Satellite Symposium of the 59th Annual meeting of the Japan Geriatrics Society

The 3rd NCGG – ICAH Symposium

(September 7th to 8th, 2017, @Education and Innovation Center for Geriatrics and Gerontology, NCGG)

Program

National Center for Geriatrics and Gerontology

Day1-Thursday 7 September 2017 @ Education and Innovation Center for Geriatrics and Gerontology, NCGG	
10:00 I 10:15	**Opening remarks** **Kenji Toba** (President, National Center for Geriatrics and Gerontology, Japan) **Kung-Yee Liang** (President, National Yang Ming University, Taiwan)
10:15 I 12:15	**Session I** **Definition and Epidemiology of Cognitive Frailty** 【Modulators】 **Hsing-Jien Kung** (President Emeritus, National Health Research Institute, Taiwan) **Hidenori Arai** (National Center for Geriatrics and Gerontology, Japan) **Liang-Kung Chen** (Taipei Veterans General Hospital, Taiwan) Definition and implication of cognitive frailty **Hiroyuki Shimada** (National Center for Geriatrics and Gerontology, Japan) Prevalence and prognosis of cognitive frailty **Wei-Ju Lee** (Taipei Veterans General Hospital Yuanshan Branch, Taiwan) Predicting all-cause mortality among older people with cognitive frailty **Taiki Sugimoto** (National Center for Geriatrics and Gerontology, Japan) Cognitive Frailty associates with ADL decline in older adults with MCI: Longitudinal analysis **Chih-Kuang Liang** (Kaohsiung Veterans General Hospital, Taiwan) The benefit of multi-dimensional intervention for community dwelling older people with cognitive frailty: a nationwide clustered randomized controlled trial **Rei Otsuka** (National Center for Geriatrics and Gerontology, Japan) Nutritional epidemiology for physical frailty and cognitive decline: findings from NILS-LSA *Discussion* *photography*
12:15 I 13:15	*Lunch*
13:15 I 15:15	**Session II** **Frailty and Neuroimaging** 【Modulators】 **Liang-Kung Chen** (Professor, Taipei Veterans General Hospital, Taiwan) **Katsuhiko Yanagisawa** (Director, National Center for Geriatrics and Gerontology, Japan) **Yukiko Nishita** (National Center for Geriatrics and Gerontology, Japan) Physical frailty and cognitive functions: findings from NILS-LSA **Chia-Shu Lin** (National Yang Ming University, Taiwan) Can chewing make your brain smarter? - Revisiting the current neuroimaging evidence and its clinical implications in geriatric medicine **Shosuke Satake** (National Center for Geriatrics and Gerontology, Japan) Experience of using the Kihon Checklist in the outpatient clinic **Chih-Ping Chung** (National Yang Ming University, Taiwan) Cerebral venous drainage in aging **Yasumoto Matsui** (National Center for Geriatrics and Gerontology, Japan) Implementation of Integrated Healthy Aging Clinic to investigate frailty, sarcopenia and locomotive syndrome in the clinical setting **Shu-Chun Chuang** (National Health Research Institute, Taiwan) Life style and cognitive frailty : findings from HALST *Discussion*

15:15 I 15: 30	***Coffee break***
15:30 I 17: 30	**Session III** **Interventions and cognitive function**
	【Modulators】 **Ching-Hui Loh** (Veterans Affairs Council, R.O.C., Taiwan) **Takashi Sakurai** (National Center for Geriatrics and Gerontology, Japan)
	Chih-Cheng Hsu (National Health Research Institute, Taiwan) Frailty prevention for the elderly through home-based exercise and nutrition intervention
	Kota Tsutsumimoto (National Center for Geriatrics and Gerontology, Japan) Intervention scheme for cognitive frailty
	Chao Agnes Hsiung (National Health Research Institute, Taiwan) Cognitive frailty, related biomarkers and adverse health outcomes : Findings from the Healthy Aging Longitudinal Study in Taiwan (HALST)
	I-Chien Wu (National Health Research Institute, Taiwan) Interrelations between Mitochondrial DNA Copy Number and Inflammation in Older Adults: Identifying novel biomarker of frailty : findings from HALST
	Naoyuki Sato (National Center for Geriatrics and Gerontology, Japan) Bidirectional interaction between Alzheimer's disease and diabetes
	Tami Saito (National Center for Geriatrics and Gerontology, Japan) Trajectories of frailty and subjective cognitive impairment: Findings from JAGES project
	Discussion

Day 2-Friday 8 September 2017 @ Education and Innovation Center for Geriatrics and Gerontology, NCGG		
10:00 I 12:00	**Session IV** **Group discussion on education and research collaboration**	
	1. Cognitive frailty （Main conference room ）	**2. Aging science and bioinformatics** (Medium conference room)
		Chao-Hsiung Lin （Department of Life Sciences and Institute of Genome Sciences） Untargeted metabolomics analysis of human serum to identify age-associated biomarkers
12:00 I 13:00	*Lunch*	

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Abstracts

National Center for Geriatrics and Gerontology

Session I
Definition and Epidemiology of Cognitive Frailty

1. Definition of cognitive frailty and implications

Liang-Kung Chen
(Taipei Veterans General Hospital, Taiwan)

Traditionally, aging research has been categorized into two main trajectories, either in physical approach or cognitive approach. In physical approach, age-related declines may start from physical function, which progressively become physically frail and disability. In cognitive approach, i.e. Alzheimer;s disease, people start with mild cognitive impairment, in which people have cognitive impairment in memory domains without impairment in physical function. However, among people with advanced aging in both trajectories, they may simultaneously present with impairment in both physical and cognitive domains. The presence of both physical frailty and mild cognitive impairment has been proposed as cognitive frailty by IAGG/IANA. Although the definition clearly defined older adults with both physical and cognitive impairment, the overall prevalence was low and the potential success of intervention may be limited.

The Asian Working Group for Cognitive Frailty has modified the definition of cognitive frailty as having dynapenia plus the presence of cognitive impairment in any specific domain. Epidemiological studies from Taiwan and Japan suggested that the prevalence of cognitive frailty may exceed 10% of total older population, and the longitudinal observations showed the potential of cognitive frailty to cause disability and mortality. Nevertheless, increased mortality risk was mainly from the dynapenia, but not cognitive impairment. In the preliminary results of brain MR imaging study, older adults with cognitive frailty showed significant deficits in cerebellum and hippocampus. Based on the current understanding, cognitive frailty is a specific aging trajectory that simultaneous declines in physical and cognitive domains may be a potentially new neurodegenerative process and is associated with adverse outcomes. Preliminary intervention data clearly demonstrated the reversibility of cognitive frailty through a clustered randomized controlled trial in Taiwan. Therefore, cognitive frailty may be an early enough entity to prevent physical and cognitive aging among community-dwelling older adults.

2. Prevalence and prognosis of cognitive frailty

Hiroyuki Shimada

(National Center for Geriatrics and Gerontology, japan)

Cognitive decline is associated with physical frailty in older adults, and both cognitive impairment and physical frailty are often seen together in older people. The International Consensus Group on Cognitive Frailty provided the first definition of cognitive frailty as a condition affecting older adults, and proposed identification of cognitive frailty as a clinical manifestation characterized by the simultaneous presence of physical frailty and cognitive impairment. Cognitive frailty was defined by a consensus conference as reduced cognitive function due to either physical or brain disease, or accelerated brain aging in the absence of evident brain disease.

There have been a number of previous studies regarding the prevalence of cognitive frailty and the relationship between cognitive frailty and activities of daily living (ADL) and incidence of dementia in older adults. Previously, we reported an overall prevalence rate of cognitive frailty of only 1.1% in a cohort of 4072 older adults, and another population-based study estimated the prevalence of cognitive frailty as 1.8% to 2.5%. We considered that the low prevalence rates of cognitive frailty, which increased the risk of false negative results, would be unsuitable for primary screening in the community.

Here, we have developed a new operational definition of cognitive frailty as follows: physical frailty, ≥1 of slow walking speed and muscle weakness; cognitive impairment, ≥1 of word list memory, attention, executive function, and processing speed in the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT). This presentation will be performed to examine the relationship between the new definition of cognitive frailty and the incidence of dementia in community-living older adults using data from a Japanese national cohort study, the National Center for Geriatrics and Gerontology-Study of Geriatric Syndromes (NCGG-SGS).

3. Predicting all-cause mortality among older people with cognitive

Wei-Ju Lee

(Taipei Veterans General Hospital Yuanshan Branch, Taiwan)

Low prevalence of cognitive frailty by using the definition of IANA and IAGG may limit the numbers needed for intervention. Results of our previous studies showed that dynapenia was associated with cognitive function and the latent class analysis confirmed the clustering phenomenon and in brain deficits. We proposed a new definition of cognitive frailty defined by dynapenia plus any cognitive domain impairment to identify a meaningful numbers of at-risk population.

All participants recruited in the ILAS received comprehensive neuropsychological assessments including Mini-Mental State Examination, the Chinese Version Verbal Learning Test, the Boston Naming Test, the Verbal Fluency Test, the Taylor Complex Figure Test, the digital backward and the Clock Drawing Test. Those with impaired global cognitive function and significant impaired individual cognitive tests were excluded for analysis. Mobility subtype of frailty (dynapenia) was defined by the cutoff values from the Asia Working Group for Sarcopenia. Cognitive frailty was defined as the concomitant presence of dynapenia and any impairment of each cognitive domain.

Of 678 participants (mean 73.3±5.3 years, men 53.7%) with a median follow-up period of 28 months, 90(13.3%) were cognitive frailty and women (60%) were more predominant. In multivariate logistic regression, lower MMSE score (OR: 0.84; 95% CI: 0.79-0.89; p<0.001), higher CES-D score (OR: 1.08; 95% CI: 1.03-1.13; p=0.001) and lower MNA score (OR: 0.87; 95% CI: 0.77-0.99; p=0.030) were independent risk factors for cognitive frailty. The multivariate Cox regression model showed the significant association between cognitive frailty and mortality. (Hazard ratio: 3.18; 95% CI: 1.08 to 9.31; P=0.035)

In conclusion, this study described the epidemiology of cognitive frailty using a new operative definition and also disclosed its independent risk factors and the association with mortality in an Asian community population.

4. Cognitive Frailty associates with ADL decline in patients with MCI and mild AD: Longitudinal analysis

Taiki Sugimoto

(National Center for Geriatrics and Gerontology, japan)

Taiki Sugimoto[1,2,3,4], Takashi Sakurai[1,5]

1. Center for Comprehensive Care and Research on Memory Disorders, National Center for Geriatrics and Gerontology, Obu, Japan
2. Medical genome center, National Center for Geriatrics and Gerontology, Obu, Japan
3. Department of Community Health Sciences, Kobe University, Graduate School of Health Sciences, Kobe, Japan
4. Japan Society for the Promotion of Science, Tokyo, Japan
5. Department of Cognitive and Behavioral Science, Nagoya University Graduate School of Medicine, Nagoya, Japan

Cognitive frailty (CF) is defined by the simultaneous presence of both physical frailty and cognitive impairment in older individuals. This study aimed to clarify the significance of CF in the memory clinic. We examined the longitudinal associations of CF with basic activity of daily living (BADL), instrumental ADL (IADL) and cognitive function.

Subjects were patients who were diagnosed as mild cognitive impairment (MCI) and mild Alzheimer's disease (AD) and had MMSE score of 18 or more. Frailty was defined both by the Frailty Index (FI) and by the Cardiovascular Health Study (CHS) criteria. Subjects with pre-frailty and frailty were grouped as CF. Subjects were evaluated by Lawton index and Barthel index at the first and second visit, and those who scored lower in more than one item at the second visit were assessed as having IADL and BADL decline. Also, subjects who scored more than three points lower on MMSE at the second visit were assessed as having cognitive decline. We performed stepwise logistic regression analysis to investigate whether CF was associated with decline in BADL, IADL and cognitive function.

Of the 302 patients (females, 67.2%; age, 79.7 ± 5.8 years; follow-up period; 1.1 ± 0.2 years), prevalence of CF was 75.8% based on the FI, and CF was associated with BADL decline (OR = 2.92 [1.15 – 7.46]). Of the 202 patients (females, 70.8%; age, 78.8 ± 5.8 years; follow-up period; 1.1 ± 0.2 years), prevalence of CF was 70.8% based on the CHS criteria, and CF was associated with IADL decline (OR = 2.10 [1.05 – 4.21]). CF based on FI or the CHS criteria was not associated with cognitive decline.

CF is a risk factor for functional decline, and evaluation and intervention for CF would be a successful strategy to prevent functional decline in patients with cognitive impairment.

5. The benefit of multi-dimensional intervention for community dwelling older people with cognitive frailty: a nationwide clustered randomized controlled trial

Chih-Kuang Liang

(Kaohsiung Veterans General Hospital, Taiwan)

Background: In 2013, An International Consensus Group of I.A.N.A and I.A.G.G on "Cognitive Frailty" defined such a condition include: 1) presence of physical frailty and they published an operative definition for cognitive frailty: cognitive impairment (CDR=0.5); and 2) exclusion of concurrent AD dementia or other dementia. However, the IANA/IAGG definition for cognitive frailty gained certain research attention and modification for its operational definition was proposed. The Asian Working Group for cognitive frailty proposed a new definition by using dynapenia plus cognitive impairment in any domain. This study aimed to evaluate the potential benefits of multi-dimensional interventions for older people with cognitive frailty in the community.

Methods: This is a sub-study of THISCE, which recruited subjects with at least of the followings: 1. self-reported memory impairment, 2. loss at least one IADL and 3. gait speed < 1m/sec. THISCE is a four-year nationwide multi-center clustered RCT, and all subjects received comprehensive assessment including demographic information, living area, life style factors, self-reported medical conditions, functional survey, such as nutritional status, mood symptoms, IADL, handgrip strength, gait speed and frail status, and neuropsychologial assessments based on MoCA. We identified the subgroup with cognitive frailty based on the Asian Working Group for Cognitive Frailty.

Results: A total of 434 subjects (mean 77.2±6.4 years, women 73.3%) met our definition of cognitive frailty were identified. Using paired student T test to comparing the significant change of MoCA scores at 6th or 12th months than baseline within the groups of intervention or control, older people in intervention group improved their MoCA scores at 12th month significantly (score difference between 6th month and baseline -0.14 (SD 3.78), p value 0.616; between 12th month and baseline 0.95 (3.78), p value 0.002), and moreover, a markedly worsening of follow-up global cognitive function in control group (score difference between 6th month and baseline -0.85 (4.62), p value 0.018; between 12th month and baseline -0.91 (5.30), p value 0.037). Multiple linear regression also showed significantly intervention effect on global cognitive function at 6th and 12th month after adjusting covariates (at 6th month, standardized B 0.097, p value: 0.045; at 12th month, 0.188, p value <0.001).

Conclusion: There are significantly benefit for improving cognitive function after 6- and 12-month multi-dimensional intervention, and for those in control group, obviously decreasing global cognitive function was observed at time of 6th and 12th month.

6. Nutritional epidemiology for physical frailty and cognitive decline: findings from NILS-LSA

Rei Otsuka

(National Center for Geriatrics and Gerontology, japan)

[1] Section of NILS-LSA, Center for Gerontology and Social Science, NCGG
[2] Center for Gerontology and Social Science, and [3] National Hospital for Geriatric Medicine, NCGG

Nutrition is closely related to physical frailty and cognitive impairment in the elderly. We examined the effect of dietary and nutritional intake on the development of physical frailty and cognitive impairment in community-dwelling older Japanese.

The National Institute for Longevity Sciences - Longitudinal Study of Aging (NILS-LSA), a comprehensive longitudinal study of aging, started in 1997 at the National Center for Geriatrics and Gerontology (NCGG). Subjects in this study were 2,300 residents aged 40 to 79 years who were age- and sex-stratified random samples selected from the area around the NCGG. Participants were examined at the NILS-LSA examination center every 2 years from 1997 to 2012 and were followed-up from 2012 to 2017. Nutrition and food intake were calculated based on 3-day dietary records with photographs. Physical frailty was assessed by the modified criteria of the Cardiovascular Health Study, which included weight loss, weakness, exhaustion, slow walking speed, and low physical activity. Cognitive function was assessed by the Mini-Mental State Examination for the subjects ≥ 60 years.

In this presentation, the recent nutritional findings from the NILS-LSA cohort will be shown. First, compared to less varied diets, moderately to highly varied diets containing fish, soy bean, and dairy products prevented cognitive decline. Second, higher meat and dairy consumption to ensure sufficient protein and fat intake prevented physical frailty than that of lower consumption. These findings suggest that a healthy diet that includes a variety of foods with sufficient protein and fat might be effective for preventing cognitive decline and physical frailty.

Session II
Frailty and Neuroimaging

1. The relationship between physical frailty and cognitive function: Findings from NILS-LSA

Yukiko Nishita
(National Center for Geriatrics and Gerontology, japan)

Yukiko Nishita[1)], Akinori Nakamura[2)], Takashi Kato[2)], Rei Otsuka[1)],
Kengo Ito[2)], Hidenori Arai[3)]

[1)] Section of NILS-LSA, NCGG,
[2)] Department of Clinical and Experimental Neuroimaging, NCGG,
[3)] Center for Gerontology and Social Science and National Hospital for Geriatric Medicine, NCGG

Summary

It has been proposed that cognitive frailty is the simultaneous presence of physical frailty and cognitive impairment. To understand the underlying mechanisms for progression of cognitive frailty, it is essential to accumulate more evidence on the relationships between physical frailty and cognitive functions. The purpose of this presentation is to investigate the relationships between (1) physical frailty and some cognitive test scores and (2) physical frailty and regional brain volumes.

Subjects in the study were approximately 900 community-dwelling Japanese aged 65 or older who participated in the National Institute for Longevity Sciences – Longitudinal Study of Aging (NILS-LSA). Physical frailty was assessed by the modified criteria of the Cardiovascular Health Study, which included weight loss, weakness, exhaustion, slow walking speed, and low physical activity. Cognitive function was assessed by Mini-mental state examination and the six subtests in Wechsler Adult intelligence scale- revised, which included Information, Similarities, Picture completion, Digit symbol substitution, Forward digit span, and Reverse digit span. The regional gray matter volumes were evaluated from 3D-T1 MR images using Statistical Parametric Mapping (SPM 8) and FreeSurfer software.

In this presentation, the following results are shown. (1) Physical frailty was closely associated with the Digit symbol substitution test, which assesses information processing speed. The cross-lagged effects model showed that the digit symbol substitution test score was related to subsequent physical frailty score in two years; however, physical frailty was not associated with subsequent the digit symbol substitution test score. (2) Slow walking speed was significantly correlated with less regional brain volumes in the hippocampus, amygdala, and fusiform gyrus. The results suggest that the progression of physical frailty is associated with the reduction in the regional cortical volumes related to memory and social recognition.

2. Can chewing make your brain smarter? - Revisiting the current neuroimaging evidence and its clinical implications in geriatric medicine

Chia-Shu Lin

(Taipei Veterans General Hospital, Taiwan)

Traditionally, aging research has been categorized into two main trajectories, either in physical approach or cognitive approach. In physical approach, age-related declines may start from physical function, which progressively become physically frail and disability. In cognitive approach, i.e. Alzheimer;s disease, people start with mild cognitive impairment, in which people have cognitive impairment in memory domains without impairment in physical function. However, among people with advanced aging in both trajectories, they may simultaneously present with impairment in both physical and cognitive domains. The presence of both physical frailty and mild cognitive impairment has been proposed as cognitive frailty by IAGG/IANA. Although the definition clearly defined older adults with both physical and cognitive impairment, the overall prevalence was low and the potential success of intervention may be limited.

The Asian Working Group for Cognitive Frailty has modified the definition of cognitive frailty as having dynapenia plus the presence of cognitive impairment in any specific domain. Epidemiological studies from Taiwan and Japan suggested that the prevalence of cognitive frailty may exceed 10% of total older population, and the longitudinal observations showed the potential of cognitive frailty to cause disability and mortality. Nevertheless, increased mortality risk was mainly from the dynapenia, but not cognitive impairment. In the preliminary results of brain MR imaging study, older adults with cognitive frailty showed significant deficits in cerebellum and hippocampus. Based on the current understanding, cognitive frailty is a specific aging trajectory that simultaneous declines in physical and cognitive domains may be a potentially new neurodegenerative process and is associated with adverse outcomes. Preliminary intervention data clearly demonstrated the reversibility of cognitive frailty through a clustered randomized controlled trial in Taiwan. Therefore, cognitive frailty may be an early enough entity to prevent physical and cognitive aging among community-dwelling older adults.

3. Experience of using the Kihon Checklist in the outpatient clinic

Shosuke Satake
(National Center for Geriatrics and Gerontology, japan)

Recently, frailty has been an important issue in the geriatric field because this concept could be a key factor for prolonging healthy life expectancy in the older population. Therefore, it is important for geriatricians to identify frail elderly earlier in order to take appropriate preventive measures against deterioration of senior's health status. In Japan, the Kihon checklist (KCL) has been introduced to identify at-risk elderly of requiring care or support in the preventive long-term care insurance system. However, this checklist has not been utilized in a clinical setting as it was developed for screening the older population independent of the frailty concept. This checklist is comprehensive for assessing physical, social, and mental functions of seniors' lives. Therefore, it is also conceivable for us to use it for screening frailty in a clinical setting. Based on the total KCL scores we could classify older adults into 3 groups, robust, pre-frail and frail, with a significant predictive ability for adverse health outcomes, such as an incidence of dependency or mortality, in a population-based longitudinal observational study. In NCGG, especially in our geriatric department, the KCL is utilized as a screening tool to identify frailty and problematic domains. Also, geriatric outpatients with frailty assessed by the total KCL score showed a tendency to use more drugs, especially hypnotics, sedatives, antidepressants, and laxatives. In this presentation, we will demonstrate our preliminary results.

4. Cerebral venous drainage in aging

Chih-Ping Chung
(National Yang Ming University, Taiwan)

Chronic cerebro(spinal) venous insufficiency (CCSVI) is a theory emerged after clinical observations that extracranial (mainly internal jugular vein) drainage venous abnormalities are associated with neurological diseases including certain age-related neurological disorders and neurodegenerative diseases.

The present talk will suggest the future direction and potential solutions for research to prove the theory, e.g. extracranial drainage venous abnormalities are one etiology of these neurological diseases by influencing cerebrospinal venous drainage:

The causal relationship between extracranial drainage venous abnormalities and neurological diseases.

Clinical longitudinal studies would give clues.

Animal models of extracranial drainage venous abnormalities are needed. Besides the causal relationship, they are also tools to explore the mechanisms.

The pathophysiological consequence of each extracranial drainage venous abnormality.

The study targets should be inspired from known associated neurological diseases

The etiologies of these extracranial drainage venous abnormalities.

One possibility is that these extracranial drainage venous abnormalities are just bystanders or biomarkers of these associated neurological diseases. There might be another etiology which contributes to both extracranial venous abnormalities and certain neurological disease.

5. Implementation of Integrated Healthy Aging Clinic to investigate frailty and sarcopenia in the clinical setting

Yasumoto Matsui

(National Center for Geriatrics and Gerontology, japan)

Although frailty, sarcopenia, and locomotive syndrome are key concepts for the prevention of disability, the assessment of these has not been completely established yet and thus is not widely used in clinical practice. At our hospital, we newly opened an Integrated Healthy Aging Clinic (The Locomo-Frail Center in Japanese), which is a novel diagnostic system for comprehensive evaluation of problems among older patients through multidepartment and multidisciplinary cooperation to assess their physical frailty status and sarcopenia. Here we introduce the assessment system and report the preliminary results of 160 patients (60 men and 100 women; mean age: 77.5±6. 4 years [60–94 years]) who were assessed between March and June 2017 and fulfilled the disease registration criteria.

In addition to the questionnaires concerning basic attributes (e.g., age, sex, education family etc.), higher cognitive function, sociability, frailty, locomotive syndrome, comorbidities, medications, nutrition, spinal radiography, DXA, thigh CT scan, body composition, blood biochemical profile, and motor functions (walking speed, grip strength, timed up and go, SPPB -walking, balance, chair rise, total score-, one leg standing time, two locomotive syndrome tests, ankle dorsiflexion angle measurement, etc.) were assessed.

Based on the Asian Working Group for Sarcopenia criteria, 49 patients had sarcopenia, 34 had presarcopenia, and 77 did not have sarcopenia. Regarding frailty, 52 were frail, 90 prefrail, and 18 robust. Regarding locomotive syndrome, 119 patients had locomotive syndrome level 2, 34 level 1, and 7 patients did not satisfy the criteria of locomotive syndrome.

Comparisons of various physical functions were made among three groups of frail, prefrail and robust patients and many of the functions showed significant differences between frail and robust or prefrail groups.

Frailty, sarcopenia, and locomotive syndrome are concepts aimed for disability prevention, but the progression stages evaluated by each criterion were different.

6. Life style and cognitive frailty : findings from HALST

Shu-Chun Chuang

(National Health Research Institute, Taiwan)

Physical Frailty is often associated with cognitive impairment, possibly because of common underlying pathophysiologic mechanisms. The most studied risk factors include cardiovascular risk factors, nutrition, inflammation, and mental health. Promoting physical activity and a healthy diet, engaging in an active and socially integrated lifestyle, and obtaining an ideal amount of daily sleep are common primary preventive measures. HALST is an ongoing longitudinal study which includes 5664 participants who were ≥55 years old. By the time of this preliminary analysis, 2320 participants had completed the second wave data collection (~5 years apart). Preliminary results showed that good social networking and high vegetable intake at baseline were associated with both lower prevalence of physical frailty and MMSE impairment at second wave. Physical activity was associated with frailty but not MMSE impairment. Future directions include conducting more sophisticate analyses, such as latent class analysis, which might help to class high risk population. We wish the final results from this study would help in designing interventions to delay physical and mental degradation and the subsequent adverse health outcomes and improve overall quality of life.

Session III
Interventions and cognitive function

1. Frailty prevention for the elderly through home-based exercise and nutrition intervention

Chih-Cheng Hsu
(National Health Research Institute, Taiwan)

The proportion of the elderly population has increased rapidly worldwide. Frailty is a common geriatric syndrome. Exercise and comprehensive dietary management have been shown beneficial to frailty prevention and its reversal. However, center-based exercise and nutrition interventions may cause high attrition rate. We developed a home-based exercise and nutrition intervention protocol for frail and pre-frail elders. A total of 319 (pre)frail subjects were recruited and randomized into 4 groups: home-based exercise (n=79), nutrition (n=83), exercise and nutrition combination (n=77), and control groups (n=80). We provided intervention for 3 months and then followed up for another 3 months. The nutrition intervention included individualized nutrition education with designed dishware for balanced diet as well as food supplementations (mixed nuts and milk powder). In the end of the 6-month follow-up, our results show that home-based exercise and combination interventions are feasible for the elderly. Individualized home-based exercise interventions can help to improve physical performance and frailty status. Nutritional intervention may be helpful to improve nutrition status and mental health for the elderly. In addition, nutritional intervention can act as a supplemental remedy to the exercise program for frailty prevention.

2. Intervention scheme for cognitive frailty

Kota Tsutsumimoto
(National Center for Geriatrics and Gerontology, japan)

Cognitive frailty is defined as the simultaneous presence of not only physical frailty, but also cognitive impairment. Thus, the intervention for older people with cognitive frailty should be considered to improve both physical function and cognitive function. Our group investigated that cognitive and physical activities effectively to improve both physical and cognitive function in elderly with mild cognitive impairment using a single-blinded, randomized, controlled trial. In this program, the participants conducted the exercises combined physical and cognitive tasks into what we called “cognicize.” For example, participants played word games while doing stepping exercises. The combined activity program involved weekly 90-min sessions for 40 weeks focused on physical and cognitive activities. The control group attended 90-min health promotion classes thrice during the 40-week trial period. In the results, Compared to the control group, the combined activity group showed significantly greater scores on the Mini-Mental State Examination (difference = 0.8 points, P = .012) and Wechsler Memory Scale-Revised–Logical Memory II (difference = 1.0, P = .004), significant improvements in mobility and the non-memory domains and reduced left medial temporal lobe atrophy in amnestic mild cognitive impairment (Z score difference = -31.3, P < .05). Combined physical and cognitive activity program including “cognisize”improves or maintains cognitive and physical performance in older adults with mild cognitive impairment, especially the amnestic type. In future, we should conduct this program for older people with cognitive frailty in order to

3. Cognitive frailty, related biomarkers and adverse health outcomes : Findings from the Healthy Aging Longitudinal Study in Taiwan (HALST)

Chao Agnes Hsiung
(National Health Research Institute, Taiwan)

"Cognitive frailty" was proposed and defined as an heterogeneous clinical manifestation characterized by the simultaneous presence of both physical frailty and cognitive impairment with exclusion of AD dementia or other dementias. We will study whether concurrent physical frailty and cognitive impairment, compared with physical frailty alone increase adverse health outcomes (functional disability assessed by ADL, IADL, hospitalization, poor quality of life based on SF-12 PCS). The findings are from the Healthy Aging Longitudinal Study in Taiwan (HALST), a population-based cohort of over 5000 Chinese in Taiwan aged 55 and above. The associations of physical frailty (CHS criteria: 0=robust, 1-2=pre-frail, 3-5=frail) with and without cognitive impairment (MMSE<26) and adverse outcomes were estimated, controlling for age, gender, education, comorbidity, smoking, alcohol consumption, betel nut chewing, depressive symptoms. Compared to robust noncognitively impaired, physical pre-frailty with cognitive impairment was associated with a 2.83 ($p<0.0001$), (1.88, $p=0.0052$) increased prevalence (incidence) of functional disability, a 2.07 ($p<0.0001$), (1.65, $p=0.03$) increased prevalence (incidence) of poor QOL. Cognitively impaired frail individuals had a 7.56 ($p<0.0001$), (5.75, $p<0.0001$) fold increased prevalence (incidence) of functional disability, a 9.06 ($p<0.0001$), (8.23, $p<0.0001$) fold increased prevalence (incidence) of low QOL. Some possible biological biomarkers include inflammatory markers (eg CRP, IL-6, TNFR1), cholesterol, serum albumin etc..

4. Interrelations between Mitochondrial DNA Copy Number and Inflammation in Older Adults: Identifying novel biomarker of frailty : findings from HALST

I-Chien Wu
(National Health Research Institute, Taiwan)

Background: Interplays between inflammation and mitochondrial biology are reported. Here, we examined the cross-sectional interrelationships of mitochondrial DNA copy number (mtDNACN) and inflammation and their interaction with physical functioning.
Methods: A total of 1990 community-dwelling adults aged 65 years and older who were participating in the Healthy Aging Longitudinal Study in Taiwan underwent measurements of peripheral-blood leukocytes MtDNACN, multiple inflammatory markers, grip strength and gait speed.
Results: Principal components analysis revealed two inflammatory factors: factor 1 (high-sensitivity C-reactive protein [hs-CRP], white blood cell count, fibrinogen and interleukin-6 [IL-6]); factor 2 (tumor necrosis factor receptor 1, D-dimer and soluble interleukin-6 receptor). Participants with severe physical functioning impairment (low grip strength and gait speed) had higher ($P < .05$) levels of factor 1 and 2, but not mtDNACN, than did those with moderately impaired (low grip strength or gait speed) and normal physical functioning. MtDNACN was negatively related to factor 1 ($r = -0.221$, $P < .001$) but not factor 2 ($r = -0.002$, $P = .938$). Increased factor 1 was strongly associated with higher odds of physical functioning impairment in those with a low mtDNACN (adjusted odds ratios [OR] of moderate physical function impairment 1.21, 95% CI 1.01 to 1.44; adjusted OR of severe physical function impairment 1.52, 95% CI 1.25 to 1.85) but not in those with a high mtDNACN (P for interaction = .016).
Conclusions: A low mtDNACN was associated with an inflammation exhibiting elevated hs-CRP, IL-6, fibrinogen, and white blood cell count, and strengthened the association of this inflammation with physical functioning impairment.

5. Bidirectional interaction between diabetes and Alzheimer's disease

Naoyuki Sato
(National Center for Geriatrics and Gerontology, japan)

Clinical studies have suggested that diabetes is associated with neurodegeneration and Alzheimer's disease (AD). However, the mechanisms underpinning this association have not been elucidated fully. Diabetes causes neurodegeneration through changes in glucose metabolism, insulin signaling and vascular function and structure and the modification of b-amyloid (Ab)/tau.
In turn, neurodegeneration influences systemic glucose metabolism through behavioral changes, memory disturbances, hypothalamic dysfunction and possibly plasma/peripheral Ab. The exploration of the molecular, cellular and inter-organ mechanisms of the bidirectional interaction between diabetes and neurodegeneration/AD is expected to contribute to development of next-generation therapeutic options for dementia caused by neurodegeneration/AD.
In this session, I will also introduce two newly developed tools for cognitive frailty.

6. Trajectories of frailty and subjective cognitive impairment: Findings from JAGES project

Tami Saito

(National Center for Geriatrics and Gerontology, japan)

Aim

This study examined the associations between frailty, subjective cognitive impairment (SCI), and onset of basic activities of daily living (BADL) disability among community-dwelling older adults.

Methods

We obtained data from the Japan Gerontological Evaluation Study (JAGES) project. Data for 66332 functionally independent older adults were linked to the Long-term Care Insurance (LTCI) records for a 3-year follow-up period. The incident BADL disability was defined as a new registration in the LTCI records with care need level II and above. We assessed the Kihon Check List (KCL), a simple self-administered questionnaire, developed by Ministry of Health, Labour and Welfare, and designated respondents with scores ≥8 points as frail, and between 4 and 7 points as pre-frail. The SCI items were also assessed using the KCL.

Findings

Among the analyzed, 53.3%, 31.5%, and 15.2% were categorized as being robust, pre-frail, and frail, respectively. A multivariate Cox proportional hazards model showed that the pre-frail and frail groups were at a significant excess risk for incident disability compared to the robust group (hazard ratio [HR]: 1.78 and 3.45, respectively). The difference remained significant after controlling for the SCI score. Similarly, the association between SCI and BADL disability was significant regardless of frailty level. The interaction effect of frailty with SCI on incident mortality was not significant; however, our additional analysis showed that respondents with both frailty and SCI were 4.5 times more likely to develop incident disability than those who had neither frailty nor SCI. The risk of developing incident disability was higher in respondents with both frailty and SCI than those with only frailty or only SCI.

Conclusions

An excess risk for BADL disability was observed in frail older adults, particularly in those with concurrent SCI. No synergetic effect of concurrent frailty and SCI was found.

Session IV
Group discussion on education and research collaboration

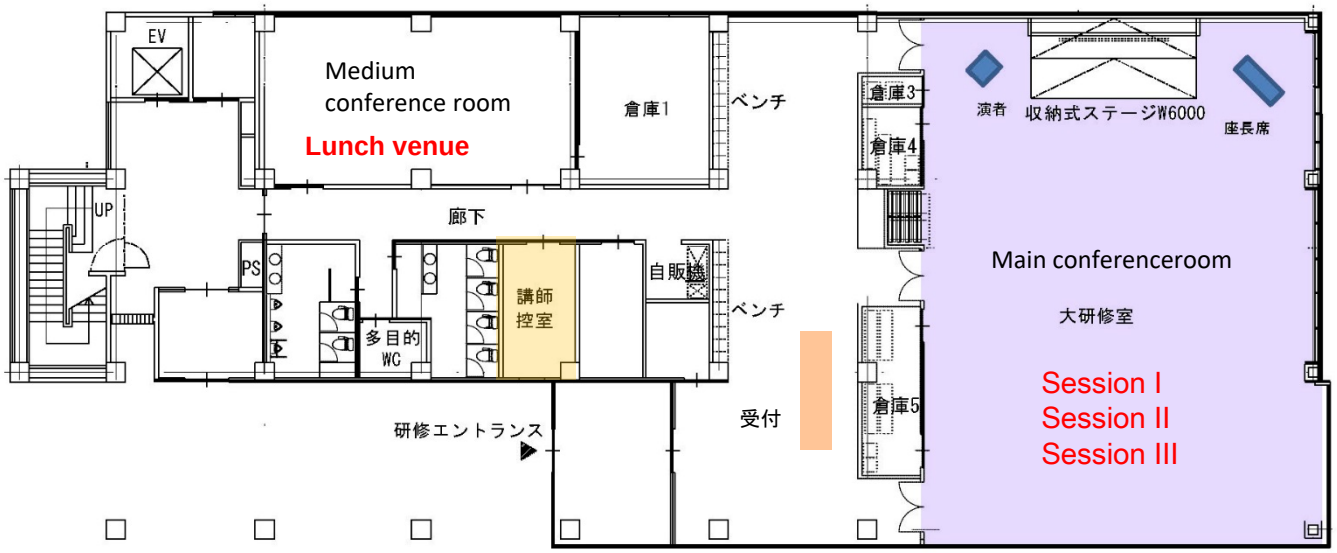
Aging science and bioinformatics

1. Untargeted metabolomics analysis of human serum to identify age-associated biomarkers

Chao-Hsiung Lin
Department of Life Sciences and Institute of Genome Sciences）

The proportion of the elderly population has increased rapidly worldwide. Frailty is a common geriatric syndrome. Exercise and comprehensive dietary management have been shown beneficial to frailty prevention and its reversal. However, center-based exercise and nutrition interventions may cause high attrition rate. We developed a home-based exercise and nutrition intervention protocol for frail and pre-frail elders. A total of 319 (pre)frail subjects were recruited and randomized into 4 groups: home-based exercise (n=79), nutrition (n=83), exercise and nutrition combination (n=77), and control groups (n=80). We provided intervention for 3 months and then followed up for another 3 months. The nutrition intervention included individualized nutrition education with designed dishware for balanced diet as well as food supplementations (mixed nuts and milk powder). In the end of the 6-month follow-up, our results show that home-based exercise and combination interventions are feasible for the elderly. Individualized home-based exercise interventions can help to improve physical performance and frailty status. Nutritional intervention may be helpful to improve nutrition status and mental health for the elderly. In addition, nutritional intervention can act as a supplemental remedy to the exercise program for frailty prevention.

The 3rd NCGG – ICAH Symposium



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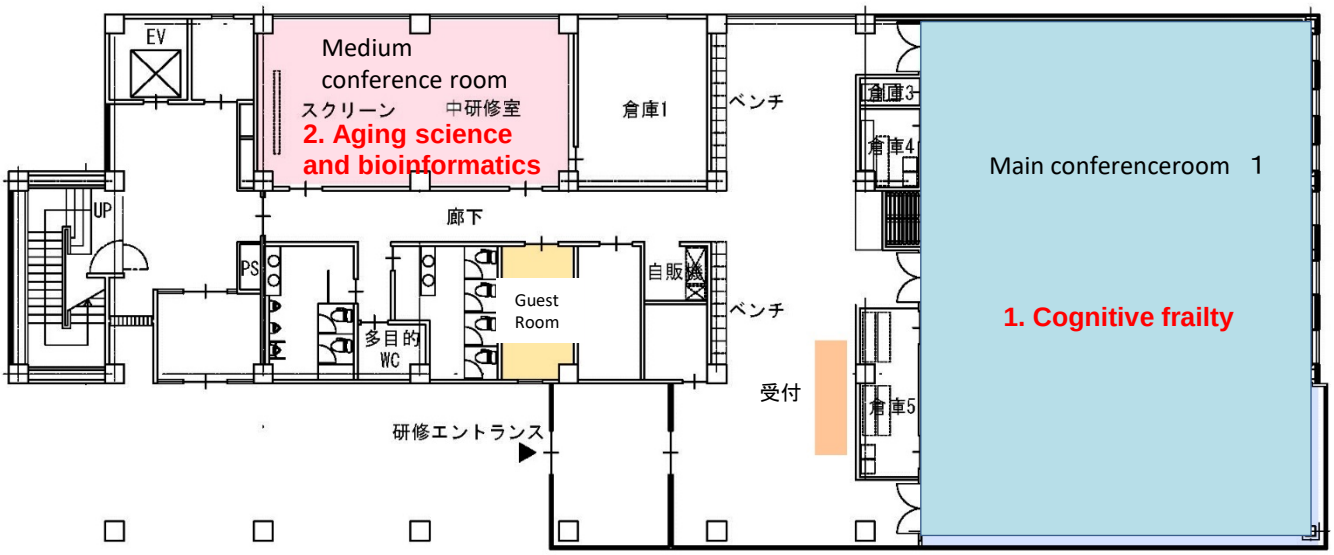
Day1 Openingremarks, Session Ⅰ, Session Ⅱ, Session Ⅲ



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Day2 Session Ⅳ Group discussion on education and research collaboration