.406	-0.247	-0.321	-0.360
trouble			0.400		0.370	0.055	0.005	0.000	0.070	0.007
IHD	0.550	0.360	0.468	0.570	0.376	0.066	0.085	0.260	0.079	0.067
DM	-0.049	-0.026	-0.209	-0.088	-0.395	-0.154	-0.038	0.064	0.034	0.033
Infectious diseases	-0.451	0.314	0.234	0.077	0.091	0.203	0.159	0.046	0.328	-0.060
Bone fracture	0.271	-0.350	0.091	0.325	0.410	0.238	-0.095	0.077	0.094	0.178
CVD	-0.469	0.085	0.165	-0.007	-0.066	0.354	0.192	-0.248	-0.055	0.086

^{*} p < 0.05.

Relationship between VAS scores of QOL and laboratory data/personal histories were analyzed using multivariate regression analysis, corrected with age, sex, and period of hemodialysis (HD) therapy, cardio-thoracic ratio (CTR), blood urea nitrogen (BUN), hemoglobin (Hb), albumin (Alb), blood access trouble, ischemic heart disease (IHD), diabetes mellitus (DM), infectious diseases, bone fracture and cerebrovascular disease (CVD).

Each number indicates the standard β of each independent variable.

et al reported that there was a higher risk of depression in male patients and patients with religious beliefs.¹⁶ Meanwhile, various methods for depression screening have been used, for example, Beck's Depression Inventory (BDI),¹⁷ and the Center for Epidemiological Studies Depression Screening Index (CES-D).¹⁸ We used GDS-15 as it was a self-assessed questionnaire composed of 15 yes

or no questions and required only a few minutes to complete and score. ¹⁹ In Japan, Schreiner et al. reported that the cut-off score of 6 for GDS-15 in Japanese individuals, had a sensitivity of 97.3% and a specificity of 95.9%, which was the same as that reported for western individuals. ²⁰ In our study, few or no antidepressant agents were prescribed to patients with a depressive mood. Therefore,

We would like to ask you some questions about your feeling for the last month. On each question, circle "yes" or "no", please.

- (1) Are you basically satisfied with your life? (yes/no)
- (2) Have you dropped many of your activities and interests? (yes/no)
- (3) Do you feel that your life is empty? (yes/no)
- (4) Do you often get bored? (yes/no)
- (5) Are you in good spirits most of time? (yes/no)
- (6) Are you afraid that something bad is going to happen to you? (yes/no)
- (7) Do you feel happy most of the time? (yes/no)
- (8) Do you often feel helpless? (yes/no)
- (9) Do you prefer to stay at home, rather than going out and doing new things? (yes/no)
- (10) Do you feel you have more problems with memory than most? (yes/no)
- (11) Do you think it is wonderful to be alive now? (yes/no)
- (12) Do you feel pretty worthless the way you are now? (yes/no)
- (13) Do you feel full of energy? (yes/no)
- (14) Do you feel that your situation is hopeless? (yes/no)
- (15) Do you think that most people are better of than you are? (yes/no)

Fig. 2. Geriatric Depression Scale-15. We used this form translated into Japanese.

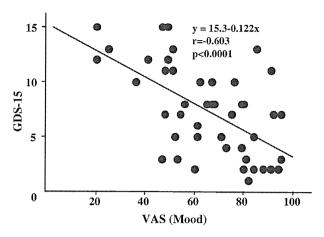


Fig. 3. Correlation between GDS-15 score and VAS in mood in elderly HD patients.

a prospective study to test the effect of antidepressants on OOL in elderly HD patients remains to be investigated.

As might be expected, the score of QOL item of mood "very depressed to very good mood" and that of GDS-15, were significantly correlated with each other by univariate regression analysis in elderly HD patients (Fig. 3). These data indicate that the VAS of "mood" can be used to support GDS scores for depression.

Concerning the relationship between QOL and laboratory data/ personal histories, it is noteworthy that better sleep was inversely correlated with the existence of blood access trouble, which indicated that the sleeping position (for example, resting one's head against one's arm) is one of the reasons of blood access obstruction. It is notable that female sex and the low values of CTR were correlated with better family relationships, friendship or economical status. These data might be due to the nature of female genes in comparison to those of males.

This study has some limitations. Although it is the first investigation to use VAS to assess psychosocial QOL in elderly HD patients, the sample size was small. In order to establish the validity and reliability of VAS in examining QOL, a study with a larger sample size should be performed.

In conclusion, elderly HD patients have a lower score of QOL than healthy elderly individuals. VAS could be a convenient tool to examine psychosocial QOL for the elderly.

Acknowledgments

We would like to thank Toshiko Hori, Kazuko Nishiyama, and Masanori Shibata for technical assistance in giving the questionnaire to participants. No conflict of interest (financial or non-financial) is declared.

- 1. The statistical survey by the Japanese Society for Dialysis Therapy. Website. http://docs.jsdt.or.jp/overview/index.html.
- 2. Mittal SK, Ahern L, Flaster E, Maesaka JK, Fishbane S. Self-assessed physical and mental function of haemodialysis patients. Nephrol Dial 2001;16:1387-94.
- Cagney KA, Wu AW, Fink NE, Jenckes MW, Meyer KB, Bass EB, et al. Formal literature review of quality-of-life instruments used in end-stage renal disease. Am J Kidney Dis 2000;**36**:327–36.
- Lewin NW. Adequacy of dialysis. Am J Kidney Dis 1994;**24**:308—15.

 Matsubayashi K, Wada T, Okumiya K, Fujisawa M, Taoka H, Kimura S, et al.

 Comparative study of quality of life in the elderly between in Kahoku and in Yaku.

 Nippon Ronen Igakkai Zasshi 1994;**31**:790—9 [In Japanese, English abstract].
- Matsubayashi K, Okumiya K, Osaki Y, Fujisawa M, Doi Y. Quality of life of old people living in the community. Lancet 1997;350:1521-2.
- Kanamori H, Nagai K, Matsubara T, Mima A, Yanagita M, lehara N, et al. Comparison of psychosocial quality of life in hemodialysis patients between elderly and non-elderly using visual analogue scale: the importance of appetite and depressive mood. Geriatr Gerontol Int. doi:10.1111/j.1447-0594.2011. 00731.x. [Epub ahead of print].
- 8. Lamping DL, Constantinovici N, Roderick P, Normand C, Henderson L, Harris S, et al. Clinical outcomes, quality of life, and costs in the North Thames dialysis study of elderly people on dialysis: a prospective cohort study. Lancet 2000:**356**:1543-50.
- 9. Fukuhara S, Lopes AA, Bragg-Gresham JL, Kurokawa K, Mapes DL, Akizawa T, et al. Health-related quality of life among dialysis patients on three continents: the dialysis outcomes and practice patterns study. Kidney Int 2003;64:
- 10. DeOreo PB. Hemodialysis patient-assessed functional health status predicts continued survival, hospitalization, and dialysis-attendance compliance. Am J Kidney Dis 1997;**30**:204–12.
- Morrison DP. The Crichton visual analogue scale for the assessment of behaviour in the elderly. Acta Psychiatr Scand 1983;68:408-13.
- De Wit GA, Busschbach JJ, De Charro FT. Sensitivity and perspective in the valuation of health status: whose values count? *Health Econ* 2000;**9**:109–26.
- Sabbatini M, Minale B, Crispo A, Pisani A, Ragosta A, Esposito R, et al. Insomnia in maintenance haemodialysis patients. Nephrol Dial Transplant 2002;17: 852-6
- 14. Christensen AJ, Smith TW, Turner CW, Cundick KE. Patient adherence and adjustment in renal dialysis: a person x treatment interactive approach. J Behav Med 1994;17:549-66.
- Yesavage JA. Geriatric depression scale. Psychopharmacol Bull 1988;24:709-11.
- Patel SS, Shah VS, Peterson RA, Kimmel PL. Psychosocial variables, quality of life, and religious beliefs in ESRD patients treated with hemodialysis. Am J Kidney Dis 2002;40:1013-22
- 17. Finkelstein FO, Finkelstein SH. Depression in chronic dialysis patients: assessment and treatment. Nephrol Dial Transplant 2000;15:1911-3
- Lopes AA, Albert JM, Young EW, Satayathum S, Pisoni RL, Andreucci VE, et al. Screening for depression in hemodialysis patients: associations with diagnosis, treatment, and outcomes in the DOPPS. Kidney Int 2004;66:2047-53.
- Wada T, Ishine M, Sakagami T, Kita T, Okumiya K, Mizuno K, et al. Depression, activities of daily living, and quality of life of community-dwelling elderly in three Asian countries: Indonesia, Vietnam, and Japan. Arch Gerontol Geriatr 2005:41:271-80.
- Schreiner AS, Hayakawa H, Morimoto T, Kakuma T. Screening for late life depression: cut-off scores for the geriatric depression scale and the cornell scale for depression in dementia among Japanese subjects. Int J Geriatr Psychiatry 2003;18:498-505.

(6)

Geriatr Gerontol Int 2012; 12: 65-71

ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Comparison of the psychosocial quality of life in hemodialysis patients between the elderly and non-elderly using a visual analogue scale: The importance of appetite and depressive mood

Hiroshi Kanamori,^{1*} Kojiro Nagai,¹ Takeshi Matsubara,¹ Akira Mima,¹ Motoko Yanagita,^{2*} Noriyuki Iehara,¹ Hajime Takechi,³ Keiichi Fujimaki,⁵ Kazumasa Usami,⁶ Atsushi Fukatsu,¹ Toru Kita,^{2*} Kozo Matsubayashi⁴ and Hidenori Arai^{3*}

¹Department of Nephrology, Kyoto University Hospital, Departments of ²Cardiovascular Medicine and ³Geriatric Medicine, Kyoto University Graduate School of Medicine, ⁴Center for Southeast Asian Studies, Kyoto University, Kyoto, and ⁵Kita-Eijinkai Hospital, Hyogo, ⁶Taigenkai Hospital, Aichi, Japan

Aim: The number of hemodialysis (HD) patients is increasing along with their mean age in Japan. The assessment of their psychosocial status and quality of life (QOL) is therefore becoming more and more important along with laboratory data or comorbidities.

Methods: We examined the psychosocial status of 211 HD patients (72 elderly and 139 non-elderly) and compared the difference between elderly and non-elderly patients using a visual analogue scale (VAS). We then examined how QOL affected mortality rate in 3-year prospective follow up. We assessed 10 items of QOL: health condition, appetite, sleep, mood, memory, family relationships, friendship, economical status, life satisfaction in daily life, and happiness with qualified self-evaluating questionnaires along with laboratory data and comorbidities. Furthermore, we investigated the correlation between the scores of mood and geriatric depression scale (GDS)-15.

Results: There was no difference in VAS scores between elderly and non-elderly patients. Lower VAS scores for appetite and mood correlated with higher mortality in HD patients, especially in the non-elderly. VAS scores for mood correlated with GDS-15 in HD patients.

Conclusions: More attention should be paid to appetite and the diagnosis and therapy of depressive mood to improve the prognosis of HD patients, especially for the non-elderly. **Geriatr Gerontol Int 2012; 12: 65–71.**

Keyword: appetite, depressive mood, hemodialysis, quality of life, visual analogue scale.

Accepted for publication 21 June 2011.

Correspondence: Dr Hiroshi Kanamori MD PhD, Department of Nephrology, Kyoto University Hospital, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan. Email: h-kanamori@live.jp

*Present addresses: Hiroshi Kanamori, Department of Nephrology, Fukuchiyama City Hospital, Kyoto, Japan; Motoko Yanagita, Hakubi Project, Young Researcher Development Center, Career-Path Promotion Unit For Young Scientist, Kyoto University Graduate School of Medicine, Kyoto, Japan; Toru Kita, Kobe City Medical Center Hospital, Hyogo, Japan; Hidenori Arai, Department of Human Health Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan.

Introduction

With the advance of dialysis technology, the number of dialysis patients along with the proportion of older patients is increasing in Japan. According to the annual statistical survey by the Japanese Society for Dialysis Therapy from the end of 2003 to 2009, the mean age of the whole dialysis population rose from 61.5 to 65.8 years old, much older than in 1985 (50.3 years old).

In the years 2003 and 2009, there were about 220 000 and 290 000 dialysis patients in Japan, respectively. It is likely that these dialysis patients live with more mental stress, including anxiety from comorbidities, conflict with their family and social restrictions. 1 It is reported that mental and physical health-related quality of life (QOL) in hemodialysis (HD) patients is lower than that in the general population,² and that depression is one of the most important predictors of patients' prognosis,3 which is one of the main QOL factors used to evaluate patients with end-stage renal disease (ESRD).4 Therefore, we should pay more attention to QOL and the psychological problems of dialysis patients in addition to medical factors. In terms of QOL, assessment of HD patients' self-evaluation for psychosocial status (subjective QOL) is very important. Although there are some reports on psychosocial QOL in HD patients, few studies have addressed the comparison between elderly and non-elderly patients.5

The aim of this study, therefore, was to evaluate psychosocial QOL of HD patients and to compare it between the elderly and non-elderly. Furthermore, we investigate how QOL affects the mortality of HD patients in a 3-year prospective follow up.

Patients and methods

This study was performed at Taigenkai Hospital and Kita-Eijinkai Hospital, located in Japan from 2000–2003. All HD outpatients in the dialysis units (231 patients) of these two hospitals were given questionnaires. Patients 65-years-old or older were defined as "elderly", those under 65-years-old as "non-elderly". On the basis of this definition, the HD population consisted of 83 elderly and 148 non-elderly patients. This study was approved by the Ethical Committee of Kita-Eijinkai Hospital and Taigenkai Hospital and conforms to the provisions of the Declaration of Helsinki. Written informed consent for the study was obtained from each patient. Participants were given a brief explanation of the questionnaire by a medical technician or the attending physician and were asked to complete the questionnaire.

QOL assessment of subjects was carried out using a visual analogue scale (VAS). VAS is frequently used as a subjective scale of pain in the field of anesthesiology. Each VAS questionnaire ended with a summing-up graph in the form of a 100 mm bar, graded with

subjectively the worst condition on the left and best one on the right. The participant was asked to mark on the 100 mm bar how they evaluated their condition. We defined the distance (mm) from the left to the marked position as the score of VAS (0-100), with high scores indicating high QOL.6 We assessed 10 QOL items: health condition; appetite; sleep; mood; memory; family relationships; friendship; economical status; life satisfaction in daily life; and happiness, as described by Matsubayashi et al.6 The VAS (10 items of QOL) has been validated for use in the Japanese population.7 Demographic data including age, gender, and duration of HD therapy, laboratory data, which included cardiothoracic ratio (CTR), plasma level of blood urea nitrogen (BUN), hemoglobin (Hb), albumin (Alb), and comorbidities including blood access trouble, ischemic heart disease, diabetes mellitus, infectious diseases, bone fracture, cerebrovascular disease were simultaneously collected. After patients rested in the supine position for at least 5 min, systolic blood pressure was measured twice by medical staff at the bedside and the average of those was calculated. Patients were examined at the beginning of their first HD session of the week, as is done in routine medical care.

We followed these patients for 3 years prospectively. The end point for patients was the trial end or death from any cause. At first, we examined the survival analysis in elderly and non-elderly HD patients. We then investigated how QOL affects the mortality of HD patients. At the end of the 3-year observation period we also screened for depression using the geriatric depression scale (GDS)-15 with a self-assessed questionnaire (0 [good] – 15 [very depressed])⁸ and investigated the correlation between the scores of the GDS-15 and QOL item mood, which was also examined simultaneously.

Data were analyzed using JMP v. 6.0.0 (SAS Institute Inc., Cary, NC, USA). For patient age, duration of HD and laboratory data, means were analyzed using t-test. For patient gender and comorbidities, frequencies were analyzed using χ^2 for independence test. Medians of QOL scores were calculated and analyzed using Mann-Whitney *U*-test. According to the average score of each VAS from all patients, a survival rate curve was analyzed by Kaplan-Meier analysis followed by log-rank test. Correlation between each score of QOL and mortality rate was analyzed using multivariate Cox regression analysis corrected for age, gender, duration of HD therapy, laboratory data and comorbidities. Correlation between the scores of GDS-15 and mood was analyzed using univariate regression analysis. Statistical significance was considered to be a P value of <0.05.

Results

Questionnaires were given to 231 patients and the response rate was 100%. However, answers from 211

Table 1 Characteristics, laboratory data and comorbidities in hemodialysis (HD) patients

	Elderly patients (n = 72)	Non-elderly patients $(n = 139)$	P value
Age (years, means \pm S.D.)	71.8 ± 5.6	52.4 ± 9.3	< 0.0001
Sex (male)	58.3%	64.7%	0.3613
Duration of HD (years, means \pm S.D.)	6.9 ± 5.0	8.5 ± 6.9	0.0696
SBP (mmHg, means \pm S.D.)	155 ± 23	153 ± 22	0.6046
CTR (%, means \pm S.D.)	50.2 ± 4.9	48.0 ± 5.0	0.0025
BUN (mmol/L, means \pm S.D.)	26.0 ± 6.5	28.4 ± 5.8	0.0073
Hb (g/L, means \pm S.D.)	87.8 ± 14.4	94.7 ± 15.6	0.0033
Alb (g/L, means \pm S.D.)	38.5 ± 5.7	42.4 ± 4.9	< 0.0001
Blood access trouble	58.5%	57.6%	0.9175
IHD	28.6%	25.7%	0.7410
DM	53.1%	42.7%	0.2567
Infectious diseases	18.4%	5.7%	0.0549
Bone fracture	17.1%	23.8%	0.4111
CVD	13.3%	17.4%	0.5614

Patient characters were compared between elderly and non-elderly. Data are expressed as means ± S.D. or incidence of each disease (%). Alb, albumin; BUN, blood urea nitrogen; CTR, cardiothoracic ratio; CVD, cerebrovascular disease; DM, diabetes mellitus; Hb, hemoglobin; IHD, ischemic heart disease; SBP, systolic blood pressure.

Table 2 Median of quality of life (QOL) scores in hemodialysis patients

Items of QOL	Elderly patients $(n = 72)$	Non-elderly patients $(n = 139)$	P value
Health condition	50	49	0.3047
Appetite	76.5	82	0.2415
Sleep	53	54	0.8906
Mood	62	60	0.6133
Memory	45	51	0.0948
Family relationships	91.5	89	0.1982
Friendship	88	80	0.3215
Economical status	70.5	51.5	0.0512
Satisfaction in daily life	68	57	0.0903
Happiness	71	67	0.4419

QOL scores were compared by Mann–Whitney U-test between elderly and non-elderly hemodialysis patients for each item of QOL. There was no significant difference between elderly and non-elderly hemodialysis patients.

patients (91.3%) were used for the analysis, because the rest were incomplete. Table 1 demonstrates patient characteristics, laboratory data, and comorbidities. The mean age of elderly and non-elderly HD patients was 71.8 ± 5.6 and 52.4 ± 9.3 , respectively (P < 0.0001). There was no significant difference in the proportion of gender or the duration of HD between the two groups. For the 10 items of QOL, there was no significant difference in VAS scores between elderly and non-elderly HD patients (Table 2).

In the 3-year prospective follow up, the number of deceased patients was 44 and the mortality rate was 21.8%. We also investigated the correlation between VAS scores in the QOL items and survival rate by

univariate analysis according to the average score of each QOL. The Kaplan–Meier analysis according to the VAS score of each QOL item in elderly and non-elderly HD patients is shown in Table 3. We found that higher VAS scores of health condition, appetite, sleep, mood and satisfaction in daily life were associated with better survival in non-elderly patients, but not in elderly patients.

On the other hand, higher VAS scores in appetite, mood, friendship, and satisfaction in daily life were significantly associated with better survival in non-elderly HD patients according to multivariate Cox regression analysis adjusted for age, gender, and duration of HD therapy, clinical data including CTR, BUN, Hb, Alb

Table 3 Kaplan–Meier analysis by each item of quality of life (QOL) in hemodialysis patients in elderly and non-elderly

	Cut-off point	Elderly patients $(n = 72)$ P value	Non-elderly patients ($n = 139$) P value
Health condition	50 <= vs 49 =>	0.4824	0.0138
Appetite	75 <= vs 74 =>	0.6832	0.0021
Sleep	59 <= vs 58 =>	0.8158	0.0059
Mood	62 <= vs 61 =>	0.8342	0.0047
Memory	$53 \le vs 52 =>$	0.7448	0.1317
Family relationships	$78 \ll vs 77 \implies$	0.4242	0.3575
Friendship	$74 \le vs 73 =>$	0.3438	0.5439
Economical status	$54 \le vs 53 =>$	0.5022	0.1990
Satisfaction in daily life	$61 \le vs 60 \Longrightarrow$	0.5047	0.0420
Happiness	66 <= vs 65 =>	0.7771	0.4040

Correlation between mortality and each item of QOL was analyzed by Kaplan–Meier analysis, followed by log–rank test. Cut off point (according to the average score of each QOL) is shown.

and comorbidities (appetite: relative risk [RR] = 0.931, P = 0.0041; mood RR = 0.938, P = 0.0005; friendship: RR = 0.949, P = 0.0317; satisfaction in daily life: RR = 0.967, P = 0.0178) (Table 4, right). Statistical significance was also found in family relationships (RR = 0.967; P = 0.0009) and friendship (RR 0.977; P = 0.0180) for all HD patients (Table 4, left), and appetite in elderly patients (RR = 1.048; P = 0.0247) (Table 4, center).

We then assessed the correlation between mood and GDS-15 in HD patients. There was an inverse correlation between VAS scores for mood and GDS-scores among all HD patients (r = -0.585, P < 0.0001), and when divided into elderly (r = -0.603, P < 0.0001) and non-elderly patients (r = -0.610, P < 0.0001).

Discussion

In this study we have shown that there is no difference between elderly and non-elderly HD patients in 10 psychosocial QOL items. However, better appetite, mood, and satisfaction in daily life were associated with better survival in non-elderly HD patients by Cox regression analysis and Kaplan-Meier analysis; no relationship was found between the scores of those QOL items and laboratory data/comorbidities (data not shown). These results indicate more attention should be paid to appetite, depressive mood, and satisfaction in daily life to improve the survival especially in non-elderly HD patients.

We found no significant difference in QOL between elderly and non-elderly HD patients. Few reports have addressed the relationship between age and QOL in HD patients. Tovbin *et al.* demonstrated that age is not associated with self-evaluated individualized QOL according to life domains including health, family, work/studies,

economic situation and leisure.⁵ Kutner *et al.* reported that prevalence of sleep disorders is not clearly associated with an increasing age of patients, and that elderly patients often report better psychosocial adjustment to dialysis than younger patients.⁹ Leinau *et al.* reported that the prevalence of depression is not restricted to older participants (≥60 years 31%; ≤60 years; 22%).¹⁰ These studies are consistent with our study showing no difference in QOL assessments between elderly and non-elderly HD patients.

Quite a number of studies have been reported in terms of QOL in HD patients. Most of the studies used the Kidney Disease Quality of Life (KDQOL) or Short Form 36 (SF-36) questionnaire and have reported that QOL of HD patients is markedly disturbed compared to that of the general population in both physical and mental components.² In Japan, a study using SF-36 reported that QOL sores of HD patients were lower than the national standard in all of eight scales, indicating disturbed physical and psychosocial QOL.11 However, in the KDOOL and SF-36 questionnaires the participants need to answer as many as 36 questions, which might be time consuming and require them to be patient to some extent. Japanese people, especially the elderly, are not used to multiple choice questionnaires and may have some difficulties responding to 36 questions. Therefore, we used a VAS that can be completed quickly, because participants only have to put a mark on the 100 mm bar. 12 Inter-rater reliability (r = 0.74, P < 0.05) and test-retest reliability (r = 0.82, P < 0.05) of the VAS score has been already confirmed.6 For the VAS examination we assessed 10 items of QOL, and the rate of available answers was as high as 91.3% in HD patients. Previous studies have reported that VAS scores of health conditions in dialysis patients were 58.13 Although more tests might be needed to prove further

Table 4 Correlation between mortality and each visual assessment scale (VAS) score of quality of life (QOL) items in hemodialysis patients in total, elderly, and non-elderly patients

	Relative	Total patients (1	n = 211)	Relative	Elderly patients $(n = 72)$	(n = 72)	Relative	Non-elderly patients $(n = 139)$	nts $(n = 139)$
	risk	95% CI	P value	risk	95% CI	P value	risk	95% CI	P value
Health condition	0.983	(0.956–1.008)	0.1866	0.987	(0.932–1.048)	0.6430	0.982	(0.939-1.026)	0.4116
Appetite	1.004	(0.988-1.023)	0.6087	1.048	(1.006-1.103)	0.0247	0.931	(0.871 - 0.980)	0.0041
Sleep	0.993	(0.976-1.011)	0.4511	1.029	(0.973-1.093)	0.3112	0.975	(0.936 - 1.009)	0.1462
Mood	0.982	(0.963-1.000)	0.0516	1.013	(0.971 - 1.053)	0.5270	0.938	(0.895-0.973)	0.0005
Memory	0.986	(0.966-1.005)	0.1393	1.020	(0.965-1.071)	0.4506	0.974	(0.937 - 1.004)	0.0881
Family relationships	0.967	(0.948-0.986)	0.0009	1.006	(0.945-1.076)	0.8544	0.965	(0.918-1.006)	0.0979
Friendship	0.977	(0.958-0.996)	0.0180	0.994	(0.916 - 1.067)	0.8763	0.949	(9.898-0.996)	0.0317
Economical status	1.001	(0.985 - 1.016)	0.9219	0.993	(0.940 - 1.035)	0.7229	0.990	(0.964-1.014)	0.4187
Satisfaction in daily life	0.660	(0.974-1.005)	0.1762	1.015	(0.982 - 1.046)	0.3423	0.967	(0.936 - 0.994)	0.0178
Happiness	0.988	(0.967-1.008)	0.2371	1.013	(0.972-1.052)	0.5097	0.997	(0.950-1.042)	0.8848

therapy, cardio-thoracic ratio (CTR), blood urea nitrogen (BUN), hemoglobin (Hb), albumin (Alb), and presence or absence of comorbidities including blood access trouble, Correlation between mortality and each item of VAS score of QOL was analyzed by multivariate Cox regression adjusted for age, gender, duration (years) of hemodialysis ischemic heart disease (IHD), diabetes mellitus (DM), infectious diseases, bone fracture and cerebrovascular disease (CVD) validation, our investigation is the first study to use VAS to assess psychosocial QOL in HD patients.

Anemia is considered to be an important factor for QOL and survival. As reported in western countries, there was a recent report from Japan that lower mortality risk was associated with higher Hb levels and that lower Hb levels were associated with lower QOL scores. 14 In contrast, the relationship between anemia and depression has been controversial.¹⁰ In this study we did not find any correlation between the Hb level and VAS score of any OOL items using multivariate regression analysis. It has been reported that diminished appetite is associated with a higher mortality rate from a viewpoint of malnutrition-inflammation complex syndrome (MICS).15 In this study, we analyzed data such as Alb (for nutritional status) and presence or absence of comorbidities such as infectious diseases (for inflammatory state). However, we did not find any relationship between comorbidities and Alb. These negative results might be ascribed to the small sample size in this study.

In terms of mood, a previous study found 10-35% prevalence of depression among ESRD patients.16 In this study, we assessed depressive mood by measuring the VAS score for mood. However, the score did not necessarily mean that the patients had depression. Therefore, we used GDS-15 in the third year of the prospective follow up, because it is validated for Japanese subjects¹⁷ and is a self-assessed questionnaire composed of 15 yes or no questions, requiring only a few minutes to complete and score. 18 As expected, the score of mood and that of GDS-15 was inversely correlated by univariate regression analysis in HD patients in both elderly and non-elderly patients. This indicates that the VAS of mood could be used as a relative score to assess depression to some extent. The correlation coefficient (r) was about -0.6, which means there is some discrepancy between mood and GDS. One reason that explains this discrepancy is that feelings such as anxiety might have been included in mood in our study. 19 The prevalence of depression (GDS scores 6 or more) was found to be 54.5% in our study. This relatively high prevalence of depression may be due to the screening method. In our study, little, if any, antidepressive agent was prescribed to patients with depressive mood. Therefore, a prospective study to test the effect of antidepressants on QOL in HD patients needs to be investigated.

It has been reported that the prevalence of depression is increasing with age in the general population.²⁰ However, according to a patient survey performed by the Ministry of Health, Labor and Welfare in Japan in 2005, patients with depression were distributed widely between the ages of 30 to 70. This could account for the lack of difference in mood between elderly and non-elderly HD patients.

To investigate whether poor QOL reflects a poor health condition, we assessed the relationship between health condition and QOL in elderly and non-elderly patients using regression analysis. In non-elderly patients there was a correlation between health condition and appetite, sleep and mood (r = 0.28; P = 0.0008, r = 0.29; P = 0.0006 and r = 0.51; P < 0.0001, respectively). However, the r value was relatively low (r < 0.30)except in relation to mood. In elderly patients, there was correlation between health condition and appetite, sleep and mood (r = 0.41; P = 0.0004, r = 0.38; P = 0.0012 and r = 0.65; P < 0.0001, respectively) and the r value was relatively high (r > 0.30). These results indicate that the QOL items appetite and sleep would be better markers of the health condition of elderly HD patients than non-elderly HD patients and that the QOL item mood would be a better marker of the health condition of both elderly and non-elderly HD patients. In contrast, we showed that better appetite and mood were associated with better survival in non-elderly HD patients. Furthermore, there was no relationship between the scores of these QOL items and laboratory data/comorbidities (data not shown). These data indicate the importance of QOL assessment in HD patients.

The relationship between depression and mortality rate is reported to be controversial.21 Husebye et al. reported that psychosocial variables are prognostically important for the survival of dialysis patients over the age of 70, but depression is not associated with mortality rate.²² Drayer et al. reported that depressed HD patients are younger and depression is associated with decreased QOL including sleep and increased mortality rate.²³ In terms of psychological factors, Kimmel et al. reported that there is an inverse relationship between the number of symptoms (pain, trouble with sleep, tiredness and shortness of breath) and QOL including psychological items and that no clinical parameter (duration of ESRD, serum Alb, Hb, Kt/V and Karnofsky Performance Status Scale) correlates with any measure of QOL.24 Moreover, Leinau et al. demonstrated that non-ESRD-specific conditions such as fatigue, pain, and depression are as prevalent as ESRD-specific conditions (use of a catheter for access, Hb, intact parathyroid hormone, phosphorous, and Kt/V) and highlighted the importance of diagnosing and treating non-ESRDspecific conditions to improve the health and QOL of persons with ESRD.¹¹ As reported in these latter two literatures, QOL factors such as sleep disturbance, depression and so on should be paid as much attention as clinical parameters as suggested in the guidelines

We have highlighted the need for assessment of elderly HD patients using self-evaluation for psychosocial status (subjective QOL). In this study, however, a higher QOL score for appetite, sleep, mood and satisfaction in daily life was associated with better survival

by both of univariate analysis (Kaplan–Meier analysis; Table 3) and multivariate analysis (Cox regression analysis; Table 4), in non-elderly HD patients only. These negative results in elderly patients might be ascribed to the small sample size. Actually, among the laboratory data that showed differences between elderly and non-elderly patients (Table 1), higher levels of Alb were associated with better survival in elderly patients, but there was no relationship between Alb and the scores of any QOL item (data not shown).

In conclusion, there was no difference in 10 psychosocial QOL items between elderly and non-elderly HD patients. Paying attention to appetite and depressive mood may lead to the improvement of the mortality rate of HD patients, especially for the non-elderly.

Acknowledgements

We thank Toshiko Hori (Kyoto University), Kazuko Nishiyama (Kita-Eijinkai Hospital) and Masanori Shibata (Taigenkai Hospital) for technical assistance and giving the questionnaire to participants.

- 1 Welch JL, Austin JK. Stressors, coping and depression in hemodialysis patients. *J Adv Nurs* 2001; **33**: 200–207.
- 2 Mittal SK, Ahern L, Flaster E, Maesaka JK, Fishbane S. Self-assessed physical and mental function of haemodialysis patients. Nephrol Dial Transplant 2001; 16: 1387–1394.
- 3 Levin NW. Adequacy of dialysis. Am J Kidney Dis 1994; 24: 308–315.
- 4 Cagney KA, Wu AW, Fink NE *et al.* Formal literature review of quality-of-life instruments used in end-stage renal disease. *Am J Kidney Dis* 2000; **36**: 327–336.
- 5 Tovbin D, Gidron Y, Jean T, Granovsky R, Schnieder A. Relative importance and interrelations between psychosocial factors and individualized quality of life of hemodialysis patients. *Qual Life Res* 2003; **12**: 709–717.
- 6 Matsubayashi K, Wada T, Okumiya K et al. [Comparative study of quality of life in the elderly between in Kahoku and in Yaku]. Nippon Ronen Igakkai Zasshi 1994; 31: 790– 799
- 7 Matsubayashi K, Okumiya K, Osaki Y, Fujisawa M, Doi Y. Quality of life of old people living in the community. *Lancet* 1997; **350**: 1521–1522.
- 8 Yesavage JA. Geriatric depression scale. *Psychopharmacol Bull* 1988; **24**: 709–711.
- 9 Kutner NG. Promoting functioning and well-being in older CKD patients: review of recent evidence. *Int Urol Nephrol* 2008; **40**: 1151–1158.
- 10 Leinau L, Murphy TE, Bradley E, Fried T. Relationship between conditions adressed by hemodialysis guidelines and Non-ESRD-Specific conditions affecting quality of life. Clin J Am Soc Nephrol 2009; 4: 572–578.
- 11 Fukuhara S, Lopes AA, Bragg-Gresham JL *et al.* Health-related quality of life among dialysis patients on three continents: the dialysis outcomes and practice patterns study. *Kidney Int* 2003; **64**: 1903–1910.
- 12 Morrison DP. The crichton visual analogue scale for the assessment of behavior in the elderly. *Acta Psychiatr Scand* 1983; **68**: 408–413.

- 13 De Wit GA, Busschbach JJ, De Charro FT. Sensitivity and perspective in the valuation of health status: whose values count? *Health Econ* 2000; **9**: 109–126.
- 14 Akizawa T, Pisoni RL, Akiba T *et al.* Japanease haemodialysis anemia management practices and outcomes (1999–2006): results from the DOPPS. *Nephrol Dial Transplant* 2008; **23**: 3643–3653.
- 15 Kalantar-Zadeh K, Block G, McAllister CJ, Humphreys MH, Kopple JD. Appetite and inflammation, nutrition, anemia, and clinical outcome in hemodialysis patients. Am I Clin Nutr 2004: 80: 299–307.
- 16 Christensen AJ, Smith TW, Turner CW, Cundick KE. Patient adherence and adjustment in renal dialysis: a person x treatment interactive approach. *J Behav Med* 1994; 17: 549–566.
- 17 Schreiner AS, Hayakawa H, Morimoto T, Kakuma T. Screening for late life depression: cut-off scores for the geriatric depression scale and the cornell scale for depression in Dementia among Japanese subjects. *Int J Geriatr Psychiatry* 2003; **18**: 498–505.
- 18 Wada T, Ishine M, Sakagami T *et al.* Depression, activities of daily living, and quality of life of community-dwelling elderly in three Asian countries: Indonesia, Vietnam, and Japan. *Arch Gerontol Geriatr* 2005; **41**: 271–280.

- 19 Cukor D, Coplan J, Brown C, Peterson RA, Kimmel PL. Course of depression and anxiety diagnosis in patients treated with hemodialysis: a 16-month follow-up. *Clin J Am Soc Nephrol* 2008; **3**: 1752–1758.
- 20 Konig HH, Bernert S, Angermeyer MC *et al.* Comparison of population health status in six European countries: results of a representative survey using the EQ-5D questionnaire. *Med Care* 2009; **47**: 255–261.
- 21 Kimmel PL. Psychosocial factors in dialysis patients. *Kidney Int* 2001; **59**: 1599–1613.
- 22 Husebye DG, Westlie L, Styrvoky TJ, Kjellstrand CM. Psychological, social, and somatic prognostic indicatiors in old patients undergoing long-term dialysis. *Arch Intern Med* 1987; **147**: 1921–1924.
- 23 Drayer RA, Piraino B, Reynolds IIICF *et al.* Characteristics of depression in hemodialysis patients: symptoms, quality of life and mortality risk. *Gen Hosp Psychiatry* 2006; **28**: 306–312.
- 24 Kimmel PL, Emont SL, Newmann JM, Danko H, Moss AH. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. *Am J Kid Dis* 2003; 42: 713–721.



Contents lists available at ScienceDirect

Journal of Clinical Gerontology & Geriatrics

journal homepage: www.e-jcgg.com



Original article

Differential determinants of physical daily activities in frail and nonfrail community-dwelling older adults

Minoru Yamada, RPT, PhD*, Hidenori Arai, MD, PhD, Koutatsu Nagai, RPT, Kazuki Uemura, RPT, Shuhei Mori, RPT, Tomoki Aovama, MD, PhD

Department of Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto, Japan

ARTICLE INFO

Article history: Received 14 January 2011 Received in revised form 26 January 2011 Accepted 8 February 2011

Keywords: Fear of falling Frail adults Physical function physical activity

ABSTRACT

Background/Purpose: The purpose of this study was to determine whether or not daily activities determined by average daily steps are associated with age, gender, body mass index, fear of falling, and physical functions (locomotive function, balance function, and muscle power) in community-dwelling nonfrail and frail older adults.

Methods: This is a cross-sectional study conducted in community-dwelling older adults in Japan. Based on the Timed Up and Go (TUG) test, 629 elderly adults were divided into two groups: 515 were grouped to nonfrail elderly (TUG time less than 13.5 seconds, mean age 77.0 ± 7.2 years) and 114 to frail elderly (TUG time of 13.5 seconds or more, mean age 76.1 ± 7.5 years). Daily physical activities were determined by average daily steps measured by pedometer and four other physical function tests (10-m walk test, single-leg standing, functional reach, and five-chair stand test) were performed along with the assessment of fear of falling.

Results: Stepwise regression analysis revealed that age, gender, 10-m walk test, and single-leg standing were significant and independent determinants of the average step counts in the nonfrail elderly ($R^2 = 0.282$, p < 0.001), whereas fear of falling was the only significant and independent determinant of the average step counts in the frail elderly ($R^2 = 0.119$, p < 0.001).

Conclusion: These results indicate that differential factors may be related to daily activities depending on the level of frailty in community-dwelling older adults.

Copyright © 2011, Asia Pacific League of Clinical Gerontology & Geriatrics. Published by Elsevier Taiwan LLC. All rights reserved.

1. Introduction

Physical activities show positive associations with various components of physical functions, such as walking speed, lower-limb strength, and balance and negative associations with the incidence of coronary artery disease, obesity, osteoporosis, and other causes of morbidity and mortality in elderly.^{1–4}

Higher physical activities can also improve quality of life and physical and psychological functions, facilitate independent living, and reduce the risk of dementia in older adults.^{5–8} Physical Activity Guidelines for Americans concluded that, for older adults, in addition to the well-known health benefits of a physically active

lifestyle, "strong evidence indicates that being physically active is associated with higher levels of functional health and a lower risk of falling." ⁹

However, Yoshida et al 10 showed that the association between physical fitness and ambulatory activity is affected by the level of instrumental activity of daily life in elderly women, suggesting the effect of frailty on the association. We demonstrated that the resistance training program is effective at decreasing the fear of falling in frail elderly but not in nonfrail elderly (Yamada et al, present study), indicating the difference of the effect of physical training in elderly with different physical fitness. We hypothesized, therefore, that differential factors could affect the level of physical daily activities in the presence or absence of frailty. The purpose of this study was to determine whether or not physical activities determined by average daily steps are associated with age, gender, body mass index (BMI), fear of falling, and physical function (locomotive function, balance function, and muscle power) in community-dwelling nonfrail and frail older adults.

2210-8335/\$ — see front matter Copyright © 2011, Asia Pacific League of Clinical Gerontology & Geriatrics. Published by Elsevier Taiwan LLC. All rights reserved. doi:10.1016/j.jcgg.2011.02.004

^{*} Corresponding author. Department of Human Health Sciences, Graduate School of Medicine, Kyoto University, 53 Kawaharcho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan.

E-mail address: yamada@hs.med.kyoto-u.ac.jp (M. Yamada).

2. Methods

2.1. Participants

Participants were recruited by an advertisement in a local press. We used the following criteria to screen participants in the initial interview and invited to participate in this study if he or she was aged 65 years or older , was community-dwelling, had a score of eight or more by Rapid Dementia Screening Test, 11 and was able to walk independently.

We excluded participants based on the following exclusion criteria: the presence of severe cardiac, pulmonary, or musculo-skeletal disorders; comorbidities associated with an increased risk of falls (i.e., Parkinson's disease or stroke); and use of psychotropic drugs. We obtained written informed consent from each participant in accordance with the guidelines approved by the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1975.

2.2. Definition of frailty

The definition of frailty is based on the results of previous study. The Timed Up and Go (TUG) is a simple test developed to screen basic mobility performance and has been shown to be significantly associated with activities of daily living function in frail older adults. ¹² It has been reported that elderly with a TUG score greater than 13.5 seconds have an increased risk of falls. ¹³ Therefore, frailty was defined as a TUG score greater than 13.5 seconds. Based on key components of the screening examination (TUG score greater than 13.5 seconds), 114 elderly were classified as frail, whereas 515 elderly as nonfrail.

2.3. Measurement of physical activities

A valid, accurate, and reliable pedometer, Yamax PowerWalker EX-510 (Yamax Corp., Tokyo, Japan), was used to measure free-living step counts. ¹⁴ Measurement of step counts was conducted between October and November 2010. Participants were instructed to wear the pedometer in their pocket of dominant leg for 14 consecutive days except during bathing, sleeping, and performing water-based activities. This pedometer has a 30-day data storage capacity. We calculated the averages of their daily step counts for 2 weeks.

2.4. Measurement of fear of falling

We assessed fear of falling by asking a single yes or no question, "Are you afraid of falling,?" which has a high test-retest reliability. 15 The test-retest reliability using the Kappa coefficient was 0.960.

2.5. Measurement of physical function

The participants received four other physical function tests that are widely used to identify high-risk elderly: 10-m walk test, single-leg standing, functional reach, and five-chair stand. In 10-m walk test, the participants were asked to walk as fast as possible along a 10-m straight line, with a 1 m approach at both ends, making a total length of 12 m. The time required was taken as the measured value. In single-leg standing, the length of time for which participants were able to stand on one leg with their hands placed on their waist was measured. The time was measured twice for each leg and the maximum length of time was taken. Functional reach was measured using the simple clinical apparatus consisting of a leveled yardstick secured to the wall at right acromion height as previously described. In five-chair stand, participants were asked to stand up and sit down five times as

quickly as possible and were timed from the initial sitting position to the final standing position at the end of the fifth stand.¹⁷ For each function test, the participants performed twice, and the average score was then calculated. All test measurements were completed before the daily step measurement.

2.6. Statistical analysis

The relationship between the average daily steps and physical function was investigated with the Pearson correlation coefficient. The t test and χ^2 test were used to compare the results of measurements between frail and nonfrail groups.

A multivariate analysis by means of multiple regression using a stepwise method was performed to investigate which of the age, gender, BMI, fear of falling, and five measures of physical function (i.e., 10-m walk test, TUG, single-leg standing, functional reach, and five-chair stand test) were independently associated with the average daily steps in each group.

Data were analyzed using the Statistical Package for Social Science (Windows version 18.0; SPSS Inc., Chicago, IL, USA).

3. Results

There were no significant differences in age (nonfrail = 77.0 ± 7.2 , frail = 76.1 \pm 7.5, p = 0.241), gender (nonfrail = 67.5%, frail = 67.5%, p = 0.541), height (nonfrail = 153.5 ± 7.6 cm, frail = 153.7 ± 6.1 cm, p = 0.743), weight (nonfrail = 53.0 ± 9.6 kg, frail = 53.6 ± 4.5 kg, p =0.576), and BMI (nonfrail = 22.4 ± 3.2 , frail = 22.7 ± 1.9 , p = 0.393) between the two groups (Table 1). However, all physical function tests and average daily steps were significantly different between the two groups. More fear of falling was observed (nonfrail = 39.1%, frail = 73.6%, p < 0.001), longer time was required for 10-m walk test (nonfrail = 9.9 ± 2.2 seconds, frail = 17.1 ± 6.6 seconds, p < 0.001), single-leg standing (nonfrail = 13.3 ± 12.1 seconds, frail = 3.1 ± 6.0 seconds, p < 0.001), and five-chair stand (nonfrail = 8.9 ± 3.6 seconds, frail = 17.6 \pm 8.5 seconds, p < 0.001) in frail elderly. Less functional reach (nonfrail = 25.0 ± 8.2 cm, frail = 17.9 ± 8.4 cm, p < 0.001), and average daily steps (nonfrail = 4414 ± 2726 steps, frail = 1585 ± 1013 steps, p < 0.001) were observed in frail elderly.

To determine the association of average step counts with physical functions and demography, we analyzed Pearson's correlation coefficients in frail and nonfrail elderly. Table 2 shows that average step counts in the nonfrail group were correlated with age $(r=-0.311,\ p<0.001),\ BMI\ (r=0.167,\ p<0.001),\ 10-m$ walk test $(r=-0.475,\ p<0.001),\ TUG\ (r=-0.412,\ p<0.001),\ functional$

Table 1Comparison of demography, fear of falling, and physical function and activities between nonfrail and frail elderly

Items	Nonfrail $(n = 515)$	• .	Frail gro $(n = 114)$	-	p
	Mean	SD	Mean	SD	
Age (yr)	77.0	7.2	76.1	7.5	0.241
Gender (male $= 0$, female $= 1$)	67.5		67.5		0.541^{a}
Height	153.5	7.6	153.7	6.1	0.743
Weight	53.0	9.6	53.6	4.5	0.576
BMI (kg/m ²)	22.4	3.2	22.7	1.9	0.393
Fear of falling (yes = 1 , no = 0)	39.1		73.6		$< 0.001^{a}$
10-m walking time (s)	9.9	2.2	17.1	6.6	< 0.001
Timed up & go test (s)	8.8	2.1	20.2	6.8	< 0.001
Single leg standing (s)	13.3	12.1	3.1	6.0	< 0.001
Functional reach (cm)	25.0	8.2	17.9	8.4	< 0.001
Five chair stand (s)	8.9	3.6	17.6	8.5	< 0.001
Average daily step (step)	4414.4	2726,3	1585.0	1012.6	< 0.001

BMI = body mass index; SD = standard deviation.

 $^{\rm a}$ χ^2 test.

Table 2Pearson's correlation coefficients (*r*) between average daily steps and physical functions, age, and BMI

Items	Nonfrail group $(n = 515)$	Frail group $(n = 114)$	Overall $(n = 629)$
Age (yr)	-0.311**	-0.109	0.241**
BMI (kg/m ²)	0.167**	-0.013	0.130**
10-m walking time (s)	-0.475**	-0.047	-0.448**
Timed up & go test (s)	-0.412**	-0.131	-0.450**
Functional reach (cm)	0.348**	0.175	0.406**
Five-chair stand (s)	-0.297**	-0.226*	-0.397**
Single-leg standing (s)	0.440**	0.077	0.502**

BMI = body mass index. p < 0.05; **p < 0.01.

reach $(r=0.348,\ p<0.001)$, five chair stand test $(r=-0.297,\ p<0.001)$, and single-leg standing test $(r=0.440,\ p<0.001)$. In the frail group, however, a significant association was found only with five-chair stand test $(r=-0.226,\ p<0.001)$. Figure 1 shows linear regressions between physical functions and average step counts in nonfrail and frail elderly. Average step counts had a positive association with functional reach (Fig. 1C) and negative associations with 10-m walk test (Fig. 1A) and TUG (Fig. 1B) only in nonfrail elderly. However, step counts had a negative association with five-chair stand (Fig. 1D) both in nonfrail and frail elderly.

Stepwise regression analysis revealed that age $(\beta = -0.108, p = 0.03)$, gender $(\beta = 0.255, p < 0.001)$, 10-m walk test $(\beta = -0.202, p < 0.001)$ and single-leg standing $(\beta = 0.306, p < 0.001)$ were

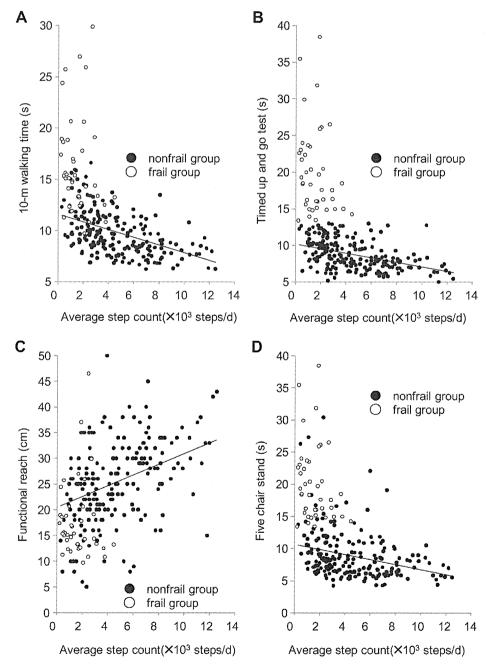


Fig. 1. Relationships between average daily steps and physical function. The physical function was associated with physical activities in nonfrail but not in frail elderly. (A) 10-m walk test; (B) Timed up and go test; (C) Functional reach; (D) Five-chair stand test.

Table 3Multiple stepwise regression analysis

Independent variables	Nonfrail group Adjusted R ² value = 0.282 standard regression value	Frail group Adjusted R ² value = 0.119 standard regression value	Overall Adjusted R ² value = 0.345 standard regression value
Age (yr)	-0.108*		-0.137**
BMI (kg/m ²)			
Gender (male = 0 , female = 1)	0.255**		0.238**
Fear of falling (yes = 1 , no = 0)		-0.356**	-0.089*
10-m walking time (s)	-0.202**		-0.172**
Timed up & go test (s)			
Functional reach (cm)			
Five chair stand (s)			-0.147**
Single leg standing (s)	0.306**		0.314**

^{*}p < 0.05; **p < 0.01.

significant and independent determinants of the average step counts in nonfrail elderly ($R^2=0.282, p<0.001$) (Table 3). Stepwise regression analysis also revealed that fear of falling ($\beta=-0.356, p<0.001$) was the only significant and independent determinant of the average step counts in frail elderly ($R^2=0.119, p<0.001$) (Table 3).

4. Discussion

In the present study, we showed that the differential factors of physical functions may relate to the daily activities in frail and nonfrail community-dwelling elderly Japanese. Our data implicate that physical daily activities can be maintained in the robust elderly with high physical function, whereas fear of falling plays a more important role for the maintenance of physical daily activities if an older adult becomes functionally impaired and frail. Previous studies also indicated that the low self-efficacy for daily activities reduces physical activity, and psychological well-being is an important predictor for staying physically active. ^{18,19} Thus, differential approaches should be taken to keep the daily activities depending on their physical fitness in elderly.

The physical functions, age, and gender were associated with daily activities in nonfrail elderly but not in frail elderly. Rantanen et al²⁰ also reported that the relationship between muscle strength and physical disability in older adults is nonlinear. Moreover, in most of previous reports, the participants were nonfrail older adults.^{1–4} Therefore, it has been assumed that there is an association between daily activities and physical functions. In addition, daily activities tended to be greater in women than in men. The reason for greater daily activities in women is often ascribed to activities, such as housework and gardening.²⁰

On the other hand, we demonstrated that fear of falling was associated with physical daily activities in frail elderly but not in nonfrail elderly. Fear of falling is shown to be associated with frailty. Several studies have indicated that people who are afraid of falling appear to enter a debilitating spiral of loss of confidence, restriction of physical activities, physical frailty, lack of social participation, falls, and loss of independence. However, Wolf et al People who are afraid to the social participation activities, physical frailty, lack of social participation, falls, and loss of independence. However, Wolf et al People who are afraid to social participation, falls, and loss of independence. On the social participation activities are social participation activities and loss of independence.

There were several limitations of this study that warrant mention. First, although we used TUG to define frailty, TUG may not be enough to define frailty. Edmonton frail scale adopts eight other domains, such as cognition, general health status, functional independence, social support, medication use, nutrition, mood, and continence other than TUG.³³ Further study is required to test the levels of these domains in this cohort. Second, participants have used pedometer measurements limited to only 2 weeks. If seasonal changes in activity pattern were taken into consideration, long-

term use would be more appropriate. Third, the participant's community was not in the rural area. The present study is the result of being restricted to older adults in the urban area.

This is the first study to demonstrate that differential factors affect daily activities depending on the level of frailty. Future work should determine whether individualized intervention can effectively improve physical activity in both nonfrail and frail elderly.

Acknowledgments

We would like to thank Nippon-Shooter Co. Ltd. for their contribution to data collection and Mr Minoru Ikeda and Mr Yusuke Terasaki for their helpful advice.

- Aoyagi Y, Katsuta S. Relationship between the starting age of training and physical fitness in old age. *Can J Sport Sci* 1990;**15**:65–71.
 Aoyagi Y, Shephard RJ. Aging and muscle function. *Sports Med* 1992;**14**:376–96.
- Aoyagi Y, Shephard RJ. Aging and muscle function. *Sports Med* 1992;14:376–96.
 Aoyagi Y, Shephard RJ. Steps per day: the road to senior health? *Sports Med* 2009;39:423–38.
- Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc 2007;39:1435—45.
- Singh NA, Clements KM, Singh MA. The efficacy of exercise as a long-term antidepressant in elderly subjects: a randomized controlled trial. J Gerontol A Biol Sci Med Sci 2001;56:M497—504.
- Mazzeo RS, Cavanagh P, Evans WJ, Fiatarone M, Hagberg J, McAuley E, et al. American College of Sports Medicine Position Stand. Exercise and physical activity for older adults. Med Sci Sports Exerc 1998;30:992-1008.
- Simons LA, Simons J, McCallum J, Friedlander Y. Lifestyle factors and risk of dementia: Dubbo study of the elderly. Med J Aust 2006;184:68–70.
- Spirduso WW, Cronin DL. Exercise dose-response effects on quality of life and independent living in older adults. Med Sci Sports Exerc 2001;33: \$5598-608.
- Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee Report, 2008. Washington, D.C.: U.S. Department of Health and Human Services: 2008.
- Yoshida D, Nakagaichi M, Saito K, Wakui S, Yoshitake Y. The relationship between physical fitness and ambulatory activity in very elderly women with normal functioning and functional limitation. J Physiol Anthropol 2010;29: 211—8.
- 11. Kalbe E, Calabrese P, Scgwalen S, Kessler J. The Rapid Dementia Screening Test (RDST): a new economical tool for detecting possible patients with dementia. *Dement Geriatr Cogn Disord* 2003;**16**:193–9.
- Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142–8.
- Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. Phys Ther 2000;80:896—903.
- Crouter SE, Schneider PL, Karabulut M, Bassett Jr DR. Validity of 10 electronic pedometers for measuring steps, distance, and energy cost. *Med Sci Sports Exerc* 2003;35:1455–60.
- 15. Reelick MF, van Iersel MB, Kessels RP, Rikkert MG. The influence of fear of falling on gait and balance in older people. *Age Ageing* 2009;**38**:435–40.
- Duncan PW, Weiner DK, Chandler J, Prescott B. Functional reach: a new clinical measure of balance. J Gerontol 1990;45:M192-7.
- Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function:

- association with self-reported disability and prediction of mortality and nursing home admission. I Gerontol 1994;49:M85-94.
- Ruuskanen JM, Ruoppila I. Physical activity and psychological well-being among people aged 65-84 years. Age Ageing 1995;24:292-6.
- Kono A, Kai I, Sakato C, Rubenstein LZ. Frequency of going outdoors: a predictor of functional and psychosocial change among ambulatory frail elders living at home. *J Gerontol A Biol Sci Med Sci* 2004;**59**:275–80.
- Rantanen T, Guralnik IM, Ferrucci L, Penninx BW, Leveille S, Sipila S, et al. Coimpairments as predictors of severe walking disability in older women. I Am Geriatr Soc 2001;49:21-7.
- Cumming RG, Salkeld G, Thomas M, Szonyi G. Prospective study of the impact of fear of falling on activities of daily living, SF-36 scores, and nursing home admission. J Gerontol A Biol Sci Med Sci 2000;55;299-305.
- 22. Delbaere K, Crombez G, Vanderstraeten G, Willems T, Cambier D. Fear-related avoidance of activities, falls and physical frailty. A prospective communitybased cohort study. Age Ageing 2004;33:368–73.
 Friedman SM, Munoz B, West SK, Rubin GS, Fried LP. Falls and fear of falling:
- which comes first? A longitudinal prediction model suggests strategies for primary and secondary prevention. J Am Geriatr Soc 2002;50:1329-35
- Lachman ME, Howland J, Tennstedt S, Jette A, Assman S, Peterson EW. Fear of falling and activity restriction: the survey of activities and fear of falling in the elderly (SAFE). J Gerontol B Psychol Sci Soc Sci 1998;53:P43—50.
- Arfken CL, Lach HW, Birge SJ, Miller JP. The prevalence and correlates of fear of falling in elderly persons living in the community. Am J Public Health 1994;84:

- 26. Howland J, Peterson EW, Levin WC, Fried L, Pordon D, Bak S. Fear of falling among the community-dwelling elderly. J Aging Health 1993;5:229–43.
- 27. Cumming RG, Salkeld G, Thomas M, Szonyi G. Prospective study of the impact of fear of falling on activities of daily living, SF-36 scores, and nursing home admission. J Gerontol A Biol Sci Med Sci 2000;55:M299-305.
- Delbaere K, Crombez G, Vanderstraeten G, Willems T, Cambier D. Fear-related avoidance of activities, falls and physical frailty. A prospective communitybased cohort study. *Age Ageing* 2004;**33**:368–73. Wolf S, Barnhart H, Kutner N, McNeely E, Coogler C, Xu T, et al. Selected as the
- best paper in the 1990s: reducing frailty and falls in older persons: an investigation of tai chi and computerized balance training. J Am Geriatar Soc 2003;51:1794-803.
- Brouwer BJ, Walker C, Rydahl SJ, Culham EG. Reducing fear of falling in seniors through education and activity programs: a randomized trial. J Am Geriatr Soc 2003-51-829-34
- Tennstedt S, Howland J, Lachman M, Peterson E, Kasten L, Jette A. A randomized, controlled trial of a group intervention to reduce fear of falling and associated activity restriction in older adults. J Gerontol B Psychol Sci Soc Sci 1998;53:384-92.
- 32. Zijlstra GAR, Van Haastregt JCM, Ambergen T, Van Rossum E, Van Eijk JTM, Tennstedt SL, et al. Effects of a multicomponent cognitive behavioral group intervention on fear of falling and activity avoidance in community-dwelling older adults: results of a randomized controlled trial. *J Am Geriatr Soc* 2009;57:2020—8.

 33. Rolfson DB, Majumdar S, Tsuyuki RT, Tahir A, Rockwood K. Validity and reli-
- ability of the Edmonton Frail Scale. Age Ageing 2006;35:526-9.