鷲見幸彦	認知症の「ひと」に寄り添うチームケア	TEAM APPROACH	18	2-5	2012
鷲見幸彦	かかりつけ医制度の現状と課題	老年精神医学雑誌	23(3)	287-293	2012
服部英幸	新規抗認知症薬の効果と限界	精神神経学雑誌	第115巻	22-31	2013
福田耕嗣 服部英幸	「ＢＰＳＤ初期対応ガイドライン」と期待される効果	Geriatric Medicine	第51巻	27-30	2013
Hattori H	Role of geriatric hospitals for dementia care in the community	PSYCHOGERIATRICS	12	124-126	2012
服部英幸	認知症の治療・ケアガイド―周辺症状(BPSD)	月刊薬事臨時増刊号	Vol.54, No.10	68-71	2012
服部英幸	認知症の人に突然、ＢＰＳＤが出現した時の評価・対応	認知症介護	第13巻2号	60-66	2012
遠藤英俊	臨床に役立つQ&A 認知症の薬の副作用で気をつけることを教えてください	Geriatric Medicine	51(1)	75-77	2013
遠藤英俊	被災と認知症	Geriatric Medicine	51(1)	79-81	2013
武地　一、藤井昌彦、遠藤英俊、鳥羽研二	認知症診療における地域連携と早期診断・早期対応に向けて－リバスチグミンの有効性と期待を含めて－	Geriatric Medicine	51(1)	83-93	2013
加藤昇平、遠藤英俊、鈴木祐太	課題実行時ｆNIRS脳機能計測データのベイジアンマイニングに基づく認知機能障害の３群判別	人工知能学会論文誌	27(2)SP-D	28-33	2012
Shohei Kato, Hidetoshi Endo, Yuta Suzuki	Bayesian-Based Early Detection of Cognitive Impairment in Elderly Using fNIRS Signals during Cognitive Tests	BIOSIGNALS		118-124	2012
加藤昇平、遠藤英俊、本間昭、佐久間拓人、渡邊恵太	高齢者の発話音韻と脳血流を用いたベイジアンマイニングに基づく認知機能障害の早期スクリーニング	The 26th Annual Conference of the Japanese Society for Artificial Intelligence	2A1-NFC-6-11	1-4	2012

Hiroyuki Shimada, Takashi Kato, Kengo Ito, Hyuma Makizako, Takehiko Doi, Daisuke Yoshida, Hiroshi Shimokata, Yukihiko Washimi, Hidetoshi Endo, Takao Suzuki	Relationship between Atrophy of the Medial Temporal Areas and Cognitive Functions in Elderly Adults with Mild Cognitive Impairment	European Neurology	67	168-177	2012
遠藤英俊	認知疾患治療ガイドライン2010に基づく薬物治療	脳外誌	21(10)	765-770	2012
遠藤英俊	認知症の薬物療法の実際とその効果	日本医師会雑誌	141(3)	555-559	2012
小長谷陽子、渡邉智之、太田壽城	地域在住高齢者の認知機能と身体活動との関連性 —4年間の縦断調査の結果から—	日本老年医学会雑誌	49	752-759	2012
小長谷陽子	地域包括支援センターにおける認知症相談の実態と課題	日本医事新報	4610	84-88	2012
小長谷陽子、渡邉智之、小長谷正明	地域在住高齢者の認知機能スクリーニングのための時計描画テスト－定量的および定性的評価による検討–	日本老年医学会雑誌	49	483-490	2012
T Watanabe, Y Konagaya, M Miyao et al.	Study of Daily Driving Characteristics in Patients with Dementia Using Video-Recording Driving recorders	JAGS	60 (7)	1381-1383	2012
小長谷　陽子	若年性認知症コールセンターへの相談	ふれあいケア	18	30-33	2012
Arai Y, Kumamoto K, Mizuno Y, Arai A	The general public's concern about developing dementia and related factors in Japan	Int J Geriatr Psychiatry	27(11)	1203-1204	2012
Mizuno Y, Arai Y	Measures to support voluntary retirement from driving in Japanese older people: driving is not just a means of transportation	J Am Geriatr Soc	60(11)	2170-2172	2012
Toyoshima Y, Washio M, Ishibashi Y, Onizuka J, Miyabayashi I, Arai Y	Burden among family caregivers of the psychiatric patients with visiting nursing services in Japan	IMJ	19(2)	127-129	2012

Washio M, Yoshida H, Ura N, Ohnishi H, Togashi T, Sakauchi F, Arai Y, Mori M, Shimamoto K	Burden among family caregivers of patients on chronic hemodialysis in Northern Japan	IMJ	19(3)	221-223	2012
Kurasawa S, Yoshimasu K, Washio M, Fukumoto J, Takemura S, Yokoi K, Arai Y, Miyashita K	Factors influencing caregivers' burden among family caregivers and institutionalization of in-home elderly people cared for by family caregivers	Environmental Health and Preventive Medicine	17	474-483	2012
Washio M, Arai Y, Oura A, Miyabayashi I, Onimaru M, Mori M	Family Caregiver Burden and Public Long-Term Care Insurance System in Japan	IMJ	19(3)	229-233	2012
Hashimoto E, Washio M, Arai Y, Sasaki R, Mori M	Depression among family caregivers of patients with dementia attending to psychiatric dispensary in northern Japan	IMJ		in press	2012
水野洋子, 荒井由美子	英国における認知症の早期診断における「かかりつけ医」の役割に関する検討：National Dementia Strategy の策定の背景に着目して	社会保険旬報	2498	14-18	2012
水野洋子, 荒井由美子	英国における認知症の早期診断における「かかりつけ医」の役割に関する検討：National Dementia Strategy の概要及び課題に着目して	社会保険旬報	2499	24-29	2012
水野洋子, 荒井由美子	認知症高齢者の自動車運転を考える家族介護者のための「介護者支援マニュアル」の概要及び社会支援の現況	Geriatric Medicine	50(2)	159-163	2012
荒井由美子, 水野洋子	認知症高齢者の自動車運転を考える：家族介護者への支援	交通安全教育	47(11)	6-15	2012
上田照子, 三宅眞里, 荒井由美子	介護保険サービスの必要量利用の可否が家族介護者に及ぼす影響	厚生の指標	59(3)	8-13	2012

山崎律子, 鷲尾昌一, 荒井由美子	在宅要介護高齢者を介護する家族の介護負担感－都市部の訪問看護サービス利用者の調査より－	臨床と研究	89(2)	228-234	2012
豊島泰子, 鷲尾昌一, 高橋裕明, 井出三郎, 荒井由美子	新型インフルエンザ(A/H1N1)流行シーズンにおける小中学生のインフルエンザワクチンの接種状況－ある学校法人の調査より－	日本公衆衛生雑誌	59(6)	390-398	2012
豊島泰子, 鷲尾昌一, 今村桃子, 荒井由美子	訪問看護ステーションの管理者のインフルエンザワクチン接種に対する意識	厚生の指標	59(12)	7-11	2012
鷲尾昌一, 豊島泰子, 山崎律子, 宇佐いづみ, 荒井由美子	家族介護者の介護負担に関連する要因－要介護高齢者の介護者の介護負担を中心に－	臨床と研究	89(12)	75(1687)-79(1691)	2012
工藤啓, 荒井由美子	健康日本21(第二次)地方計画について－加美町第Ⅱ期健康増進計画「げんき加美町21」を支援の立場から－	公衆衛生情報みやぎ	417	7-9	2013
熊本圭吾, 荒井由美子	高齢社会における希望の醸成	老年精神医学雑誌		印刷中	2013
Akishita M, Ishii S, Kojima T, Kozaki K, Kuzuya M, Arai H, Arai H, Eto M, Takahashi R, Endo H, Horie S, Ezawa K, Kawai S, Takehisa Y, Mikami H, Takegawa S, Morita A, Kamata M, Ouchi Y, Toba K.	Priorities of Health Care Outcomes for the Elderly.	J Am Med Dir Assoc.			E-pub 2013 Feb 14.
Hibi S, Yamaguchi Y, Umeda-Kameyama Y, Yamamoto H, Iijima K, Momose T, Akishita M, Ouchi Y.	The high frequency of periodic limb movements in patients with Lewy body dementia.	J Psychiatr Res	46	1590-1594	2012

Ogita M, Utsunomiya H, Akishita M, Arai H.	Indications and practice for tube feeding in Japanese geriatricians: Implications of multidisciplinary team approach.	Geriatr Gerontol Int	12	643-651	2012
Ota H, Akishita M, Akiyoshi T, Kahyo T, Setou M, Ogawa S, Iijima K, Eto M, Ouchi Y	Testosterone deficiency accelerates neuronal and vascular aging of SAMP8 mice: protective role of eNOS and SIRT1.	PLoS One	7	e29598	2012
Kojima T, Akishita M, Nakamura T, Nomura K, Ogawa S, Iijima K, Eto M, Ouchi Y.	Polypharmacy as a risk for fall occurrence in geriatric outpatients.	Geriatr Gerontol Int	12	425-430	2012
Kojima T, Akishita M, Kameyama Y, Yamaguchi K, Yamamoto H, Eto M, Ouchi Y.	Factors associated with prolonged hospital stay in a geriatric ward of a university hospital in Japan.	J Am Geriatr Soc	60	1190-1191	2012
Nagai K, Akishita M, Shibata S, Kobayashi Y, Yamada Y, Kimura S, Machida A, Toba K, Kozaki K.	Relationship between testosterone and cognitive function in elderly men with dementia.	J Am Geriatr Soc	60	1188-1189	2012
Kojima T, Akishita M, Kameyama Y, Yamaguchi K, Yamamoto H, Eto M, Ouchi Y.	High risk of adverse drug reactions in elderly patients taking six or more drugs: analysis of inpatient database.	Geriatr Gerontol Int	12	761-762	2012
Yamada Y, Eto M, Yamamoto H, Akishita M, Ouchi Y.	Gastrointestinal hemorrhage and antithrombotic drug use in geriatric patients.	Geriatr Gerontol Int	12	751-752	2012
Okochi M, Tagami S, Yanagida K, Takami M, Kodama TS, Mori K, Nakayama T, Ihara Y, Takeda M.	γ-Secretase Modulators and Presenilin 1 Mutants Act Differently on Presenilin/γ-Secretase Function to Cleave Aβ42 and Aβ43.	Cell Rep	31;3(1)	42-51.	2013

Nomura K, Kazui H, Wada T, Sugiyama H, Yamamoto D, Yoshiyama K, Shimosegawa E, Hatazawa J, Takeda M.	Classification of delusions in Alzheimer's disease and their neural correlates.	Psychogeriatrics.	12(3)	200-10.	2013
Atsushi Araki, Kouichi Kozaki, et al and the Japanese Elderly Diabetes Intervention Trial Study Group	Long-term multiple risk factor interventions in Japanese elderly diabetic patients: The Japanese Elderly Diabetes Intervention Trial—study design, baseline characteristics and effects of intervention	Geriatr Gerontol Int	12 (Suppl.1)	7-17	2012
Atsushi Araki,-Koichi Kozaki,et al and the Japanese Elderly Intervention Trial Research Group	Non–high-density lipoprotein cholesterol: an important predictor of stroke and diabetes-related mortality in Japanese elderly diabetic patients	Geriatr Gerontol Int	12 (Suppl.1)	18-28	2012
Kenji Toba, Kumiko Nagai, Sayaka Kimura, Yukiko Yamada, Ayako Machida, Akiko Iwata, Masahiro Akishita and Koichi Kozaki	New dorsiflexion measure device:A simple method to assess fall risks in the elderly	Geriatr Gerontol Int	12(3)	563-564	2012
Nagai K, Akishita M, Shibata S, Kobayashi Y, Yamada Y, Kimura S, Machida A, Toba K, Kozaki K	Relationship between testosterone and cognitive function in elderly men with dementia	J Am Geriatr Soc.	60(6)	1188-9	2012
Akishita M, Ishii S, Kojima T, Kozaki K, Kuzuya M, Arai H, Arai H, Eto M, Takahashi R, Endo H, Horie S, Ezawa K, Kawai S, Takehisa Y, Mikami H, Takegawa S, Morita A, Kamata M, Ouchi Y, Toba K	Priorities of healthcare outcomes for the elderly	J Am Med Dir Assoc	in press		

Araki A, Iimiro S, Sakurai T, Umegaki H, Iijima K, Nakano H, Oba K, Yokono K, Sone H, Yamada N, Ako J, Kozaki K, Miura H, Kashiwagi A, Kikkawa R, Yoshimura Y, Nakano T, Ohashi Y, Ito H	Long-term multiple risk factor interventions in Japanese elderly diabetic patients: The Japanese Elderly Diabetes Intervention Trial (J-EDIT)—study	Geriatr Gerontol Int.	12(Suupl. 1)	7-16	2012
Araki A, Iimiro S, Sakurai T, Umegaki H, Iijima K, Nakano H, Oba K, Yokono K, Sone H, Yamada N, Ako J, Kozaki K, Miura H, Kashiwagi A, Kikkawa R, Yoshimura Y, Nakano T, Ohashi Y, Ito H	Non–high-density lipoprotein cholesterol: an important predictor of stroke and diabetes-related mortality in Japanese elderly diabetic patients	Geriatr Gerontol Int.	12(Suupl. 1):	18-28	2012
Yoshimura Y, Kamada O, Takahashi K,、Kaimoto T, Iimuro S, Ohashi Y, Araki A, Umegaki H, Sakurai T, Hideki Ito	Relations of nutritional intake to age, gender and BMI in Japanese elderly patients with type 2 diabetes - Japanese Elderly Diabetes Intervention Trial(J-EDIT)-	Geriatr Gerontol Int.	12(Suupl. 1):	29-40	2012
Kamada C, Yoshimura H, Okumura R, Takahashi K, Iimuro S, Ohashi Y, Araki A, Umegaki H, Sakurai T, Yoshimura Y, Ito H	Optimal energy distribution of carbohydrate intake for Japanese elderly patients with type 2 diabetes – Japanese Elderly Intervention Trial (J-EDIT)	Geriatr Gerontol Int.	12(Suupl. 1)	41-49	2012
Takahashi K, Kamada C, Yoshimura H, Okumura R, Iimuro S, Ohashi Y, Araki A, Umegaki H, Sakurai T, Yoshimura Y, Hideki Ito	Effects of total and green vegetable intakes on HbA1c and triglycerides in elderly patients with type 2 diabetes mellitus – Japanese Elderly Intervention Trial (J-EDIT)	Geriatr Gerontol Int.	12(Suupl. 1)	50-58	2012

Iimuro S, Yoshimura Y, Umegaki H, Sakurai T, Araki A, Ohashi Y, Ito H	Dietary pattern and mortality in Japanese elderly patients with type 2 diabetes mellitus - Does vegetable- and fish-rich diet improve mortality ?: An explanatory study	Geriatr Gerontol Int.	12(Suupl. 1)	59-67	2012
Iijima K, Iimuro S, Ohashi Y, Sakurai T, Umegaki H, Araki A, Yoshimura Y, Ouchi Y, Ito H	Lower Physical Activity, but not Excessive Calorie Intake, is Associated with Metabolic Syndrome in Elderly with Type 2 Diabetes Mellitus: Japanese Elderly Diabetes Intervention Trial (J-EDIT)	Geriatr Gerontol Int.	12(Suupl. 1)	68-76	2012
Iijima K, Iimuro S, Shinozaki T, Ohashi Y, Sakurai T, Umegaki H, Araki A, Ouchi Y, Ito H	Lower Physical Activity is a Strong Predictor of Cardiovascular Events in Elderly Patients with Type 2 Diabetes Mellitus beyond Traditional Risk Factors: Japanese Elderly Diabetes Intervention Trial (J-EDIT)	Geriatr Gerontol Int.	12(Suupl. 1)	77-87	2012
Shinozaki T, Matsuyama Y, Iimuro S, Umegaki H, Sakurai T, Araki A, Ohashi Y, Ito H	Effective prevention of cardiovascular disease and diabetes-related events with atorvastatin in Japanese elderly patients with type 2 diabetesmellitus: adjusting for treatment changes using a marginal structural proportional hazards model and a rank-preserving structural failure time model	Geriatr Gerontol Int.	12(Suupl. 1)	88-102	2012
Umegaki H, Iimiro S, Shinozaki T, Araki A, Sakurai T, Iijima K, Ohashi Y, Ito H	Risk factors associated with cognitive decline in the elderly with type 2 diabetes; Baseline data analysis of Japanese elderly diabetes intervention trial (J-EDIT)	Geriatr Gerontol Int.	12(Suupl. 1)	103-109	2012

Umegaki H, Iimiro S, Shinozaki T, Araki A, Sakurai T, Iijima K, Ohashi Y, Ito H	Risk factors associated with cognitive decline in the elderly with type 2 diabetes:Pooled logistic analysis of a 6-year observation in the Japanese elderly diabetes intervention trial (J-EDIT)	Geriatr Gerontol Int.	12(Suupl. 1)	110-116	2012
Sakurai T, Iimuro S, Umegaki H, Araki A, Ohashi Y, Ito H	Risk factors for a 6-year decline in physical disability and functional limitations among elderly people with type 2 diabetes (J-EDIT)	Geriatr Gerontol Int.	12(Suupl. 1)	117-126	2012
Araki S, Nishio Y, Araki A, Umegaki H, Sakurai T, Iimuro S, Ohashi Y, Uzu T, Maegawa H, Kashiwagi A, Ito H	Prevalence and Risk Factors for Diabetic Maculopathy and its Relationship to Diabetic Retinopathy in Elderly Japanese Patients with Type 2 Diabetes Mellitus	Geriatr Gerontol Int.	12(Suupl. 1)	127-133	2012
Wang X, Takata T, Bai X, Oue F, Yokono K, Sakurai T	Pyruvate Prevents the Inhibition of the Long-term Potentiation Induced by Amyloid-□ through Protein Phosphatase 2A Inactivation	Journal of Alzheimer's Disease	29	1–9	2012
Matsuzawa T, Takata T, Yokono K, Ueda H, Moriwaki K, Kamae I, Urakami K, Sakurai T	A Warning Index Used in Prescreening for Alzheimer's Disease, Based on Self-reported Cognitive Deficits and Vascular Risk Factors for Dementia in Elderly Patients with Type 2 Diabetes.	International Journal of Alzheimer's Disease	in press		2012
櫻井　孝	高齢者栄養の道標	日本医事新報	No.4622	92	2012
鳥羽研二、櫻井孝、渡辺浩	国立長寿医療研究センター：高齢者総合機能評価を iPad で入力	日経メディカルオンライン	http://medical.nikkeibp.co.jp/inc/all/special/it/casestudy/201103/518775.html		2012
櫻井　孝	糖尿病の適切な治療うが認知症の予防にも	Medical Tribune	45	11	2012
櫻井　孝	認知症の診断	高崎医学	62	61-67	2012

櫻井　孝	認知症のリスクを見据えた糖尿病診療	日本臨床	70増刊号(5)	503-506	2012
櫻井　孝、浦上克哉	糖尿病と認知症	モダンフィジシャン	32	2012-2018	2012
櫻井　孝、鳥羽研二	国立長寿医療研究センター　もの忘れセンター	Cognition and Dementia	11	68-71	2012
櫻井　孝、鳥羽研二	国立長寿医療研究センター「もの忘れセンター」と認知症診療ネットワーク	Cognition and Dementia	11	84-87	2012
櫻井　孝	糖尿病	Cognition and Dementia		86-87	2012
櫻井　孝	高齢者糖尿病の血糖コントロール目標	内分泌・糖尿病・代謝内科	35	13-22	2012
櫻井　孝	専門医と実地医家との連携	医薬ジャーナル	48	115-120	2012
櫻井　孝	糖尿病治療薬による認知症治療への期待	月刊糖尿病4	9	88-97	2012
櫻井　孝、鳥羽研二	認知症の疫学と課題	月刊薬事	54	26-29	2012
櫻井　孝	認知症を伴う高齢糖尿病の管理	月刊Mebio	29	104-111	2012
Maki Y, Yoshida H, Yamaguchi T, Yamaguchi H	Relative preservation of the recognition of positive facial expression "happiness" in Alzheimer disease.	Int Psychogeriatr	25(1)	105-10	2013
Yamaguchi T, Maki Y, Yamaguchi H	Pitfall Intention Explanation Task withClue Questions (Pitfall task): assessment of comprehending other people's behavioral intentions in Alzheimer's disease.	Int Psychogeriatr	24(12)	1919-26	2012
Maki Y, Ura C, Yamaguchi T, Takahashi R, Yamaguchi H	Intervention using a community-based walking program is effective for elderlyadults with depressive tendencies.	J Am Geriatr Soc	60(8)	1590-1	2012
Maki Y, Amari M, Yamaguchi T, Nakaaki S, Yamaguchi H	Anosognosia: patients' distress and self-awareness of deficits in Alzheimer'sdisease.	Am J AlzheimersDis Other Demen	27(5)	339-45	2012

Kamegaya T, Long-Term-Care PreventionTeam of Maebashi City,Maki Y, Yamagami T, Yamaguchi T, Murai T, Yamaguchi H	Pleasant physical exercise program forprevention of cognitive decline in community-dwelling elderly with subjective memory complaints.	Geriatr Gerontol Int	12(4)	673-9	2012
Yamagami T, Takayama Y, Maki Y, Yamaguchi H	A Randomized Controlled Trial of Brain-Activating Rehabilitation for Elderly Participants with Dementia in Residential Care Homes.	Dement Geriatr Cogn Disord Extra	2	372-80	2012
Maki Y, Yamaguchi T, Koeda T, Yamaguchi H	Communicative Competence in Alzheimer's Disease: Metaphor and Sarcasm Comprehension.	Am J Alzheimers Dis Other Demen	Epub ahead of print		2012
Yamaguchi T, Maki Y, Yamaguchi H	Yamaguchi Facial Expression-Making Task in Alzheimer's Disease: A Novel and Enjoyable Make-a-Face Game.	Dement Geriatr Cogn Disord Extra	2	248–57	2012
木之下徹	訪問診療の立場からみた精神科　入院医療の役割，現状と課題アルツハイマー型認知症診療の意義とあり方を考える	老年精神医学雑誌	23(5)	578-585	2012
朝田隆，片山禎夫，木之下徹，武田章敬，宮島俊彦	認知症を抱える本人の視点	CLINICIAN	608	6-20	2012
繁田雅弘，河野禎之，安田朝子，木之下徹ほか	専門医を対象とした認知症診療のあり方とその手法に関する面接調査.	老年精神医学雑誌	23(4)	466-480	2012

Fall Prevention

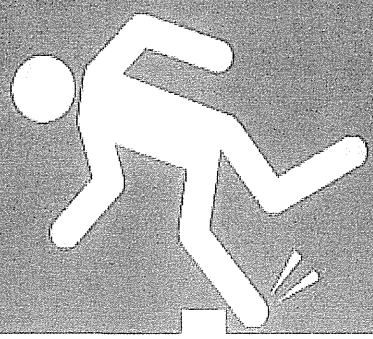
CD-ROM付

「転倒予防手帳」収載

高齢者の転倒予防ガイドライン

◇監修
鳥羽研二
国立長寿医療研究センター病院長

◇執筆
運動器の不安定性に関与する姿勢と中枢制御機能に着目した転倒予防ガイドライン策定研究班



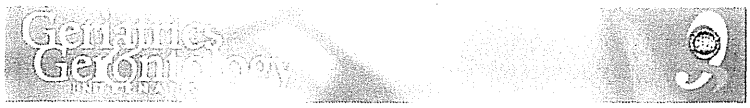
MEDICAL VIEW

やさしい 患者と家族のための

認知症の生活ガイド

国立長寿医療研究センター 内科総合診療部長　遠藤　英俊　著

医薬ジャーナル社



Association of decreased sympathetic nervous activity with mortality of elderly in long-term care

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Title: Association of decreased sympathetic nervous activity with mortality of elderly in long-term care

Abbreviated title: Autonomic nervous in long-term care elderly

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Abstract

Aim: To investigate the relationship between physical function, mortality and autonomic nervous activity measured by heart rate variability of elderly in long-term care.

Methods: Cross-sectional and longitudinal studies at hospital and health service facilities for elderly in Nagano prefecture, Japan from July 2007 to March 2011. One hundred and five long-term care elderly and 17 control elderly with independent physical function. Functional independence measure and Barthel index were determined as indices of physical function. Twenty-four-hour Holter monitoring was conducted. From RR intervals in the electrocardiogram, heart rate and standard deviations of all NN intervals in all 5-minute segments of the entire recording, power spectral density, low frequency, high frequency and LF/HF were calculated.

Results: FIM score and Barthel index were 46±26 and 30±31, respectively, in long-term care elderly. FIM and Barthel index were significantly correlated with HR and SDANN after adjustment for age, sex, cardiovascular risk factors and FIM. Furthermore, LF/HF was significantly decreased in long-term care elderly compared with control elderly after adjustment for covariates. In addition, decrease in LF/HF was an independent risk factor for mortality.

Conclusion: Low LF/HF activity was observed in long-term care elderly and was related to an increase of overall mortality.

Keywords: heart rate variability, long-term care, mortality, motor activity, sympathetic nervous system

INTRODUCTION

The number of elderly people who need long-term care (LTC) has been increasing in Japan, and it was reported that there were 4.67 million elderly in LTC in 2008 (1). One of the characteristics of elderly in long-term care is physical and cognitive dysfunction. Physical dysfunction, including slow gait, low handgrip strength, low physical activity, weight loss and exhaustion, are reported to be associated with increased overall mortality (2). In Japan, LTC elderly is defined as those who require assistance with walking, moving, and washing their face, body and mouth, representing functional disability and high mortality (3). Thus, it is important to maintain or increase physical function in LTC elderly.

The underlying causes of physical dysfunction in Japanese LTC elderly include cerebrovascular disease, dementia, fractures, falls, weakness due to aging, and arthritis (3). Recent studies have revealed that these diseases with physical dysfunction are associated with low sympathetic nervous system activity (4-7).

Skin sympathetic reactivity (SSR) reflects sympathetic nervous system activity. Muslumanoglu et al. demonstrated that low SSR was associated with greater severity of paralysis, and depression of sympathetic reflex activity was associated with moderate or severely limited motor function in the chronic phase of ischemic cerebrovascular disease in elderly patients (5). In addition, low plasma norepinephrine and low ^{123}I-MIBG uptake were observed in patients with Lewy body dementia compared with normal healthy subjects (6, 7). RR intervals in the electrocardiogram are utilized to evaluate heart rate variability (HRV), which reflects autonomic nervous system activity (8). In practice, low frequency/high frequency (LF/HF), a marker of sympathovagal balance or sympathetic modulation, showed a positive correlation with respiratory and skeletal muscle strength in chronic obstructive pulmonary disease (4). Moreover, decreased LF/HF was related to overall mortality in frail elderly (9).

In addition to measurement of SSR, norepinephrine spillover and ^{123}I-MIBG scintigraphy uptake, heart rate variability (HRV) have been recently used as markers of autonomic nervous function (8). HF was reported to reflect parasympathetic nervous system activity and LF/HF to represent sympathovagal balance or sympathetic modulation. In addition, decreased HRV was associated with cardiovascular disease (CVD) (10), cardiac death (11) and all-cause mortality (9). Whereas HRV is known to

decrease with the aging process (12, 13), little is known about the relationship between sympathetic nervous activity and mortality in LTC elderly.

In the Framingham heart study, a cohort study in American community-dwelling people, mortality and HRV were investigated in the elderly, and it was not shown that low LF/HF correlated with mortality (14), whereas in a cohort study of frail elderly, low LF/HF was significantly correlated with both frailty and mortality in the Women's Health and Aging Study-I (WHAS-I) (9).

Aging attenuates sympathetic nervous modulation (12, 13), and previous studies suggested that low sympathetic nervous activity might be associated with physical and cognitive dysfunction. However, only some of the subjects were frail or LTC elderly (9, 14), and there is little evidence describing the relationship between physical function, mortality and sympathetic nervous activity in LTC elderly. In particular, few studies have focused on the specific characteristics of sympathetic nervous activity in LTC elderly. Therefore, we investigated the relationship between sympathetic nervous activity, measured by HRV, and physical function and mortality in elderly in LTC.

METHODS

Study design and participants

This observational study analyzed 105 consecutive elderly persons in LTC aged 75 years or older who were admitted to a rehabilitation unit or a health service facility for elderly that provided rehabilitation. All hospitals and health service facilities were located in Nagano prefecture, Japan. Inclusion criteria were elderly in LTC aged 75 years or older receiving rehabilitation. Exclusion criteria were treatment of acute phase diseases within the last two weeks, arrhythmia, administration of anti-arrhythmia drugs or β-blockers, malignancy, and neurodegenerative diseases other than dementia. As a control of this study, we recruited 17 elderly outpatients with intact activities of daily living (ADL) who were matched for age, sex, and CVD risk factors. The same inclusion and exclusion criteria were adopted in these control subjects. Medical records were reviewed to obtain information of medical history of CVD such as hypertension, diabetes mellitus, hyperlipidemia, chronic heart failure and ischemic heart disease, which was confirmed by the patients or their family. This study protocol was approved by the institutional review board of the facility. Written informed consent was obtained from all subjects or their families.

Heart rate variability

Ambulatory Holter recording was performed for 24 hours using QR2100 (Fukuda M・E Kogyo, Japan) and processed with HS1000VL (Fukuda M・E Kogyo, Japan). For time domain analysis, the standard deviations of all NN intervals in all 5-minute segments of the entire recording (SDANN) were calculated, and frequent domain analysis was performed with fast Fourier transform. From the power spectral density, low frequency (LF, 0.04~0.15Hz), high frequency (HF, 0.15~0.40Hz), and low frequency/high frequency (LF/HF) were determined.

Anthropometric, physical function and hematologic measures

Height, weight and body mass index (BMI) were measured before Holter monitoring. Functional independence measure (FIM) (15) and Barthel index (16) were determined in order to assess physical function. Venous blood samples were obtained from subjects in the morning after an overnight fast. Blood cell counts and serum levels

of chemical parameters were determined by a commercial laboratory (Health Science Research Institute, Yokohama, Japan).

Statistical analysis

Data were analyzed using SPSS software (Ver.11.0.1J, SPSS Japan Inc., Japan). Mann-Whitney U test for continuous variables and $\chi 2$ test for categorical variables were used to compare controls and LTC elderly. Pearson correlation coefficient was calculated and standardized multiple regression analysis of HRV indices was performed with age, sex, FIM, Barthel index, and blood nutritional data as covariates. Multiple regression analysis was used to calculate Cox hazard ratio, with adjustment for age, sex, clinical risk factors and FIM. Kaplan-Meier survival rate was computed for HRV indices.