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An Association of the First Three Days' Oral Energy Intake with Post-Hospital Daily Living Activities in Hospitalized Females Above 75 Years Old

Tsunou A[1,2], Hokotachi Y[1,3] and Amagai T[1*]

[1]Administration Food Sciences and Nutrition Major, Graduate School of Human Environmental Sciences, Mukogawa Women's University, Nishinomiya, Japan

[2]Department of Clinical Nutrition, Kita-Uwa Hospital, Kita-Uwa, Japan

[3]Department of Clinical Nutrition, Takarazuka Dai-ichi Hospital, Takarazuka, Japan

***Corresponding author:**

Teruyoshi Amagai,
Administration Food Sciences and Nutrition Major, Graduate School of Human Environmental Sciences, Mukogawa Women's University,
Nishinomiya, Japan, 663-8558,
Tel: +81-798-45-9855;
Fax: +81-798-45-9855;
E-mail: amagaipedteruyoshi@gmail.com

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Abbreviations:

ADL: activities of daily living; Alb: serum albumin concentration; BMI: body mass index; CCI: Charlton comorbidity index; CRP: C-reactive protein; Δ ADL: change of ADL calculated by ADL at discharge minus ADL at admission; Hb: hemoglobin concentration; NPC/N: non-protein calorie/ nitrogen ratio; PN: parenteral nutrition; PO: oral nutrition; OR: odds ratio; CP: cut-off value of DEI; DEI: an average daily energy intake during the first 72 hours after admission (kcal/ kg of actual body weight); LOS: length of stay in hospital; ROC: the receiver operating characteristic; T-Bil: serum total bilirubin concentration

[#]Author Contributions:

Tsunou A, Hokotachi Y. These authors have contributed equally to this article.

1. Abstract

To test hypothesis that an early oral energy intake during hospitalization is associated with enhancing an activity of daily living (ADL) at discharge. All consecutive female older inpatients aged ≥ 75 years, admitted to a single institution, were recruited. The collected data were demographics, blood test, nutritional, and outcome parameters, included changes of pre- and post-hospital ADL (Δ ADL) The Δ ADL in all individuals was defined by living places into dichotomy, favorable (F) and unfavorable (U) for Δ ADL ≥ or < 0, respectively. **1:** All collected data in two groups was compared. **2:** To determine which factor is associated with Δ ADL, multivariate logistic regression analysis was conducted. **3**: To test hypothesis that oral daily energy intake (DEI) is associated to maintain post-hospital ADL, ROC curve analysis was conducted to draw cutoff value of DEI during the first three days of hospitalization to maintain post-hospital ADL. The results were the followings: 67 out of 131 subjects, whose median age and BMI were 87.0 years and 18.4 kg/ m^2, respectively. 1) DEI were significantly larger in Group-F (25.7 vs. 17.5 kcal/kg, respectively, p=0.001), 2) DEI at admission were proved determinant factors, 3) the cutoff value of DEI was 25 kcal/ kg to maintain post-hospital ADL. We concluded that daily energy intake ≥ 25 kcal/kg orally taken during the first three days of hospitalization was associated with maintaining post-hospital ADL among female inpatients aged ≥ 75 years, and vice versa.

2. Background

The aging society has rapidly developed in the developed countries, such as Japan as the leading country in this area, followed

by Italy and Germany. The World Health Organization (WHO) and the United Nations define an "aging society" as one in which more than 7% of the population is 65 years or older, followed by an "aged society", "super-aged society", and so-called "super-super-aged" society as a society in which more than 14%, 21%, and 28% of the population is 65 years or older [1]. Giving that Japan is the leading country to reach to super-aging society all over the world, the year to reach to above mentioned four type aged-societies in Japan were 1970, 1994, 2007, and 2019, respectively. These are calculated that three durations for growing every 7% of four type societies were 24, 13, and 12 years, respectively [2]. Regardless of rapid changes of social structures, such as growth of aging population, there is scant evidence or observation that older adult seems live healthier than their parents did. Ageism also has been reported to be more pervasive than sexism or racism and the integrated health care system is proposed to be required by World Health Organization [3]. To make health care system enhancing active more in health among older adults, in this study, we hypothesized that an appropriate oral energy intake during an early periods of hospitalization is associated with post-hospital live more active. The reason why we paid our attention to the early in-hospital period was that most stresses under medical and surgical insults to the older adult patients might be considered as a more severe insult during an early period rather than later, unless they failed to achieve recovery from cytokine attack even with the efforts of medical treatments. Furthermore, the reason why we selected female rather than male as study subject was because average life expectancy (HL, years) has been reported longer in female (87.14 vs. 80.98 years). Even in this context, focusing on period of non-healthy life expectancy (NHL, years) which is defined and calculated by the equation that ordinary life expectancy (years) minus healthy life expectance (years) as the relevant indicator of unhealthiness in oldest adults. NHL is as longer in female than in male (12.35 vs. 8.84 years, respectively) as HL [3]. These facts are interpreted that female older adults must be no longer live healthy and they live on supports in daily living over 12 years at their last of lives. Under these social circumstances, if influential factors on post-hospital living activity are able to identify among nutritional management during hospitalization, female older inpatients might shorten NHL.

3. Aim

To test hypothesis that an oral energy intake during early periods of hospitalization was associated with post-hospital ADL.

4. Outcome Measures

The primary outcome was change of Activities of daily living (ΔADL) between pre- and post-hospitalization. The second outcomes included the length of hospitalization, the highest CRP during hospitalization, free days of antibiotics, daily prescribed drugs at discharge.

4.1. ADL Stratification: ADL was evaluated by living institutes or home because living institutes was determined by governmental officers according to ADL strictly evaluated as shown in Table 1. This was the reason why living place was chosen as ADL parameter in older adults. An individual ADL of pre-and post-hospitalization were stratified into six levels (Table 1). For explaining each level of ADL, several objective instances are described in the followings: 1) level 1 meant dead during hospitalization, ADL2) level 2 and 6 meant complete dependency and independency in ADL, respectively, l3) level 5 institutes accept older adults who live on medical checks by routinely, 4) level 4 could accept and includes daily visiting services, 5) the difference between level 4 and 3 was that level 4 has training program for rehabilitation and physical function of female residents in this level was less impaired than in level 3, 6) the level 1 included dead during hospitalization, 7) although the larger figures was corresponding to more independent living activities, the figure itself did not always correspond to relative changes of ADL. In this ADL definition, the integral figures of ADL were not always identical to an absolute severity of physical functional impairment. In other words, comparing level 6 and 3, level 3 did not mean two times severe ADL compared with that in level 6.

Table 1: The definition of living activity before and after hospitalization.

ADL	Living environments	Medical care	Nursing care	Short stay	Long staying	Self-cooking
6	Home	×	×	×	○	○
5	Social welfare facility	×	×	○	○	×
4	Nursing care facility for the olde adults	△	○	○	○	×
3	Nurisng care health facility	△	○	○	△	×
2	Another hospital	○	○	○	△	×
1	Death during hositalization	×	×	×	×	×

Determining an individual Δ ADL expressed numerical character (ADL after hospitalization minus ADL before hospitalization), all subjects was divided into dichotomy, favorable (F) and unfavorable (U), by each Δ ADL. When the figure of Δ ADL was zero or plus, the subject was assigned to Group-F, and the others were to Group-D.

5. Collected Data

1) demographics, including age, sex, body weight, body mass index (BMI, expressed in unit of kg /m^2), Charlson comorbidity index (CCI) [4] to evaluate individual comorbidity, and activity of daily life (ADL) evaluated by dichotomy of independence or dependence of daily physical activity. Here, a dependence was defined as daily living with the others' supports and independence was opposite. These data were evaluated at admission, **2) blood test parameters,** including serum C-reactive protein (CRP) and hemoglobin concentration (Hb) measured during hospitalization as necessary, **3) nutritional parameters,** including daily energy intake (DEI: kcal of daily energy intake through all available routes / kg of actual body weight (BW) measured at admission) for the first 72 hours between second and fourth day after admission. Here, the reason why the first day after admission was excluded from the study period was to avoid data inconsistency by different admission clock time, some with lunch or dinner, and the others without.

6. Methods

All above mentioned data was collected from recruited subjects divided into two groups, according to change of ADL between pre- and post-hospitalization. The inclusion criteria of subjects were consecutive female older inpatients, aged ≥ 75 years, admitted to a single institution between April and September. 2017. The exclusion criteria were as the follows: 1) the length of stay in hospital < 72 hours because the shorter stay could not enough to test influential effects on clinical outcomes, 2) primary purpose of admission was not treatment but palliative, 3) nutritional support route did not oral, but with enteral or parenteral, 4) liver or renal dysfunction defined as serum total bilirubin level > 1.5 mg/dL, or serum creatinine level > 1.5 mg/dL, respectively, because of possibilities of their adverse effects on outcome through nutrients metabolism or excretion. Then, all data was analyzed in three different methods described later (Figure 1).

Given the nature of this study, the requirement for informed patient consent was considered unnecessary.

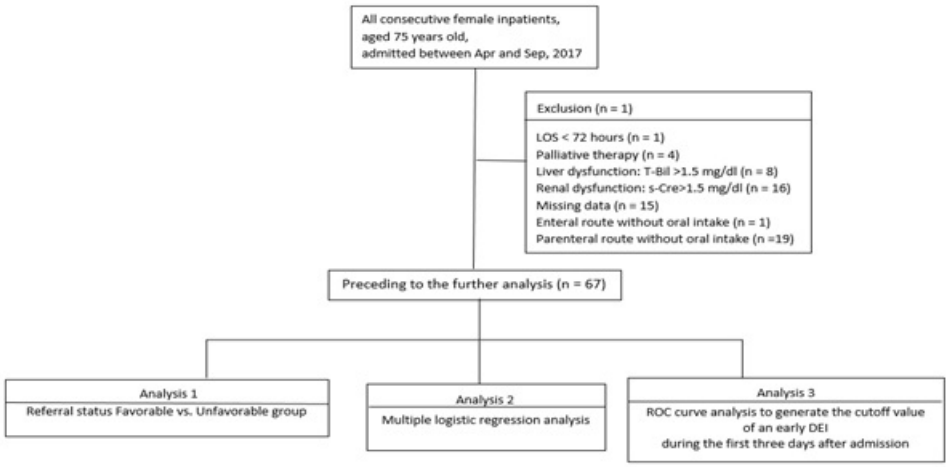

Figure 1: Flow chart of the study

6.1. Analysis 1

After dividing all subjects into two groups, group F and D, all collected data was compared between two groups to extract influencing factors on ADL after hospitalization.

6.2. Analysis 2

To determine which factors are associated with post-hospital ADL, multivariate logistic regression analysis was conducted using factors taken in analysis 1 and each factor were expressed by odds ratio (OR), its 95% Confidence interval (CI), and p-value.

6.3. Analysis 3

Limited If nutritional factor was proved as an influential on post-hospital ADL in analysis 2, to test hypothesis that nutritional intakes at an early period in hospitalization is associated with post-hospital ADL, the receiver operating characteristic (ROC) curve analysis was conducted and the cutoff value of DEI during the first 72 hours after admission was calculated.

6.4. Statistical Analysis

The outcome parameters in the two groups were divided into different categories and compared using the Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. In the ROC curve analysis, the area under the curve (AUC) and the 95% confidence interval (CI) were also determined. The AUC with a 95% CI was considered if the AUC was 1.0, and an AUC of 0.5 was not considered to be confident. The point with the larger Youden index, equal to [sensitivity + (specificity – 1)], was defined as the superior cutoff point. Two-sided p value of < 0.05 was considered statistically signifi-

cant. All analyses were performed using SPSS Statistics version 24 (IBM Corp., Armonk, NY, USA).

7. Results

One hundred and thirty-one female inpatients were recruited. After excluding 64 according to exclusion criteria, the remaining 67 subjects were remained and were proceeding to the further three analyses (Figure 1). The all subjects were distributed into two groups, favorable and unfavorable group (Table 2, Table 3).

Table 2.1: Favorable group

			ADL before hospitalization					
			6	5	4	3	2	
			Home	Social welfare facilities	Nursing care acilities for the elderly	Nusring care health facilities	Another Hospital, Clicics	Total
ADL after hospitalization	6	Home	30	0	0	0	1	31
	5	Social welfare facilities	0	8	0	0	1	9
	4	Nursing care acilities for the elderly	0	0	9	0	1	10
	3	Nursing care health facilities	0	0	0	0	0	0
	2	Another Hospital, Clicics	0	0	0	0	1	1
	1	Dead	0	0	0	0	0	0
		Total	30	8	9	0	4	51

Table 2.2: Unfavorable group

			ADL before hospitalization				
			6	5	4	3	2
			Home	Social welfare facilities	Nursing care acilities for the elderly	Nusring care health facilities	Another Hospital, Clicics
ADL after hospitalization	6	Home	0	0	0	0	0
	5	Social welfare facilities	2	0	0	0	0
	4	Nursing care acilities for the elderly	2	0	0	0	0
	3	Nursing care health facilities	1	0	0	0	0
	2	Another Hospital, Clicics	4	2	2	0	0
	1	Dead	0	1	1	0	1
		Total	9	3	3	0	1

Table 3: Comparison of collected data between discharge status, Favorable vs. Unfavorable.

Discharge status	Total	Favorable	Unfavorable	P Value
Demographics	67	51	16	
Age*, years	87 (82, 94)	87 (86, 93)	89 (83, 95)	0.56
Height*, cm	145 (140, 148)	145 (140, 148)	144 (140, 150)	0.988
Body weight*, Kg	40.0 (33.6, 44.8)	39.2 (33.0, 44.3)	42.8 (38.1, 50, 3)	0.087
BMI*, kg/m2	18.4 (16.9, 21.0)	17.9 (16.5, 20.7)	20.1 (18.4, 23.6)	0.032
CCI score	1 (1, 2)	1 (1, 2)	2 (1, 3)	0.229
Blood test				
Hb, g/dl	11.2 (9.8, 12.4)	11.2 (9.5, 12.1)	11.8 (9.8, 14.1)	0.162
Alb, mg/dl	3.3 (2.9, 3.7)	3.3 (2.9, 3.7)	3.3 (2.8, 3.6)	0.256
CRP, mg/dl	1.65 (0.32, 9.56)	1.75 (0.31, 9.62)	1.61 (0.46, 3.99)	1.000
Nutritional data				
Total Daily energy intake (PO+PN), kcal/kg/day	22.9 (14.8, 27.7)	25.7 (19.3, 28.8)	17.5 (8.8, 23.2)	<0.001
Oral Daily energy intake (PO only), kcal/kg/day	22.2 (14.8, 27.3)	23.2 (18.0, 28.6)	16.2 (8.1, 21.2)	<0.001
Total Daily protein intake, g/kg/day	1.0 (0.7, 1.3)	1.1 (0.8, 1.4)	0.6 (0.4, 1.0)	0.001
NPC/N	110 (100, 119)	110 (100, 118)	111 (89, 124)	0.825
Outcome parameters				
∆ ADL**	0 (0, 0)	0 (0, 0)	-3 (-4, -2)	<0.001
Death, n (%)	3 (4)	0 (0)	3 (19)	0.012
Length of hositalization, days	19 (12, 34)	18 (10, 30)	32 (14, 47)	0.064
Highest CRP, mg/dl	2.71 (0.46, 9.73)	2.71 (0.32, 12.53)	2.51 (0.62, 4.62)	0.977
Free days of antibiotics	28 (23, 28)	28 (21, 28)	28 (28, 28)	0.093
Number of medication at disharge	4 (1, 5)	4 (2, 5)	2 (0, 6)	0.134

7.1. Result 1- Result of Analysis 1

The favorable group showed significantly higher total and orally taken daily energy and protein intake (Table 4). Meanwhile, the severity of comorbidity expressed by CCI did not differ between two groups.

Table 4: Results of multiple logistic regression analysis for determining living dependence level in female inpatients 75 years and older.

Independent Variable	OR (95% CI)	P value
Daily energy intake (kcal/kg/day)	13.98 (2.09-93.38)	0.006
ADL	6.68 (1.24-35.95)	0.027

7.2. Result 2- Result of Analysis 2

The multivariate logistic regression analysis showed that DEI was proved to influent on post-hospital ADL. In other words, insufficient energy intake was significantly associated with lowering post-hospital ADL.

7.3. Result 3- Result of Analysis 3

As our working hypothesis that smaller energy intakes for the first three days in hospitalization was proved worsening post-hospital ADL, to get the cutoff value of DEI to identify older female inpatients who has poor post-hospital ADL, ROC curve analysis showed that the cutoff value of DEI was 24.4 kcal/kg. This result is interpreted that average DEI for the first three days in hospitalization ≤ 24.4 kcal/kg of actual body weight seems associated with worsening post-hospital ADL and vice versa.

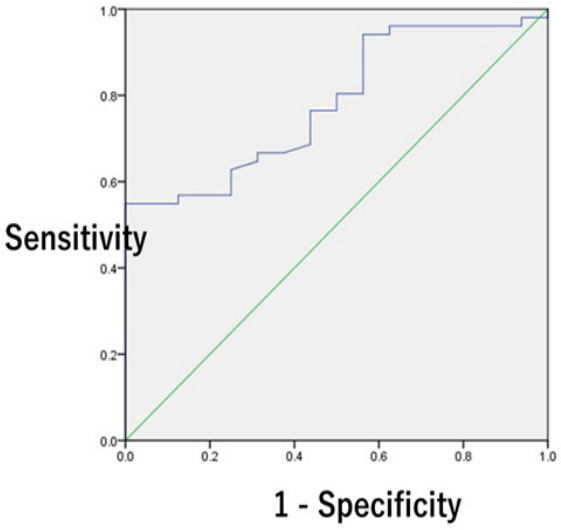

Figure 2: Results of receiver operating characteristic curve analysis to draw cutoff value of DEI (kcal/kg/ of actual body weight). The cutoff value of DEI for maintaining ADL after hospitalization could be determined at 24.4 kcal/kg, with an area under the curve of 0.782 ($p<0.05$).

8. Discussion

The ADL after hospitalization seems to depend on various factors, such as age, severity of the primary reason for hospitalization, comorbidities [6], and physically functional dependent activity [7, 8]. The present study also adds an importance of nutritional route and amount of energy intake during an early period as an association factor with post-hospital ADL.

8.1. Why Does an Oral Route Impact On Post-Hospital ADL in Older Patients?

An ability to eat might secure the possibilities of simultaneous chewing and swallowing. In stroke patients, for instance, an oral feeding has been reported as a predictor of recovery from dysphagia [9]. In another study, the authors observed that improvements of Functional Independence Measure (FIM) score and Dysphagia Severity Scale (DSS) have been good predictors of physical functional recovery from dysphagia also in stroke patients [10]. Contrary to stroke patients, measurements of FIM or DSS in daily basis could not always be available in non-stroke. Considering these reasons, an oral DEI was selected as a parameter of physical functional recovery of chewing and swallowing capacity. Our results could be interpreted that oral intake at an early period in-hospital seems a mirror of post-hospital ADL. In other words, an availability of oral route seems an indicator of post-hospital daily life in older female inpatients. In these contexts, we would emphasize that an oral energy intake could be helpful surrogate of post-hospital physically functional dependence.

8.2. The Cutoff Value of DEI During an Early In-Hospital to Maintain Post-Hospital ADL

From the result of ROC curve analysis, 24.4 kcal/kg/ day was drawn as the cutoff value of DEI during the first three days after admission. To avoid cumbersome in daily clinical settings, 25 rather than 24.4 kcal/ kg at admission seems feasible because of its simplicity. DEI equal to resting energy expenditure must vary with age, body size, body composition, mainly fat-free mass (FFM), and also metabolic stress [11]. When nutritional management is planned to prevent adverse events even after discharge, a provision over the cutoff value of DEI could enhance post-hospital ADL unless they have hypercytokinemia and immune-mediated injury with excess catabolism [12]. However, it also must be considered that this value is limited in the older female adult patient. In other words, when this value is providing the baseline energy amount at an early period of hospitalization, it seems reasonable to calculate additional energy amount depending FFM and metabolic stress. Given the nature of the subjects of this study, this lowest DEI amount must not extend to male, and younger adults aged < 75 years. Regardless of these, to our knowledge, this cutoff value seems to be the first report to secure post-hospital ADL in female older inpatients.

8.3. Which Cutoff Value for Older Female Inpatients Is Feasible Predictor, 25 Or 30 Kcal /Kg?

In ESPEN guideline for geriatric population, 30 kcal/kg as DEI has been recommended [13]. However, as ESPEN guideline defined the old population aged at ≥ 65 years, whereas the average age was older by 15 years in this study. In addition, because there must exist a great heterogeneity and large individual variation of energy requirement, additional age might lower energy requirement. Moreover, ESPEN guideline does not describe gender effects on energy requirement. In our study, the subjects were limited in female gender because of their longer non-healthy life expectancy as described earlier. Female older adults have been reported to have less FFM, which must affect energy expenditure more than fat composition dose, as a study has shown gender differences in energy expenditure and energy requirement [14]. From these aspects of gender and FFM differences, DEI might lower than ESPEN guideline states. However, a daily energy intake set at 25 kcal/kg might be tested prospectively not only in female but in male, and aged ≥ 75 vs. < 75 years in the further analyses.

9. Limitations

Several limitations of this study must exist. Frist, a small sample size, a single institution, and retrospective study fashion must prevent our conclusion from generalization. To draw conclusive findings, a larger sample size in prospective study must be necessary. In addition, male older adult study must be required. Second, although our result showed that ADL was stratified by living places by the official judgement which was decided based on requirements of medical and/or nursing care, and requirements of long or short rehabilitation programs. This novel methodology to measure physical activity level (ADL) must be validated. Third, although oral intake was focused to consider chewing and swallowing functions, their objective oropharyngeal function was not measured. In reported studies, as oropharyngeal dysphagia has been observed in one- third of patients discharged not to home, but to nursing home [15]. From these observations, although oropharyngeal function seems a strong influential factor on ADL functions, this must be collected to analyze in the further studies to clarify the objective importance of oral route. Fourth, to draw DEI (kcal/ kg) in the present study, a well- allocated study in different EDI set at 25, 30, and the others between them will make solid evidence. Fifth, there has been reported an association between dementia and post-hospital physical status in hospitalized old patients [16]. In our study, cognitive impairment was not included in measured parameters. A co-existence of dementia is predictor of adverse hospitalization outcomes and delayed discharge from hospital [17, 18]. Furthermore, delirium, in the older adult patients has been reported as a high risk factor of poor outcome [19], a cognitive and delirium must also be included to draw more comprehensive conclusion in the further studies. Lastly, as the frailty due to malnutrition has

been reported to have poor discharge outcomes [20-22], we made hypothesis that an early energy management is associated with discharge status. To confirm that a frailty diagnosed at admission is association with poor discharge outcome, an identification of frailty also must be added to analytical parameters in the further studies.

10. Conclusions

Among female inpatients aged ≥ 75 years, daily energy intake ≥ 25 kcal/kg orally taken during the first three days of hospitalization was associated with maintaining post-hospital ADL, and vice versa.

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