

看護師、介護支援専門員では理解度に有意な向上は認められなかったが、訪問介護員では、勉強会開始時 52.5±8.9 点から 1 年後の点数が 62.1±10.2 点と著しい上昇が認められ、栄養ケアに関しての理解度が深まったと言えた ($p<0.01$)。

③ 外来嚥下造影検査（日帰り）について

平成 22 年度に構築した地域の介護施設の入所者および病院を受診した外来患者に対し、複数回の外来受診を行わず、1 日で嚥下造影検査、評価、指導までのサービスを受けられるシステムを構築した。また、検査の手順を説明したフローチャート式のオリジナルのパンフレットを作成した。現在、外来および施設からの申し込みで嚥下造影検査が実施されており、システム構築からこれまでに、施設および在宅から 7 件の依頼があり、検査を実施した。

D. 考察

平成 22 年度より栄養ケア連携のためのシステム作りを行い、今回のモデル地区においては施設間および職種間の連携ができあがりつつある。本研究において、モデル事業を実施し、浮かび上がった一番の問題点は、栄養ケアが必要な利用者が一番近い存在であるサービス事業者の職員は、専門的な知識を学ぶ機会がないまま、食事介助などの業務を行っているのが現状であるということである。今回の勉強会に参加していたサービス事業者の方々は、遅い開始時間にも関わらず、複数回参加している人がほとんどである。また、勉強会後の質疑応答の時間においても、積極的に勉強会の内容への質問をし、普段の職場での自身

の対応法などを熱心に質問している。同時に、同じ職種同志での意見交換も行っている。介護施設が一気に増加し、サービス事業者を量産したのは良いが、やはり知識不足は否めない。食事介助に関しては、利用者の生命に関わることも少なくなく、今回のモデル事業として実施したような形態の勉強会の継続が必要と考えられた。さらに、要介護者に一番近い存在である訪問介護員や介護支援専門員らが、栄養ケアの必要性の有無および摂食・嚥下障害のリスク者の拾い上げを行い、早い段階で地域の病院への紹介、その後、リスクのあるものに対しては多職種によるケアが即座に開始されるようなシステム作りが、全国で必要と考えられる。

E. 結論

今後は、日本の高齢化率のさらなる上昇に合わせ、病院、施設、居宅に摂食・嚥下に関わる職種である管理栄養士、言語聴覚士などの配置率をあげていくことと、小規模の地域ごとの栄養ケアの連携をとり、介護保険の利用者の一番近い存在である介護支援専門員および訪問介護員を含めた地域の勉強会を継続することが必要と考えられた。

F. 健康危険情報

なし

G 研究発表

1. 和文原著

1) 榎裕美、加藤恵美、葛谷雅文：高齢者栄養ケアの実際 地域栄養ケア連携モデル. 臨床栄養 118 : 704-709.2011

2. 学会発表

- 1) 榎裕美、ほか：食事形態がもたらす要介護高齢者の健康障害について 日本静脈経腸栄養学会（名古屋），2011.2
- 2) 榎裕美、ほか：要介護高齢者の食事形態と介護負担感との関連について 日本老年医学会（東京），2011.6
- 3) Enoki H., et al.: Association between type of diet and low level of caregiver burden 9th Asia / Oceania Congress of Geriatrics and Gerontology (Melbourne, Australia), October 2011
- 4) 榎裕美、ほか：施設要介護高齢者の経口摂取悪化の要因についての検討 日本静脈経腸栄養学会（神戸），2012.2

Ⅲ. 研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Kuzuya M, Izawa S, Enoki H, Hasegawa J.	Day-care service use is a risk factor for long-term care placement in community-dwelling dependent elderly.	Geriatr Gerontol Int.		In press	2012
Kuzuya M.	Process of Physical Disability among Older Adults - Contribution of Frailty in the Super-aged Society.	Nagoya J. Med. Sci.	74	31-37	2012
Kuzuya M, Hasegawa J, Hirakawa Y, Enoki H, Izawa S, Hirose T, Iguchi A.	Impact of informal care levels on discontinuation of living at home in community-dwelling dependent elderly using various community-based services.	Arch Gerontol Geriatr.	52(2)	127-132	2011
葛谷雅文、榎裕美、井澤幸子、広瀬貴久、長谷川潤.	要介護高齢者の経口摂取困難の実態ならびに要因に関する研究.	静脈経腸栄養	26(5)	1265-1270	2011
広瀬貴久、長谷川潤、井澤幸子、榎裕美、葛谷雅文.	鬱の程度は、在宅療養要介護高齢者の死亡、入院の原因となるか— the Nagoya Longitudinal Study of Frail Elderly(NLS-FE)より.	日本老年医学会雑誌	48(2)	163-169	2011
葛谷雅文.	低栄養、栄養障害.	日本老年医学会雑誌	48(6)	659-661	2011
葛谷雅文.	低栄養<高齢者特有の症状に対応する—老年症候群>.	内科	108(6)	1011-1016	2011
Kikutani T, Tamura F, Tohara T, Takahashi N, Yaegki K.	Tooth loss as risk factor for foreign-body asphyxiation in nursing-home patients.	Arch Gerontol Geriatr.		In press	2012
Kikutani T, Yoshida M, Enoki H, Yamashita Y, Akifusa S, Shimazaki Y, Tamura F.	Relationship between nutrition status and dental occlusion in community-dwelling frail elderly people.	Geriatr Gerontol Int.		In press	2012
Takahashi N, Kikutani T, Tamura F, et.al.	Videoendoscopic Assessment of Swallowing Function to Predict the Future Incidence of Pneumonia of the Elderly.	J Oral Rehabil.		In press	2011
Yoshida M, Kikutani T, Yoshikawa M, Tsuga K, Kimura M, Akagawa Y.	Correlation between dental and nutritional status in community-dwelling elderly Japanese.	Geriatr Gerontol Int.	11	315-319	2011
榎裕美、加藤恵美、葛谷雅文.	地域栄養ケア連携モデル.	臨床栄養	Vol.118 No.6	704-709	2011.5

IV. 研究成果の刊行物・別刷



ORIGINAL ARTICLE

Day-care service use is a risk factor for long-term care placement in community-dwelling dependent elderly

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Aims: To identify predictors of long-term care placement and to examine the effect of day-care service use on long-term care placement over a 36-month follow-up period among community-dwelling dependent elderly.

Methods: This study was a prospective cohort analysis of 1739 community-dwelling elderly and 1442 caregivers registered in the Nagoya Longitudinal Study for Frail Elderly. Data included the clients' demographic characteristics, basic activities of daily living, comorbidities, and use of home care services, including the day-care, visiting nurse, and home-help services, as well as caregivers' demographic characteristics and care burden. Analysis of long-term care placement over 36 month was conducted using Kaplan-Meier curves and multivariate Cox proportional hazards models.

Results: Among the 1739 participants, 217 were institutionalized at long-term care facilities during the 36-month follow-up. Multivariate Cox regression models, adjusted for potential confounders, showed that day-care service use was significantly associated with an elevated risk for long-term care placement within the 36-month follow-up period. Participants using a day-care service two or more times/week had significantly higher relative hazard ratios than participants not using such a service.

Conclusion: The results highlight the need for effective measures to reduce the long-term care placement of day-care service users. Policy makers and practitioners must consider implementing multidimensional support programs to reduce the caregivers' willingness to consider long-term care placement. *Geriatr Gerontol Int* 2011; ●●: ●●-●●.

Keywords: community, day-care service, elderly, long-term care placement, nursing home.

Introduction

Japan introduced a universal-coverage long-term care insurance (LTCI) program in April 2000.^{1,2} This program brought a radical change from traditional, family-based care toward elderly care involving socialization and the integration of medical care and welfare

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services. There are two types of services covered by LTCI: community-based services and institutional services. Community-based services include various programs such as the home-help service, visiting bathing service, visiting rehabilitation, day care (rehabilitation), visiting nurse service, assistive device leasing, short stays (temporary stays at nursing facilities), in-home medical care, and care management services, care services provided by for-profit private homes, and allowance for the purchase of assistive devices and home renovation. In theory, the applicant can choose any certified providers and listed services.

In practice, a major role is played by a “care manager,” a licensed professional who has passed an examination and undergone brief training, who draws up a care plan and a weekly schedule of service provision for individual seniors. It is essential that the care plan must be approved by the client or the client’s family, and new care managers can be requested at any time if care plans prove inadequate. The maximum amount of reimbursement in the LTCI system is capped according to the care level.^{3,4} Elderly beneficiaries pay a 10% co-payment for services received.

The aims of LTCI home care programs are to reduce the care burden of caregivers, maintain and improve the functional abilities and well-being of elderly people, and decrease the use of institutional care services and mortality. However, there is little evidence of how community-based services affect care recipients’ outcomes, the subjective burden of caregivers or reduce the use of institutional care services.

The Nagoya Longitudinal Study for Frail Elderly (NLS-FE) compares outcomes of the use of different care services provided by the LTCI program; it was designed to provide a structured comparison of services and a comprehensive standardized assessment instrument.^{5,6} Day-care service, which includes “day care” and “day rehabilitation,” is provided in designated centers and is one of the major LTCI community-based services. Day-care service is a facility-based daytime program of nursing care, rehabilitation therapies, supervision and socialization that enables frail, older people, who are in poor overall health and have multiple comorbidities and varying physical or mental impairments, to remain active in the community. The individual visits the facility once or several times a week and then returns to his or her own home.

Although one of the aims of day-care service is to minimize or delay the possibility of institutionalization and maximize the potential for care recipients to maintain an independent life in the community, only a limited number of studies have examined the impact of day-care service on long-term care (LTC) placement among community-dwelling older adults. Moreover, most of these studies have targeted patients with dementia. Previous studies targeting dementia have

demonstrated that day-care use is associated with nursing home placement in persons with Alzheimer’s disease.^{7,8} However, the effect of using day-care service on the LTC placement of community-dwelling, frail elderly with various chronic diseases remains unknown, although it has been reported that day-care services reduce caregiving time and provide respite to caregivers.^{9,10}

In the present prospective cohort study using the NLS-FE cohort, we examined whether day-care service use among community-dwelling older people using various community-based services under LTCI in Japan influenced LTC placement during a 36-month follow-up period. Analysis of LTC placement over the 36-month was conducted using Kaplan–Meier curves and multivariate Cox proportional hazards models.

Methods

Subjects

The present study employed baseline data of the participants in the NLS-FE and data on the mortality of these patients during the 36-month follow-up. Details of participants and the NLS-FE have been published elsewhere.^{5,6} The study population initially consisted of 1875 community-dwelling dependent elderly (632 men and 1243 women, age 65 years or older) who were eligible for LTCI, lived in Nagoya City and received various home care services from the Nagoya City Health Care Service Foundation for Older People, which has 17 visiting nursing stations associated with care-managing centers. These NLS-FE participants, who were enrolled between 1 December 2003 and 31 January 2004, were scheduled to undergo comprehensive in-home assessments by trained nurses at the baseline and at 6, 12, 24, and 36 months. At 3-month intervals, data were collected about any events participants experienced, including admission to the hospital, LTC admission and mortality. Per the procedures approved by the institutional review board of Nagoya University Graduate School of Medicine, participants provided written informed consent and, for those with substantial cognitive impairment, a surrogate (usually the closest relative or legal guardian) or family caregivers provided it.

Data collection

Data were collected from standardized interviews with patients or surrogates and caregivers conducted at clients’ homes and from care-managing center records by trained nurses. The data included clients’ demographic information, depressive symptoms as assessed by the short version of the Geriatric Depression Scale (GDS-15),¹¹ and a rating for the seven basic activities of daily living (ADL) (feeding, bathing, grooming, dressing, using the toilet, walking, and transferring) using

summary scores ranging from 0 (total disability) to 20 (no disability).¹² The interview with participants also included questions about using care services, including day-care service, which includes day care and day rehabilitation, visiting nurse service, and home-help service programs, as well as medical services. In addition, the weekly frequency with which clients used these services was obtained.

Information obtained from care-managing center records included data on the following physician-diagnosed chronic conditions: ischemic heart disease, congestive heart failure, cerebrovascular disease, diabetes mellitus, dementia, cancer, and other diseases comprising the Charlson comorbidity index,¹³ which represents the sum of a weighted index that takes into account the number and seriousness of preexisting comorbid conditions.

Data were also obtained from caregivers concerning their own personal demographic characteristics and their subjective burden as assessed by the Japanese version of the Zarit Burden Interview (ZBI),¹⁴ which is a 22-item self-report inventory that examines the burden associated with functional behavioral impairments in the home care situation.

For the analysis, 136 of the original 1875 participants were excluded because of missing data regarding service use or confounding/intermediary variables, leaving 1739 in the analysis. Of these 1739 participants, 412 could not complete the GDS-15 because of severe cognitive impairment or communication impairment. Also, among the 1739 older participants, 1442 participants had primary caregivers. Of these 1442 caregivers, 289 could not or refused to complete the ZBI.

We defined three types of care facilities providing LTCI as LTC facilities: nursing homes, care health facilities for the elderly, and group homes for elders with dementia. We assessed LTC placement over 36 months using event reports at 3-month intervals. LTC placement was confirmed by visiting nurses or care-managing center records. Placement time was defined as the number of months (3-month intervals) between the baseline interview and the event report of LTC placement. We censored participants living at home after 36 months of follow-up ($n = 773$), at death ($n = 401$), or at dropout ($n = 248$).

Statistic analysis

The Student's *t*-test and χ^2 test were used to compare differences at baseline between users and nonusers of day-care service. To create ideal model, we first evaluated the association between each covariate and LTC placement using univariate Cox proportional hazards model. LTC placement over 36 months was estimated for each group (day-care service use once or multiple times per week, and nonusers) using the Kaplan–Meier

method. We then evaluated the impact of day-care service use and weekly frequency of service use on the overall model with a series of Cox proportional hazards models, which included gender, age, ADL status, presence or absence of dementia, and caregiver's sex, age and ZBI score. The risk of a variable was expressed as a hazard ratio (HR) with a corresponding 95%CI. All analyses were performed using the SPSS v. 11 (Chicago, IL, USA). $P \leq 0.05$ was considered significant.

Results

When the baseline characteristics were compared between day-care service users and nonusers, older age, a higher Charlson comorbidity index, and a lower GDS-15 score were observed in day-care service users than in nonusers (Table 1). Higher prevalence rates of cerebrovascular disease and dementia were also observed in day-care service users. The rates of nursing service use, home-help service use and living alone among day-care service users were lower than those of nonusers. Among caregivers' variables, the rate of male caregivers was significantly lower for day-care service users than nonusers. Higher ZBI score was detected in users' caregivers.

Among the 1739 participants, 217 participants were institutionalized at LTC facilities during the 36-month follow-up period. A higher rate of LTC placement was observed in day-care service users than in nonusers ($n = 143$, 18.5% vs. $n = 74$, 7.7%, $P < 0.001$) (Table 1). Among the 1327 participants who could complete the GDS-15, 150 participants were institutionalized at LTC facilities during the 36-month follow-up period. Of the 412 who could not perform the GDS-15, 67 were institutionalized at LTC facilities during the 36-month follow-up period. A higher LTC placement rate was observed in the participants who could not complete GDS-15 test than in those who could (16.3% vs. 11.3%, $P = 0.008$). There were no significant differences in LTC placement rate between participants living alone and those living with others (12.8% vs. 12.4%, $P = 0.802$). Furthermore, there was no significant difference in the LTC placement rate between participants living with caregivers who completed the ZBI and those who did not (13.0% vs. 11.1%, $P = 0.375$).

Cox hazard regression and Kaplan–Meier models

Table 2 shows the results of the unadjusted univariate Cox hazard regression analysis, which suggested that LTC placement within the 36-month follow-up period was associated with older age, a lower function of basic ADL, day-care service use, and the presence of dementia (Table 2). Among caregivers' variables, only higher care burden was associated with LTC placement. Figure 1A shows Kaplan–Meier curves exploring the

Table 1 Baseline characteristics of the 1739 care recipients and the 1442 caregivers

	Day-care service User	Nonuser	P-value
Care recipients (<i>n</i> = 1739)			
Men/women (% of men/total)	256/518 (33.1)	319/646 (33.1)	0.994
Age, years (mean, SD) [†]	81.4 (7.7)	80.2 (7.5)	0.002
Basic ADL, range: 0–20 (mean, SD) [†]	13.0 (5.9)	13.5 (6.7)	0.099
Charlson comorbidity index, range: 0–35 (mean, SD) [†]	2.2 (1.5)	1.8 (1.6)	<0.001
GDS-15 (range: 0–15), mean (SD) ^{†‡}	6.1 (3.6)	6.8 (3.7)	0.002
Chronic diseases (% of total)			
Ischemic heart disease	12.4	12.0	0.809
Congestive heart failure	8.7	8.4	0.845
Cerebrovascular disease	42.8	27.6	<0.001
Diabetes mellitus	12.4	11.7	0.659
Dementia	44.2	22.6	<0.001
Cancer	8.0	10.1	0.142
Visiting nurse service use (% of total)	38.1	54.0	<0.001
Home-help service use (% of total)	42.4	50.5	0.001
Regular medical checkups (% of total)	55.3	60.7	0.023
Living alone (% of total)	17.3	28.1	<0.001
Hospitalization during 36-month follow-up (% of total)	42.5	41.0	0.537
Long-term care placement during 36-month follow-up (% of total)	18.5	7.7	<0.001
Caregiver variables (<i>n</i> = 1442)			
Men/women (% of men/total)	137/553 (19.9)	217/535 (28.9)	<0.001
Age (years), mean (SD) [†]	63.4 (12.3)	64.3 (12.4)	0.177
Relationship to care recipient (% of total)			
Spouse	35.4	42.8	
Child	35.8	37.1	<0.001
Daughter-in-law	25.7	15.4	
Others	3.2	4.7	
ZBI score, range: 0–88 (mean, SD) ^{‡§}	30.1 (16.8)	26.8 (17.0)	0.001

[†]Student's *t*-test, others were analyzed by χ^2 test (user vs.nonuser). [‡]GDS-15, geriatric depression scale, *n* = 1327. [§]ZBI, the Zarit Burden Interview. *n* = 1153.

association between weekly frequency of day-care service use and time to LTC placement (3-month intervals). The risk of LTC placement was higher for participants who used day-care service more frequently than those who used it less frequently.

Table 3 shows the results of the series of Cox proportional hazards models that examine the HR of day-care service use to LTC placement during the 36-month follow-up period. The sequential adjustment had minor influences on the association between day-care service use and LTC placement during the 36-month follow-up period. The HR for the fully adjusted models was 2.34 (95%CI = 1.60–3.41).

In the Cox regression model adjusted for potential confounders, participants with more frequent use of day-care service had a significantly higher relative HR than participants with less frequent use of the service (Fig. 1B). Although there was no significant association between using day-care service once per week and the

risk of LTC placement, participants using a day-care service two or more times per week had a significantly higher relative HR than participants not using the service.

Discussion

In the present study we demonstrated that day-care service use was associated with LTC placement during the 36-month study period among community-dwelling frail elderly using various community-based services under the LTCI program in Japan. Many previous studies have examined predictors of LTC placement in study samples, but these have been limited to people with dementia and there have been fewer evaluations of risk factors for LTC placement in community samples.^{15–19} Few studies have comprehensively investigated how both caregiver and recipient characteristics influence LTC placement.¹⁹ Previous observations

Table 2 Univariate Cox proportional hazards model to identify predictors of long-term care placement over 36 months

Variable	Univariate HR [†]	95% CI	P-value
Care recipients (<i>n</i> = 1739)			
Men (vs. women)	0.75	0.56–1.02	0.067
Age (continuous)	1.04	1.03–1.06	<0.001
Living with someone (vs. living alone)	1.02	0.74–1.39	0.920
Basic ADL (range: 0–20) (continuous)	0.97	0.95–0.99	0.001
Regular medical checkups per month (no regular checkup)	1.19	0.90–1.56	0.214
Formal care use (vs. nonuse)			
Visiting nurse	1.15	0.88–1.51	0.295
Day-care service	2.42	1.83–3.21	<0.001
Home helper	0.71	0.81–1.37	0.714
Charlson comorbidity index (continuous)	1.04	0.95–1.13	0.375
GDS-15 (continuous) [‡]	1.01	0.96–1.05	0.762
Presence of chronic diseases (vs. absence)			
Ischemic heart disease	1.02	0.68–1.53	0.926
Congestive heart failure	1.16	0.73–1.84	0.523
Cerebrovascular disease	1.00	0.76–1.32	0.986
Diabetes mellitus	0.78	0.50–1.22	0.272
Dementia	3.00	2.29–3.92	<0.001
Cancer	0.84	0.49–1.44	0.520
Hospitalization during 36-month follow-up (vs. never admitted)	1.08	0.82–1.42	0.576
Caregiver variables (<i>n</i> = 1442)			
Men (vs. women)	0.95	0.67–1.33	0.752
Age (continuous)	1.01	1.00–1.02	0.059
Character of caregiver (vs. child)			
Spouse	0.90	0.64–1.28	0.555
Daughter-in-law	1.29	0.88–1.88	0.189
Others	1.21	0.60–2.43	0.596
ZBI score(continuous) [‡]	1.03	1.02–1.04	<0.001

[†]GDS-15, geriatric depression scale, *n* = 1327. [‡]ZBI, the Zarit Burden Interview. *n* = 1153. HR, hazard ratio.

demonstrated that common risk factors of LTC placement of community-dwelling elderly were older age, presence of dementia, and caregiver's burden.^{16,18,19}

Although one of the aims of day-care service is to minimize or delay the possibility of institutionalization and maximize the potential for care recipients to maintain an independent life in the community, only a limited number of studies have examined the impact of day-care service on LTC placement among community-dwelling older adults – and most of these have targeted demented patients. Previous studies targeting dementia have demonstrated that day-care use is associated with nursing home placement in persons with Alzheimer's disease.^{7,8} We expanded the target group and demonstrated a striking association between day-care service use and the risk of LTC placement for community-dwelling dependent elderly patients with various chronic diseases, even after adjusting for the presence of dementia and caregiver's burden. We clearly showed,

after adjusting for potential confounders, that the frequency of day-care service use had a negative impact on LTC admission with the 36-month follow-up period. The use of day-care service two or more times per week negatively affected LTC placement, but there was no significant association between institutionalization and the use of day-care service once a week. It is possible that participants with more comorbidities and a more depressive mood use day-care service more frequently; thus, participants using a day-care service two or more times per week were more likely to be placed in LTC facilities. However, even if comorbidity index score and GDS-15 score were included in the analysis, the association between LTC placement and the use of day-care service two or more times per week persisted (data not shown). This contrasts with our recent report that the risk of 21-month mortality among community-dwelling elderly was reduced significantly with frequent use of day-care service.⁶ The complex decision to place older

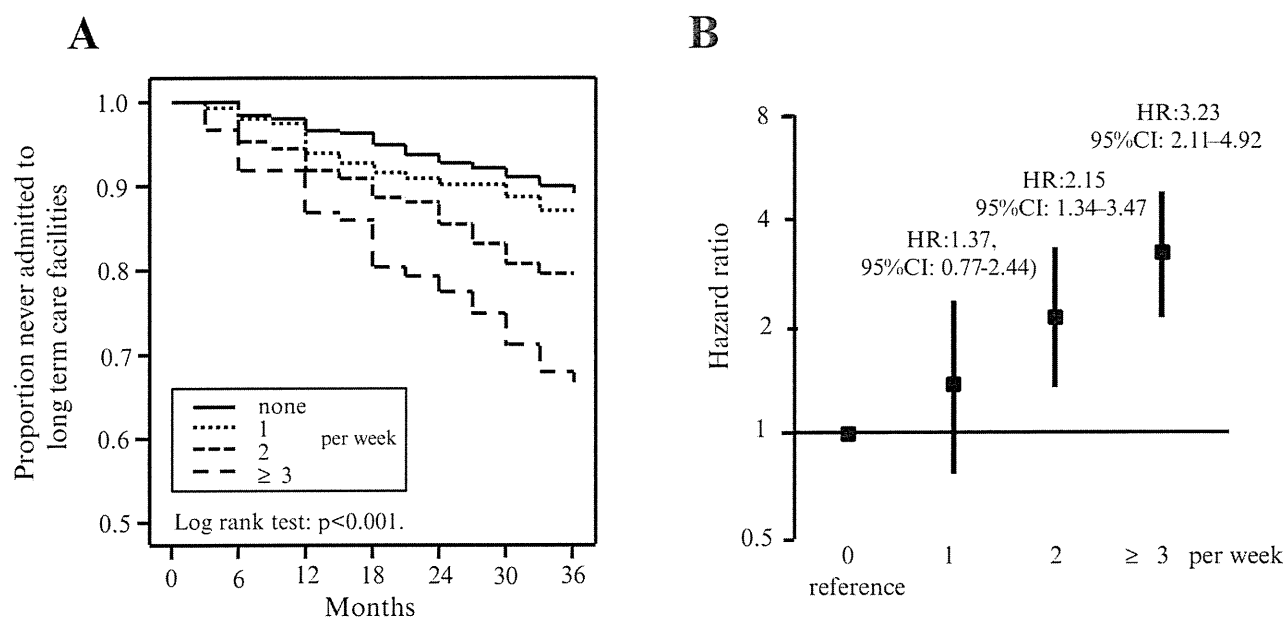


Figure 1 (A) Kaplan–Meier estimates of long-term care (LTC) placement over 36 months according to the frequency of day-care service use (times per week). The log-rank test: $P < 0.001$. (B) Risk of LTC placement based on the frequency of day-care service use (times per week), adjusting for potential confounders (recipient's gender, age, ADL status, presence or absence of dementia, caregiver's gender, age, and Zarit Burden Interview score). The y-axis is the adjusted hazard ratios (HR) on a log scale. Black squares are point estimates from a Cox proportional hazards model adjusting for potential confounders. The error bars represent 95% CI. A simple black square without confidence intervals represented the referent group, nonusers.

Table 3 Hazard ratios for long-term care placement associated with day-care service use (multivariate models)

Models	Hazard ratio	95% CI	<i>P</i> -value
Model 1 ($n = 1739$)	2.32	1.75–3.08	<0.001
Model 2 ($n = 1739$)	1.96	1.47–2.62	<0.001
Model 3 ($n = 1150$)	2.34	1.60–3.41	<0.001

Model 1 includes recipient gender and age. Model 2 includes recipient gender, age, ADL score, and presence or absence of dementia. Model 3 includes variables used in model 2 and caregiver's gender, age and Zarit Burden Interview score.

people in LTC is based on care recipient and caregiver characteristics and the sociocultural context of the recipient and caregiver. We do not know the exact reason for this negative effect of day-care service on LTC placement. There are conflicting findings in regard to the effect of day-care service on caregivers' stress, depression, subjective or objective burden, and physical and emotional well-being,²⁰ although a recent relatively large study demonstrated that day-care service had a beneficial effect on restricting caregiving time and providing respite to caregivers.^{9,10} It is possible that day-care service alone cannot satisfy the complex needs of caregivers and care recipients sufficiently to enable continued home care, and it is unlikely to change the caregiver's preference for institutional placement.²¹ Although we still do not know whether the character-

istics of caregivers and recipients, or day-care service use itself, increase the risk of LTC placement, the relief and improved mental and physical well-being of caregivers following day-care service use may enhance the willingness of caregivers to consider LTC placement. Caregivers who use day-care service or other respite services may become more aware of their level of stress and more willing to consider LTC placement as an acceptable option, especially if the service experience is positive or if the caregiver receives encouragement to institutionalize from professionals or other caregivers.²²

This study has important limitations. First, the study was not a randomized intervention trial. Japan has introduced the LTCI program, which provides various services, including day-care services, according to clients' preferences. Therefore, we could not randomize the use

of this service. Because of the observational design of the present study, differences in unmeasured factors including the severity of patients' chronic diseases, caregivers' health conditions, and quality of services may account in part for the findings. Those who use formal services may have greater need for caregiving than those who do not use formal services. The unmeasured needs that contribute to day-care service use may be stronger than the positive effects of service. Other aspects of the present study should also be considered. In the analysis, baseline data of service use was included, but changes in service use during the follow-up period were not considered. Our results may not be representative of the Japanese frail elderly in the community as a whole because the subjects in this study represented an urban population. In addition, these findings may not be generalizable to other populations given that local health practices, a variety of social and economic factors, ethnic attitudes about caring for very old people, and cost/access to day-care centers may have influenced these results.

In the present study, we showed that day-care service does not achieve the LTCI program aim of reducing the use of institutional care services of elderly people to enable them to maintain their lives at home. It may be possible that the respite for caregivers provided by day-care service is not enough to continue caregiving at home. As is true for any observational study, we cannot firmly establish a cause-and-effect relationship between day-care service use and LTC placement. In addition, the present study could not evaluate the exact reasons for the unfavorable effect of this service on LTC placement. Further studies are needed to determine why caregiving families decide to use day-care services, reasons for LTC placement, and whether day-care services meet the needs of families and care recipients throughout the caregiving career. In addition, future research should assess the quality of day-care programs and examine whether the quality of day-care services affects the LTC placement of clients. Health-care providers and care managers should recognize that day-care service use may augment LTC placement in dependent older people. Policy makers and practitioners should consider implementing a multidimensional support program to reduce caregivers' willingness to consider LTC placement.

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Disclosure statement

The authors have no conflicts of interest with any of the manufacturers of medications evaluated in this paper.

References

- Campbell JC, Ikegami N. Long-term care insurance comes to Japan. *Health Aff* 2000; **19**: 26–39.
- Ikegami K. Impact of public long-term care insurance in Japan. *Geriatr Gerontol Int* 2004; **4**: S146–S148.
- Tsutsui T, Muramatsu N. Care-needs certification in the long-term care insurance system of Japan. *J Am Geriatr Soc* 2005; **53**: 522–527.
- Tsutsui T, Muramatsu N. Japan's universal long-term care system reform of 2005: containing costs and realizing a vision. *J Am Geriatr Soc* 2007; **55**: 1458–1463.
- Kuzuya M, Masuda Y, Hirakawa Y *et al*. Underuse of medications for chronic diseases in the oldest of community-dwelling older frail Japanese. *J Am Geriatr Soc* 2006; **54**: 598–605.
- Kuzuya M, Masuda Y, Hirakawa Y *et al*. Day-care service use is associated with lower mortality among community-dwelling frail elderly. *J Am Geriatr Soc* 2006; **54**: 1364–1371.
- McCann JJ, Hebert LE, Li Y *et al*. The effect of adult day care services on time to nursing home placement in older adults with Alzheimer's disease. *Gerontologist* 2005; **45**: 754–763.
- Gaugler JE, Kane RL, Kane RA, Clay T, Newcomer R. Caregiving and institutionalization of cognitively impaired older people: utilizing dynamic predictors of change. *Gerontologist* 2003; **43**: 219–229.
- Gaugler JE, Jarrott SE, Zarit SH, Stephens MA, Townsend A, Greene R. Adult day service use and reductions in caregiving hours: effects on stress and psychological well-being for dementia caregivers. *Int J Geriatr Psychiatry* 2003; **18**: 55–62.
- Zarit SH, Stephens MA, Townsend A, Greene R. Stress reduction for family caregivers: effects of adult day care use. *J Gerontol B Psychol Sci Soc Sci* 1998; **53B**: S267–S277.
- Yesavage JA. Geriatric depression scale. *Psychopharmacol Bull* 1988; **24**: 709–711.
- Mahoney F, Barthel DW. Functional evaluation: the Barthel Index. *Md State Med J* 1965; **14**: 61–65.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–383.
- Arai Y, Kudo K, Hosokawa T, Washio M, Miura H, Hisamichi S. Reliability and validity of the Japanese version of the Zarit Caregiver Burden interview. *Psychiatry Clin Neurosci* 1997; **51**: 281–287.
- Aguero-Torres H, von Strauss E, Viitanen M, Winblad B, Fratiglioni L. Institutionalization in the elderly: the role of chronic diseases and dementia. Cross-sectional and longitudinal data from a population-based study. *J Clin Epidemiol* 2001; **54**: 795–801.
- Bharucha AJ, Pandav R, Shen C, Dodge HH, Ganguli M. Predictors of nursing facility admission: a 12-year epidemiological study in the United States. *J Am Geriatr Soc* 2004; **52**: 434–439.
- Harris Y, Cooper JK. Depressive symptoms in older people predict nursing home admission. *J Am Geriatr Soc* 2006; **54**: 593–597.

- 18 Rockwood K, Stolee P, McDowell I. Factors associated with institutionalization of older people in Canada: testing a multifactorial definition of frailty. *J Am Geriatr Soc* 1996; **44**: 578–582.
- 19 Kesselring A, Krulik T, Bichsel M, Minder C, Beck JC, Stuck AE. Emotional and physical demands on caregivers in home care to the elderly in Switzerland and their relationship to nursing home admission. *Eur J Public Health* 2001; **11**: 267–273.
- 20 Cox C. Findings from a statewide program of respite care: a comparison of service users, stoppers, and nonusers. *Gerontologist* 1997; **37**: 511–517.
- 21 Kuzuya M, Hasegawa J, Hirakawa Y *et al.* Impact of informal care levels on discontinuation of living at home in community-dwelling dependent elderly using various community-based services. *Arch Gerontol Geriatr* 2011; **52**: 127–132.
- 22 Gaugler JE, Zarit SH. The effectiveness of adult day services for disabled older people. *J Aging Soc Policy* 2001; **12**: 23–47.

**PROCESS OF PHYSICAL DISABILITY
AMONG OLDER ADULTS
— CONTRIBUTION OF FRAILITY
IN THE SUPER-AGED SOCIETY**

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ABSTRACT

One of the critical issues that Japan, well known for the world's highest proportion of older adults, a super-aged society, is currently confronting is how to prevent physical disability in old age. This issue is particularly important not only from a medical perspective such as functional prognoses but also from a socio-economic angle in view of reducing the rapid rise in the cost of medical and long-term care insurance services. Functional decline in old age results not only from acute diseases but also from frailty. Such a common and important syndrome that is increasingly prevalent with advancing age can be the cause. The present article intends to review what is known about frailty, including its definition, epidemiology, and pathophysiology, and to examine potential areas of future research.

Key Words: Frailty, Elderly, Physical disability

INTRODUCTION

Japan is at the forefront of population aging. As of 2010, the number of people age 65 or over was 29.6 million, constituting 23.1 percent of the total population and marking record highs in terms of both number and percentage.^{1,2)} This figure is the highest in the world. The speed of aging among Japan's population is much faster than that in any of the advanced Western European countries or the U.S.A. Although the elderly population of Japan accounted for only 7.1 percent of the total population in 1970, 24 years later in 1994 it had almost doubled in scale to 14.1 percent. A comparison with other countries clearly highlights the rapid progress of demographic aging in Japan.

During society's aging process, the proportion of dependent older people and long-term care (LTC) users are increasing in developed countries. In fact, Japan had more than 4,500,000 LTC users in 2008.¹⁾ There is a projected trend toward a reduced capacity of institutional care, which in turn will increase the number of severely disabled people living in the community. There is a great deal of public policy and clinical interest in effective and efficient ways to help disabled elderly individuals continue living in community settings.

As the number of elderly people with disabilities or requiring support in their activities of daily

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living increases, the demand for LTC services has also increased. Consequently, expenditures for the LTC system are growing steadily, threatening the financial sustainability of the system. To better cope with the accelerated aging of Japanese society and the growing need for nursing care of the elderly, Japan introduced a public LTC insurance (“*Kaigo Hoken*”) system in 2000.^{3,4)} This program enrolled all Japanese nationals aged 65 and older under the coverage of its insurance scheme, creating a radical change from the traditional family-based care toward the socialization of elderly care and the integration of medical care and welfare services. The aims of LTC insurance-based home care programs were not only to reduce the care burden of caregivers but also to maintain and improve functional abilities and well-being of older people, to minimize the use of institutional care services, and to reduce mortality. Under the LTC insurance program, older people who are certified as being either “assistance required” (*yo-shien*) or “care required” (*yo-kaigo*) could be provided with any community-based services depending on the certification of care need levels along with a 10% co-payment for services received.

The number of certified older adults has kept increasing, currently reaching more than 4,500,000. According to data from the Ministry of Health, Labour and Welfare, the proportion of disabled older people estimated by the rate of older adults who were judged as requiring support/care at any levels based on the certificates of LTC insurance was 9.9% when LTC insurance system was inaugurated (April, 2000). Nevertheless, certified users of LTC insurance have increased constantly, so that by 2006 the figure had increased to 16.3%.⁵⁾ Accordingly, the expenditures of LTC insurance had grown in parallel with the constant increase in beneficiaries, threatening the financial sustainability of the system. To maintain that system and to increase the quality of life for older people, it is crucial to prevent disabilities and maintain the status of their daily living activities.

REASONS FOR LONG-TERM CARE INSURANCE SERVICE USE IN OLDER PEOPLE

As shown in Fig. 1, among the younger LTC insurance beneficiaries, stroke is a major cause of eligibility for LTC insurance (*yo-kaigo*) according to the Comprehensive Survey of Living Conditions conducted by the Ministry of Health, Labour and Welfare.⁶⁾ However, the percentage of strokes declines as age increases. The percentages of arthropathy, cardiovascular

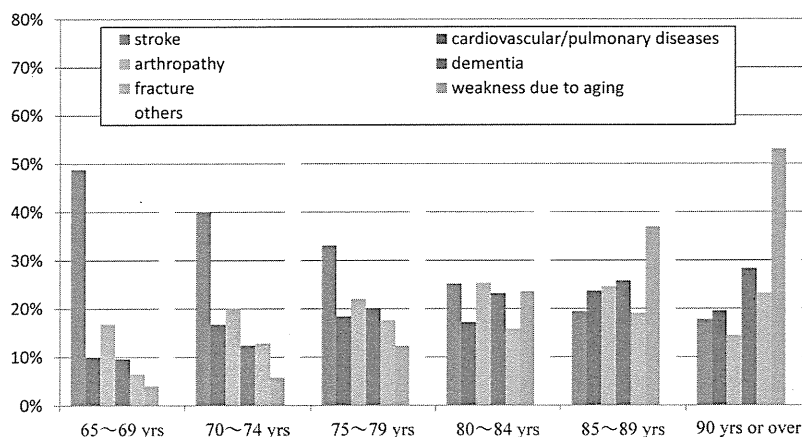


Fig. 1 Major causes of long-term care insurance eligibility (*yo-kaigo*).

FRAILITY IN THE SUPER-AGED SOCIETY

and pulmonary diseases, dementia, and fractures as causes of eligibility for LTC insurance are gradually increasing as the applicants become older. In contrast, a rapid increase was observed in the percentage of “weakness due to aging” as age increases, exceeding 50% of total applicants above age 90 or over. According to the survey, “weakness due to aging” accounts for physical dependence in 26.5% of those aged 65 or over, in 30.8% of those aged 75 or over, and 43.9% of those aged 85 or over respectively. As of 2007, it was reported that the total number of older adults certified as requiring care (*yo-kaigo*) was estimated to be about 4,400,000, which comes to a total of 1,170,000 who were certified as *yo-kaigo* due to “weakness with aging” in Japan. These data suggest that weakness as a major cause of disability in Japan’s super-aged society has already emerged.

DEFINITION OF FRAILITY

In the field of geriatric medicine, the term “frailty” has long been acknowledged among those who are engaged/involved in the care of older people. In recent years particularly since the definition has been established and become widespread, the concept of frailty has begun to draw growing attention among researchers and clinicians. Frailty may now be regarded as a geriatric syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and leading to adverse health outcomes including physical disability, falls, hospitalization, institutionalization and mortality. This would imply that a common underlying biologic process may be responsible for such a development. Concepts focusing on inflammatory processes, changes in hormonal environment and body composition support this hypothesis. This writer considers that “weakness due to aging” as described above as the major cause of *yo-kaigo* is equivalent to “frailty due to aging.”

Although there is still a lack of consensus on the definition of frailty, it has been generally accepted that it is distinct from disability and comorbidity, and that it characterizes the weakest and most vulnerable subset of older people due to the declining functions of their multiple organs. As the term “frail” has not yet achieved relevant vernacular meanings given its rather obscure definitions, it covers a wide range of common phenotypes including muscle weakness, bone fragility, very low body mass index, susceptibility to falling, vulnerability to trauma, vulnerability to infection, high risk of delirium, and severely diminished physical capabilities.

There are various proposed phenotypes of frailty among older people. Different definitions of frailty have included a variety of components including weakness, fatigue, weight loss, decreased balance, low levels of physical activity, impaired mobility and performance, and social withdrawal. In 2001, Fried *et al.* developed screening criteria for frailty as a syndrome requiring the presence of a critical mass (≥ 3) of the following clinical manifestations: weakness, weight loss, slow walking speed, fatigue, and low levels of activity.⁷⁾ That phenotype has been found to predict a variety of poor clinical outcomes, including falls, physical disability, hospitalization, and mortality.⁷⁾ Others have also reported that a combination of inactivity and weight loss is a significant predictor of disability and mortality.⁸⁾ Based on those observations, a consensus report from a group of Italian and American geriatricians has been published advocating that any criteria used to define physical frailty be based on impairments in physiological domains that include mobility, balance, muscle strength, motor processing, cognition, nutrition status including weight change, endurance (including feelings of fatigue and exhaustion), and physical activity.⁹⁾ The validity of those factors as components of frailty is provided by studies showing that in older, non-disabled persons, individual components are associated with geriatric syndromes such as falls, depression, urinary incontinence and functional impairment, which are all strong and

independent risk factors for disability and/or death.

The investigation, treatment and care of older people who are both frail and disabled constitute much of the work of geriatric assessment units. However, despite the frequency with which frailty and disability coexist, they are in fact quite separate concepts. Disability indicates a loss of function, and may arise from accidents such as a stroke or hip fracture which therefore require sustained medical care (medical or disease models of disability, see Figs. 2A and 3). Frailty

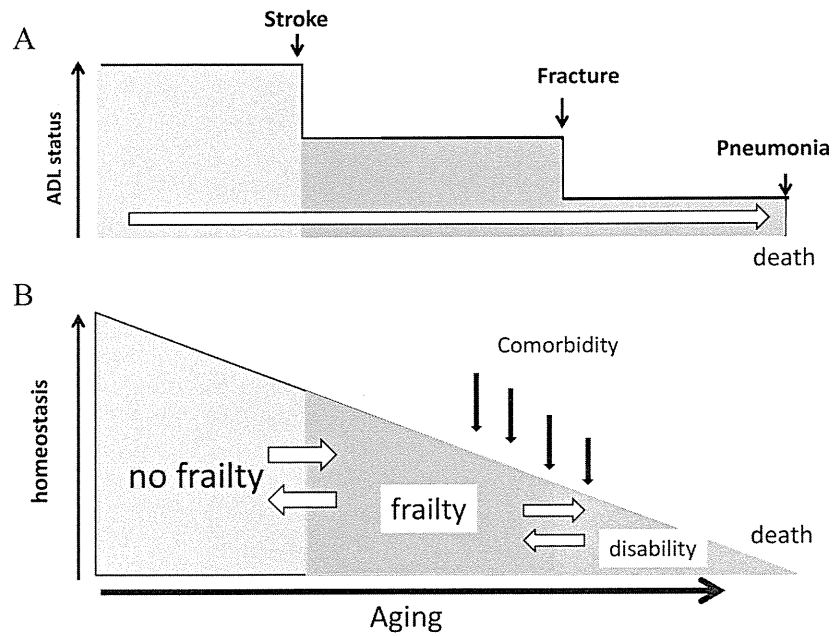


Fig. 2 Disability models for the elderly. A: Medical (disease) model of disability. B: Frailty model of disability.

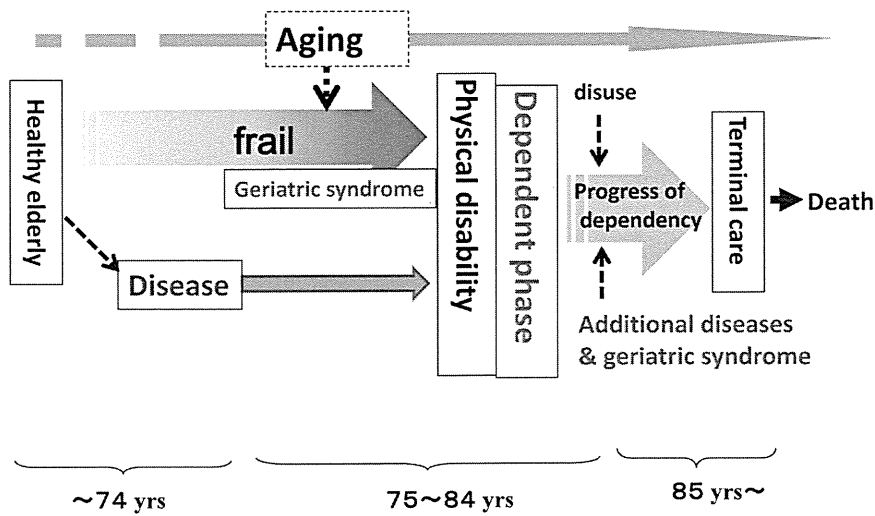


Fig. 3 Potential causes of disability and time course of death.

FRAILITY IN THE SUPER-AGED SOCIETY

indicates instability and the risk of current or further loss of function, another model of disability for the elderly (frail model, see Figs. 2B and 3). Frailty is the root cause of unstable disability and an appropriate focus for prevention, rehabilitation and public health programs in old age.

FRAILITY AND SARCOPENIA

Aging is associated with significant changes in body composition, with a substantial reduction in both fat-free mass and muscle mass together with an increase in visceral fat. Sarcopenia is a syndrome characterized by a progressive and generalized loss of skeletal muscle mass and strength entailing a risk of adverse outcomes such as physical disability, poor quality of life and eventual death. Although the definition of sarcopenia remains controversial, its prevalence among older adults under the age of 70 is roughly 25% and increases to 40% in adults 80 years or older.¹⁰ Recently, a joint European Working Group on Sarcopenia in Older People (EWGSOP) proposed a working definition.¹¹ According to EWGSOP, sarcopenia was diagnosed by the presence of low muscle mass plus either low muscle strength or low physical performance. Sarcopenia represents a risk factor for frailty, loss of independence, and physical disability.¹² Impaired mobility resulting from muscle loss is predictive of major physical disability and mortality, and is associated with poor quality of life along with social and health care needs.¹³ Several mechanisms may be involved in the onset and progression of sarcopenia. Its possible causes are multi-factorial and can include disuse, changing endocrinal functions, chronic diseases, inflammation, insulin resistance, and nutritional deficiencies. Sarcopenia is thus rightly considered a major component in the pathway leading to frailty (Fig. 4).¹⁴

CAUSES OF FRAILITY

There is currently no exact universally accepted consensus concerning the causes of frailty, which probably reflects the complexity of multiple interconnected physiological processes which become dysregulated with age. Those physiological processes/pathways include immune/inflammatory processes, neuroendocrine deregulation, mitochondrial dysfunction, hormonal changes, oxidative stress, and metabolic alterations (Fig. 4).

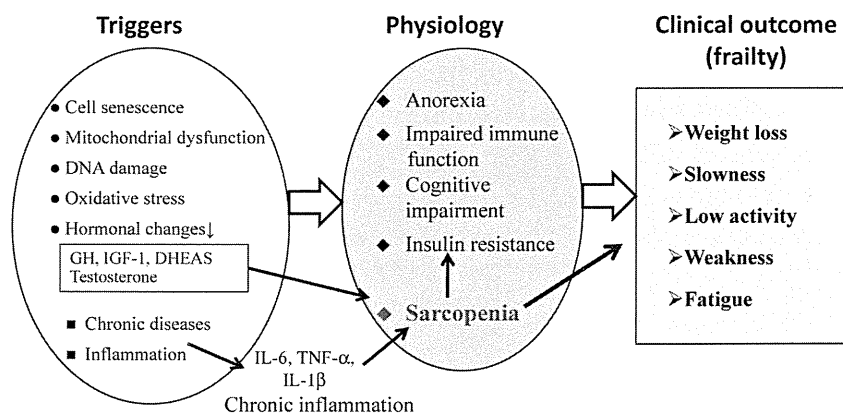


Fig. 4 Conceptual framework of specific physiological system changes that may contribute to underlying vulnerability and clinical manifestations of frailty.

In particular, evidence has been presented that supports a significant role of inflammation in the process of frailty. It has been suggested that during the aging process, a primary dysregulation of the mechanisms that initiate, modulate and block an inflammatory response often occurs. In fact, it has been demonstrated that among the elderly there are high plasma levels of circulating pro-inflammatory cytokines, including tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and interleukin-1 (IL-1) in older persons.¹⁵⁾ Such pro-inflammatory mechanisms have also been suggested to be implicated in the development of sarcopenia due to the effects of increased cytokines on reduced muscle protein synthesis and increased protein degradation (Fig. 4).

Several age-related hormonal changes have been linked to the frailty syndrome and to its components (Fig. 4). Among the latter, the hormonal relationship with the decrease in muscle strength has received the most attention. While testosterone, growth hormone (GH) and insulin-like growth factor I (IGF-1) were most intensely studied in this context, open questions still remain with regard to the clinical relevance and the effect of replacement therapy.

While a proposal for the involvement of a molecular and physiological pathway sounds attractive, it requires further substantiation. We also need to continue studying the role of other potential components that contribute to the frailty that comes with aging. It is possible that the biological, psychological, social and environmental factors that interact across the course of life are determinants of the onset of frailty. The components of frailty may include those identified by Fried (decreased physical activity, weakness, diminished endurance, slowness, undernutrition) along with added cognitive, psychological and perhaps social components. The pathway from frailty to its adverse outcomes is also affected by various biological, psychological, social and societal modifiers.

CLINICAL ASPECTS OF FRAILTY

The concept of the presence of a frailty phase during the aging process seems to be quite important, since a considerable number of older people become physically disabled through their frailty status rather than through an abrupt onset of acute medical conditions such as strokes and hip fractures as described above. This process, unique to older individuals, is not observed in younger people. However, the working definition of frailty, based on Fried's criteria,⁷⁾ is only based on physical symptoms and signs. It neglects other potentially important components of the syndromes such as mood, cognitive, sensory impairments and the socioeconomic aspects of older adults' lives. It is unsatisfactory to define frailty in the physical domain alone, since there are several other phenomena that are yet to be examined but that are commonly observed in the state of frailty.

Gill *et al.* have demonstrated that frailty is a dynamic process characterized by frequent transitions among frailty states (nonfrail, prefrail, and frail) over time (Fig. 2B).¹⁶⁾ This may illustrate the usefulness of the frailty concept for clinical practice. Some physicians may even regard frailty as an example of the medicalization of old age and be suspicious about its prevention. However, the overall consequences are that the frail elderly are at higher risk of accelerated physical and cognitive decline, disability, and finally death. Needless to say, from a practical point of view, the early identification of a propensity to frailty would prove useful in preventing or delaying its more severe clinical consequences.

From a clinical perspective, two issues are particularly important: first, the identification of the causes of frailty and its association with chronic inflammation and other factors; and second, the development of substantiated strategies for the prevention of frailty. Interventions have been made among older adults that targeted correlates or specific components of frailty. First-line treatments

FRAILITY IN THE SUPER-AGED SOCIETY

for primary frailty include an adequate diet with sufficient protein, vitamins and mineral intake, regular physical exercise such as stretching, walking, and lifting weights to preserve and increase muscle mass and strength.

CONCLUSION AND REMARKS

In conclusion there is a growing consensus that frailty is a syndrome that can be identified and measured clinically, and that it is distinct from disability and comorbidity. Frailty is a state of reduced homeostasis leading to increased vulnerability and the risk of adverse outcomes. It results from the impact of multiple system impairment with critical changes in its reserve capacities, especially in its metabolic, cardiovascular, musculoskeletal, immunologic and neurologic systems. It represents a dynamic, complex interaction of biological, psychological, cognitive and social factors as well as a complex interplay of assets and deficits.

Prevention must not only focus on diseases but also on the frailty that is crucial to the well-being of older people in a super-aged society. To establish better strategies for preventing frailty, it is also essential to improve our understanding of the causes and trajectory of frailty in the context of the demography and epidemiology of an older population.

REFERENCES

- 1) http://www8.cao.go.jp/kourei/whitepaper/w-2011/zenbun/23pdf_index.html. Accessed November 10, 2011.
- 2) http://www8.cao.go.jp/kourei/whitepaper/w-2010/zenbun/22pdf_index.html. Accessed November 10, 2011.
- 3) Ikegami K. Impact of public long-term care insurance in Japan. *Geriatr Gerontol Int*, 2004; 4: S146–S148.
- 4) Tsutsui T, Muramatsu N. Care-needs certification in the long-term care insurance system of Japan. *J Am Geriatr Soc*, 2005; 53: 522–527.
- 5) Status of Long-Term Care Insurance System: Health and Welfare Services for the Elderly (10). Annual Health, Labour and Welfare Report 2008–2009 White Papers & reports MHLW, Japan; [<http://www.mhlw.go.jp/english/wp/hw3/dl/10-06.pdf>], Accessed: November 10, 2011.
- 6) <http://www.mhlw.go.jp/toukei/list/20-19.html>. Accessed: November 10, 2011.
- 7) Fried LP, Tangen C, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: Evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*, 2001; 56A: M1–M11.
- 8) Chin A, Paw MJ, Dekker JM, Feskens EJ, Schouten EG, Kromhout D. How to select a frail elderly population? A comparison of three working definitions. *J Clin Epidemiol*, 1999; 52: 1015–1021.
- 9) Ferrucci L, Guralnik JM, Studenski S, Fried LP, Cutler GB Jr, Walston JD. Interventions on Frailty Working Group. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: A consensus report. *J Am Geriatr Soc*, 2004; 52: 625–634.
- 10) Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ, Lindeman RD. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol*, 1998; 147: 755–763.
- 11) Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M. European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010; 39: 412–23.
- 12) Roubenoff R. Sarcopenia and its implications for the elderly. *Eur J Clin Nutr*; 2000; 54: S40–S47.
- 13) Fried LP, Guralnik JM, 1997. Disability in older adults: Evidence regarding significance, etiology, and risk. *J Am Geriatr Soc*, 1997; 45: 92–100.
- 14) Kuzuya M. Impact of sarcopenia and frailty on elderly health. *Nihon Ronen Igakkai Zasshi*, 2009; 46: 279–285.
- 15) Franceschi C, Bonafè M, Valensin S, Olivieri F, De Luca M, Ottaviani E, De Benedictis G. Inflamm-aging: an evoluzinary perspective on immunosenescence. *Ann NY Acad Sci*, 2000; 908: 244–254
- 16) Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. *Arch Intern Med*, 2006; 166: 418–423.