表1　対象者の背景ならびに死亡場所ごとの相違

	全体	入院死	自宅死	p^*
	n＝1,875	n＝347	n＝107	
要介護者因子				
女性，n（%）	1,243（66.3）	185（53.3）	71（66.4）	0.017
年齢，mean（SD）**	80.6（7.7）	82.2（7.8）	86.4（7.9）	＜0.001
bADL，mean（SD）**	12.8（6.6）	10.0（7.1）	8.4（7.1）	0.053
要介護度				
要支援＋要介護1，n（SD）	719（38.3）	87（25.1）	16（15.0）	
要介護2＋3，n（SD）	655（34.9）	110（31.7）	38（35.5）	0.091
要介護4＋5，n（SD）	501（26.7）	150（43.2）	53（49.5）	
Charlson Comorbidity Index，mean（SD）**	2.0（1.6）	2.5（1.7）	2.3（1.5）	0.497
定期的な受診（%）	59.5	65.7	74.8	0.079
訪問看護サービスの使用（%）	50.8	70.1	66.9	0.532
デイサービスの使用（%）	43.8	34.6	38.6	0.451
訪問介護サービスの使用（%）	46.9	46.7	43.5	0.559
ショートステイの使用（%）	9.3	10.1	13.1	0.382
慢性期疾患（%）				
冠動脈疾患	10.7	10.0	13.2	0.388
うっ血性心不全	8.5	11.3	15.4	0.294
脳血管障害	34.3	36.8	46.2	0.107
糖尿病	12.0	16.1	4.4	0.004
認知症	35.3	42.7	55.7	0.032
高血圧	24.3	18.7	20.6	0.674
悪性腫瘍	9.1	18.7	6.6	0.006
主介護者因子				
主介護者有り（%）	1,568（83.6）	316（91.1）	96（89.7）	0.674
主介護者年齢，mean±SD	64.0（12.5）	66.3（12.1）	64.2（11.3）	0.128
主介護者性（女性，n（%））	1,180（75.2）	250（79.1）	78（81.3）	0.649
主介護者・配偶者，n（%）	633（40.4）	147（46.5）	25（26.0）	＜0.001
介護負担（Zarit，mean±SD）	28.9（17.0）	30.9（16.1）	29.4（16.7）	0.460

*，入院死と在宅死との比較
**，student t-test．それ以外はカイ2乗検定
bADL：basic ADL：range，0～20，Charlson comorbidity index：range，0～9．
Zarit：the Zarit Burden Interview．：range，0～88．

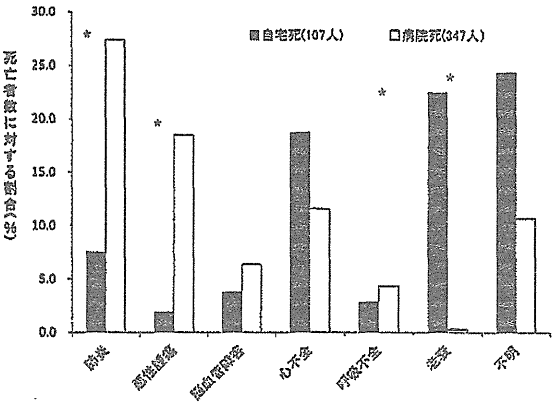

図　自宅死，病院死の死因別の割合
*p＜0.001．それ以外は両群に有意差なし

対象のセレクションバイアスの結果である可能性がある．

厚生労働省が発表した平成23年の人口動態統計によると，65歳以上の死亡原因の順位として，「悪性新生物」，「心疾患」，「肺炎」，「脳血管疾患」，「不慮の事故」の順となっている．それに次いで「老衰」が挙げられており，その割合は4.2%である[7]．

本研究では，自宅死において「老衰」の占める割合が22.4%，「心不全」が18.7%と多かった．また死因別では「老衰」，「心不全」の対病院死に対する自宅死の割合はそれぞれ96%と33%で他の死因に比べて自宅死の割合が高かった．この理由としては，自宅死の場合，直接死因の断定が困難なこと，また病院と異なり，種々の検査を施行することが困難なことが考えられ，正確な死因が不明となり，結果として老衰，心不全が死因の上位となっ

表2　病院死と比較した自宅死との関連因子（Cox 比例ハザード分析）

	univariate				multivariate model 1				multivariate model 2			
	HR	95%CI		p	HR	95%CI		p	HR	95%CI		p
要介護者因子												
女性（vs 男性）	1.73	1.10	2.72	0.018	1.17	0.58	2.36	0.668	0.99	0.47	2.06	0.969
年齢（continuous）	1.07	1.04	1.10	<0.001	1.06	1.02	1.11	0.004	1.06	1.02	1.11	0.007
bADL score（continuous）	0.97	0.94	1.00	0.054								
要介護度（vs 要支援＋要介護1，n＝103）												
要介護2＋3，n＝148	1.88	0.98	3.59	0.057	1.96	0.83	4.63	0.124	1.58	0.64	3.87	0.319
要介護4＋5，n＝203	1.92	1.04	3.57	0.038	1.64	0.70	3.84	0.253	1.51	0.62	3.68	0.360
Charlson comorbidity index（continuous）	0.95	0.83	1.10	0.496								
定期的な診察（n＝308 vs 無，n＝146）	1.55	0.95	2.52	0.081								
慢性疾患の有無												
冠動脈疾患	1.37	0.67	2.79	0.389								
うっ血性心不全	1.43	0.73	2.79	0.296								
脳血管障害	1.47	0.92	2.36	0.108								
糖尿病	0.24	0.08	0.68	0.007	0.26	0.08	0.87	0.029	0.24	0.07	0.86	0.028
認知症	1.68	1.04	2.72	0.033	1.54	0.87	2.72	0.139	1.63	0.90	2.93	0.106
閉塞性肺疾患	0.84	0.37	1.89	0.669								
悪性腫瘍	0.31	0.13	0.74	0.008	0.29	0.10	0.85	0.024				
主介護者因子												
主介護者有り，n＝412（vs 無，n＝42）	0.86	0.41	1.77	0.675								
女性，n＝328（vs 男性，n＝84）	1.14	0.64	2.04	0.649								
配偶者，n＝172（vs 非配偶者，n＝240）	0.40	0.24	0.67	<0.001	0.91	0.40	2.10	0.830	0.93	0.39	2.23	0.877
年齢（continuous）	0.99	0.97	1.00	0.141								
ZBI score（n＝341，(continuous)）	0.99	0.98	1.01	0.459								
訪問看護サービスの使用（vs 未使用）	1.16	0.73	1.86	0.532								
デイケア（サービス）の使用（vs 未使用）	0.84	0.53	1.32	0.451								
訪問介護サービスの使用（vs 未使用）	1.14	0.74	1.76	0.559								
ショートステイ使用（vs 未使用）	1.34	0.69	2.60	0.384								
主な死亡原因												
肺炎	0.21	0.10	0.46	<0.001					0.13	0.05	0.34	<0.001
心不全	1.76	0.98	3.17	0.058								
脳卒中	0.57	0.19	1.70	0.317								
悪性腫瘍	0.08	0.02	0.35	0.001					0.06	0.01	0.42	0.005
老衰	100.05	13.34	750.19	<0.001								

HR：hazard ratio，95%CI：95% confidence interval
要介護者疾患の「悪性腫瘍」は死因に悪性腫瘍があるため，多変量解析には投入せず．
死因「老衰」は入院死因が一人であるため，多変量には投入しなかった．
ZBI score：the Zarit Burden Interview score

てしまうのではないかと思われる．

本研究で自宅での死亡と多変量解析で有意な関連にあった項目は，要介護者要因としては年齢と併存症として糖尿病，悪性腫瘍（負の関係）のみで，介護者，使用サービス要因としては有意なものは存在しなかった．さらに死因としては肺炎，悪性腫瘍は自宅での死亡とは負の関連にあった．今までの報告では認知症のある高齢者の死亡場所については，50% から 92% がナーシングホームで死亡し，3% から 46% が病院で死亡しているとの報告がある[8]．また，Motiwala らの報告[9]によると，カナダのオンタリオ州における高齢者の 49.2% が病院で死亡し，30.5% が療養型施設，9.6% が自宅ケアを受けての自宅死，10.7% が自宅ケアを受けないでの自宅死となっている．この死亡する場所に最も大きく影響を与えているのは併存症であり，悪性腫瘍の診断は自宅ケアを受けての自宅死を増やし，認知症の存在は療養型施設での死亡となることが多いとされている．また，認知症と悪性腫瘍の存在は，それぞれ病院死とは負の相関を示すとの報告もある[10]．今回の我々のコホートでは悪性腫瘍は今までの報告[11][12]と異なり，病院死が多かった．平

成23年（2011）人口動態統計（確定数）の概況によると，悪性腫瘍で死亡したもののうち，病院死は87.8%，自宅死は8.2%となっており，今回の報告とほぼ同じ傾向となっている．日本での病院での悪性腫瘍の看取りが多い理由の一つは，まだ在宅での緩和ケアサービスが十分行き届いていないことにも原因がある可能性がある．現に日本においても，また諸外国においても在宅緩和ケアサービスの導入により，悪性腫瘍患者の在宅での看取りが増えることが報告されている[14][15]．また肺炎による死亡も自宅では少なかった．基本的には自宅療養中の高齢者が誤嚥性肺炎を起こしても，多くの場合が病院に搬送されていることがうかがわれる．認知症の存在は自宅での死亡との関連は単変量では認められるものの，多変量ではその関連は消失している．

今回の調査では糖尿病の存在は自宅死と強い負の関連を示していた．糖尿病の存在そのものが病院死と関連あるかは不明だが，糖尿病の合併症が入院の危険度を高め，死亡の危険度を増加させるとの報告もある[16]．つまり糖尿病を基盤とした動脈硬化性疾患が入院と関連し，ひいては病院死と強い関連が認められたのかもしれない．

今まで自宅死を規定する因子を検索する報告が国内外多数存在しているが，そのほとんどが悪性腫瘍の患者である．悪性腫瘍患者での自宅死に関連する因子に関するシステミック・レビューでは身体機能が低下している，自宅での死亡を希望している，在宅医療の導入，身内と同居している，長期間の家族からの介護が受けられる，などの因子が報告されている[17]．今回の調査では登録から死亡までの期間において，在宅死と病院死との間に差を認めなかった．しかし，この期間は介護が始まってからの期間ではなく，本調査の登録からの期間であるため，この結果から在宅死と病院死での看取りでの介護期間によるものかどうかの結論づけることはできない．

今回登録時の種々の看護保険サービスの使用は自宅での死亡との関係は見いだされなかった．一つは今回の解析に使用したのは登録時のサービス使用であり，臨死期にはサービス利用が変化していた可能性がある．今まで数は少ないものの，地域での終末期における在宅サービス導入が死亡場所に与える影響があるかどうかの検討がなされ，結論的にはサービス使用介入により自宅での死亡が増加するわけではないことが報告されている[18]．実際，日本では介護保険サービスが2000年より開始されたが，日本における自宅での死亡率はその後増加したわけではなく，平成22年度の報告では自宅での死亡は全死亡の12.6%と報告されている[6]．

介護者の介護負担は少なくとも日本の調査でもがん患者に限った調査ではあるが，自宅での死亡が困難な要因になっている[19]が，今回は介護負担は死亡場所との有意な関連は認められなかった．しかし，これまた介護負担感はあくまでも登録時の評価であり，終末期とは異なる可能性が高い．

今回の調査研究には多くの限界が存在している．今回の前向き調査では施設入所の時点で，フォローアップを終了するプロトコールであったため，実際には施設入所後に死亡する高齢者を把握できていない．また，死因の情報は訪問看護師または介護支援専門員（全員看護職）を経由しており，実際の死亡診断書の死因とは異なる可能性がある．また，前述したとおり，特に介護保険サービスの内容，介護負担感をはじめとする主介護者情報などは登録時のものであり，この3年間の観察期間中に変更があった可能性があり，これの考慮が今回の解析ではなされていない．また先行研究でも報告されているように看取りの場所を決定する因子として大きく関連することが報告されている[6][20]，本人または家族の意思などの項目が欠如している．定期受診の有無も自宅死との関連が認められなかったが，これまで訪問診療の有無と死亡場所について検討した報告は見られていない．定期受診には訪問診療と外来通院の2群が考えられ，それには要介護高齢者のADL（通院できるかできないか）が影響していると考えられ，今後さらなる検討が必要である．また，今回在宅医療，特に訪問診療の導入と看取り場所の解析が欠如している．在宅での看取り要件として，在宅療養の不安解消，さらには信頼できる在宅診療医の存在が大きな要件になっている[3]．従って，今回はデータ欠如により解析ができなかったが，訪問診療の利用，特に24時間対応が必要とされる在宅支援診療所の使用と自宅での看取りとは関連があることが想像される[21]．

今回の3年間の自宅療養中の要介護高齢者の診取りを決定する因子としては，限られた調査項目の中では，要介護者の年齢，あとは併存疾患ならびにその死因のみが関連項目として抽出された．今回の調査で把握できていない，本人や家人の意思表示，希望，死亡前の訪問診療，訪問看護サービスの使用などの項目を追加した，さらなる調査が必要と思われる．

本論文に関して，開示すべき利益相反は存在しない．

なお本研究の一部は三井住友海上財団より研究助成（平成18～20年）を受けて実施した．

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Place and cause of death in community-dwelling disabled elderly people

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Abstract

Aim: To examine the place and cause of death in community-dwelling disabled elderly people.

Methods: The baseline data of 1,875 participants and their caregivers in the Nagoya Longitudinal Study for Frail Elderly were used for the analysis. Cox proportional hazard models were used to assess the associations between the variables and the place of death during the 3-year follow-up period.

Results: During the observation period of three years, 454 died (hospital death: 347, home death: 107). In total, the rates of pneumonia-, cancer- and heart failure-related death were 22.7%, 14.5%, and 13.2%, respectively. Among the home deaths, 22.4% were age-related deaths and 18.7% were heart failure-related deaths. Females, older, and participants with dementia were more likely to die at home, while those with cancer or a spouse caregiver were more likely to die in the hospital. There were no differences in the levels of caregiver burden or formal service use between the cases of home and hospital death. Multivariate Cox hazard models revealed that home death was associated with an older age and the absence of diabetes mellitus and cancer at baseline.

Conclusions: We demonstrated that death at home among community-dwelling disabled elderly is associated with an older age, and the absence of diabetes mellitus and cancer. Due to the lack of important factors that should be addressed, a further study is required in the future.

Key words: *Home death, Hospital death, Cause of death, Home-dwelling elderly*

(Nippon Ronen Igakkai Zasshi 2013; 50: 797–803)

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Clinical Nutrition 29 (2010) 47–53

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original Article

The impact of malnutrition and nutrition-related factors on the development and severity of pressure ulcers in older patients receiving home care☆

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ARTICLE INFO

Article history:
Received 27 November 2008
Accepted 31 May 2009

Keywords:
Family caregiver
Home care
Malnutrition
Medical staff
Pressure ulcer

SUMMARY

Background & aims: To investigate the impact of nutritional status and nutrition-related factors on the development and severity of pressure ulcers acquired in the home care setting.

Methods: Two hundred and seven home care offices in Japan were selected at random and 290 patients with home-acquired pressure ulcers and 456 patients without pressure ulcers were analyzed. Data on nutritional status, caregiver knowledge, and health professional's nutritional management were collected. Pressure ulcers were categorized as superficial or full-thickness.

Results: Malnutrition was significantly and most strongly associated with higher rate of the pressure ulcer after adjusting for other risk factors (OR, 2.29; 95% CI, 1.53–3.44). Assessment of the patient's nutritional status and adequate dietary intake by a health professional were significantly associated with lower odds for developing pressure ulcers (OR, 0.43, 0.47; 95% CI, 0.27–0.68, 0.28–0.79, respectively). Malnutrition was also significantly and most strongly associated with more severe pressure ulcers (OR, 1.88; 95% CI, 1.03–3.45). Assessment of a caregiver's nutritional knowledge by a health professional was a significant preventive factor for severe pressure ulcers.

Conclusion: The quality of home care for risk factors such as pressure redistribution has improved, making nutritional management a more crucial factor in pressure ulcer prevention.

1. Introduction

Pressure ulcers (PUs) are common in frail or bed-ridden older people and are associated with increased mortality and decreased quality of life.[1–3] Recently, the home-acquired PU is becoming one of the serious problems as the number of older patients receiving home care was increasing. The prevalence of home-acquired PUs was estimated to be 9.1% and was associated with higher mortality.[4,5]

Malnutrition is one of the well-known factors for PU development in hospitals and nursing homes.[6–8] In the home care setting, however, there have been few studies on the relationships between malnutrition and the PU development although the prevalence of malnutrition was as high as approximately 50%.[9] Previously, one study on home-acquired PU prevalence did not investigate the nutritional status.[4] Another study reported that there was no significant association between nutritional risk using the subcategory of the risk assessment tool and PU development in the home care setting.[10] However, this study did not examine the influence of nutritional status in relation to other preventive cares for PU. In more recent years, it is possible that the quality of nutritional management remains as issue of PU management because the quality of other general PU prevention such as the use of pressure redistribution mattresses is improving. Therefore, malnutrition may have greater relative influence on the development of home-acquired PUs under this conditions.

Furthermore, it was reported that 27.0–48.8% of home-acquired PUs were full-thickness PUs,[4,11] which is greater than the proportion in hospitals where the approximate prevalence is 10%.[1,12] Full-thickness PUs tend to be accompanied by undermining or infection, they do not heal easily and require extended care once they occur. While the majority of patients with full-thickness PUs were malnourished even in the hospital,[13] the association between malnutrition and the development of severe PUs remains uncertain in the home care setting.

Abbreviation: PU, Pressure ulcer.

☆ Conference presentation: None.

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doi:10.1016/j.clnu.2009.05.018

In addition, one of the reasons for the higher prevalence and severity of PU and malnutrition in the home care setting is insufficient preventive nutritional care.[11] For example, the nutritional guidelines for PU care were used less frequently in the home care setting than in hospitals or nursing homes.[14] This could be attributed to a limited continuity of care by health professionals and a lack of knowledge on the part of the family caregivers in the home care settings. Therefore, in order to promote effective nutritional managements which was proved to reduce the risk of PU development in hospitals or nursing homes,[15] it is necessary to investigate the association of caregiver's and health professional's roles in nutritional management with the development and severity of PUs in the home care settings.

The aims of this study were 1) to describe the characteristics of nutritional status and nutrition-related factors related to PU prevention and 2) to investigate the impact of these factors on the incidence of PUs by their severity after adjustment for other risk factors in the home care setting.

2. Methods

2.1. Participants

This case-control study was conducted in the home care setting in January 2008. All 2688 home care offices registered to the Home Care Nursing Associations in Japan were stratified according to prefecture, and 20% of the offices were selected ($n = 537$) using a random number table. After questionnaires were mailed to the selected offices, each office identified all patients with home-acquired PUs (PU group) as well as one or two control patients without PUs (non-PU group) who were similar to the patients with PUs in terms of age and sex. Because there were a limited number of patients in any particular office, strict matching, such as complete agreement of care level, was not possible within each office. Inclusion criteria were 1) age of 65 years or older, and 2) no history of PU in the non-PU group, or a history of at least one home-acquired PU in the PU group. Patients were excluded if their age, sex, or care level were unknown. Patients in the PU group with unknown PU status (incidence location, depth, or other status) or without documentation about their situation before PU development were also excluded. The study protocol was approved by the Institutional Review Board of Kanazawa University.

2.2. Questionnaire

The questionnaire was developed by conducting a semi-structured interview of 10 health professionals who had engaged in home care for patients with PU. Five nurses, two physicians, and three caseworkers were selected. Twenty-one key factors for PU incidence were obtained and divided into four categories: patient factors (11 factors), caregiver factors (5 factors), health professional's home care process (5 factors), and PU management (13 factors). A draft questionnaire was prepared based on both this interview and the literature review. After face and content validity were confirmed by a multidisciplinary research team and a pre-test was conducted, the questionnaire was finalized. The primary nurses for each patient answered or asked caregivers to answer items on the questionnaire. These items included demographic characteristics, general risk factors, and nutrition-related factors for the development and prevention of PUs. The primary nurses also reported PU status and location. For the PU group, the statuses of variables were determined for the period preceding the development of PUs, whereas patients in the non-PU groups were asked to respond regarding the preceding one month.

2.3. Demographic characteristics

Primary nurses were asked about the patient's age, sex, independence level, comorbidities, family, and caregiver's age. Independence level was evaluated according to the certified care level in Japan: not certified, support level 1–2, and care level 1–5. Care levels 1–5 were divided into two groups: care level 1 or 2 (patients have difficulty in moving independently) and care level 3–5 (patients are almost bed-ridden and require continuous care). Family type was categorized as living alone or not. Caregiver's age was categorized as "65 years of age or older" or "younger than 65 years".

2.4. Risk factors for PU development

To determine risk factors for PU development, nurses were asked about the patient's mobility in a bed and chair and the presence of extreme bony prominence, joint contracture, edema, excess moisture on skin, and urinary and fecal incontinence, which are listed in the Japanese PU care plan by the Ministry of Health, Labor, and Welfare.

To evaluate variables about PU prevention, questions regarding the caregiver's knowledge about the frequency of position changes and the use of a pressure-redistributing mattress were asked. In addition, nurses were asked whether they had conducted risk assessments for each risk factor. The type of mattress used was also determined and the variable about the use of an air-cell mattress was used for analysis.

2.5. Nutritional status and nutrition-related factors

Primary nurses in each office reported on patient nutritional status. Malnutrition was determined by the presence of at least one of the followings based on the previous studies in hospitals or nursing homes: body mass index of 18.5 or lower, serum albumin of 3.0 g/dl or less, or hemoglobin of 11.0 g/dl or less.[16,17] The cut-off points were lowered to reduce the false-positive rate for thin Japanese older people. Because the above objective nutritional assessments were not required by the Japanese long-term care insurance in the home care setting, following statuses were also assessed subjectively to evaluate malnutrition in addition: weight loss, edema, or inadequate energy intake. Due to these current institutional limitations in the home care setting, we assumed that it was difficult to collect the full set of nutritional data in this study. Therefore, malnutrition was evaluated comprehensively based on the above signs by each nurse rather than using the single specific indicator.

In addition, primary nurses reported on caregivers' knowledge about nutritional management for PU prevention and the subjective and objective degree of dietary intake on an average day.

Nutritional management by health professionals, consisting of nutritional assessment and nutritional intervention, was also evaluated by the questionnaire. Regarding nutritional intervention, primary nurses reported whether the patients received nutrients by any route. Nutritional route was categorized as oral, enteral, or parenteral. The absence of nutritional intervention was if the patient received neither regular food intake nor nutrients by any route. For nutritional assessment, primary nurses were asked whether they conducted risk assessments for patient's nutritional status, caregiver's knowledge of nutritional preventive strategies, the degree of dietary intake, and whether they had consulted with a registered dietician.

2.6. Outcome measures

Data regarding PU status, including depth, sites, and the number of home-acquired PUs, were collected from the medical charts in each office. The primary outcome measure was whether the patient had a home-acquired PU; the secondary outcome was the depth of the PU, which was assessed by each primary nurse. PU depth was evaluated by DESIGN,[18] and categorized as "d" for superficial ulcers or "D" for full-thickness ulcers. If patients had multiple PUs, the most severe one was included in the analysis.

2.7. Statistical analysis

Data are reported as means (standard deviation, SD) for continuous variables or numbers (percent) for categorical variables. Univariate analyses were conducted using t-test or chi-squared test.

First, multivariate logistic regression analysis was conducted in order to determine whether malnutrition was an independent risk factor for PU development. The model was adjusted for demographic characteristics and other risk factors that were associated with PU development in univariate analysis.

Second, univariate analysis was conducted to determine the more detailed nutrition-related factors for PU development. Associations between each independent variable were checked by chi-squared test. If the variables were highly associated with each other, only one of the variables was included in the multivariate model. Then, factors associated with PU development at $p < 0.2$ in univariate analysis were included in the multivariate logistic regression analysis using the stepwise method. Entry and stay significance levels were set at $p = 0.15$. The final model was adjusted for demographic characteristics (Model 1) and for both demographic characteristics and risk factors other than nutrition that had a significant association with PU development in univariate analysis (Model 2). Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated. The goodness-of-fit of the model was evaluated by the Hosmer–Lemeshow test. If p-values for this test were not significant, the model was considered a good fit.

Because primary nurses could answer questions about patient characteristics (questions for patients or caregivers) only when they had conducted a risk assessment (questions for nutritional management by health professionals), the above analyses were conducted separately for the patient and caregiver model and for the nutritional management model. In addition, the latter model was adjusted only for patient demographic characteristics (Model 1) to avoid multicolinearity because variables related to PU management including the assessment of a caregiver's knowledge about position changes and mattress use were highly associated with nutritional management by a health professional.

The same analytical process was conducted for the PU group alone in order to investigate variable associations with PU severity. The dependent variable was PU severity dichotomized as superficial ulcers or full-thickness ones. The statistical significance level was set at 0.05. All analyses were conducted using Statistical Analysis System version 9.1 (SAS Institute, Inc., Cary, NC).

3. Results

3.1. Patient characteristics

Two hundred and seven offices participated in this study (38.5% of 537 offices). This number corresponded to 7.8% of all 2688 registered offices in Japan. Fig. 1 shows the flowchart of participant selection. Of 1069 enrolled patients who met inclusion criteria, 255 patients with PU and 68 patients without PU were excluded. The most frequent reason for exclusion in the PU group was that PUs had developed in the non-home care setting. Finally, 290 patients with PUs and 456 patients without PUs were eligible. The mean age of all participants was 82.7 years (SD, 8.9). The PU group tended to be older and more functionally impaired than the non-PU group (Table 1; $p = 0.084$ and 0.078, respectively). In addition, the PU group had less cerebrovascular disease ($p = 0.001$) and diabetes ($p = 0.044$) than the non-PU group. More than half of family caregivers in both groups were 65 years of age or older. Almost half of the patients in both groups used an air-cell mattress for PU prevention (46.8% for PU group and 44.9% for non-PU group, $p = 0.666$).

3.2. Pressure ulcer status

Table 2 displays the information regarding PU status. One hundred fifty-seven patients (54.1%) had superficial PUs and the remainder (45.9%) had a full-thickness PUs. The most frequent site of PU development was the sacrum (46.6%), followed by the trochanter and the heel. One hundred ninety-four patients (66.9%) had only one ulcer and the remainder (33.1%) had multiple home-acquired PUs.

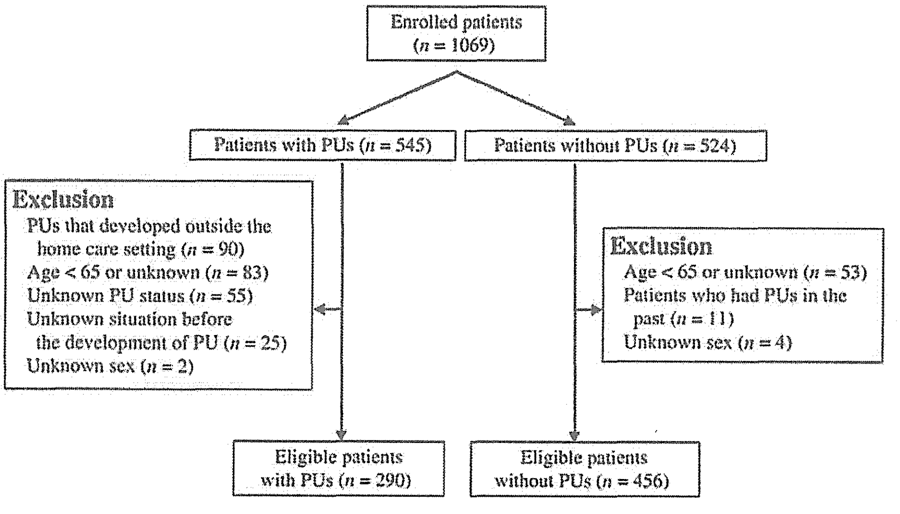

Fig. 1. Flowchart of participant selection.

Table 1
Demographic characteristics of study participants.

		With PU (n = 290)	Without PU (n = 456)	p-value
Mean age in years (SD)		83.4 (9.0)	82.2 (8.8)	0.084
Sex, n (%)	Male	115 (39.7)	188 (41.2)	0.670
	Female	175 (60.3)	268 (58.8)	
Care-need certification, n (%)[a]	Not certified	7 (2.2)	10 (2.2)	0.078
	Support level	8 (2.5)	22 (4.8)	
	Care level 1-2	18 (6.2)	49 (10.8)	
	Care level 3-5	256 (88.6)	374 (82.2)	
Cerebrovascular disease, n (%)		99 (34.1)	214 (46.9)	0.001
Cancer, n (%)		25 (8.6)	36 (7.9)	0.723
Infectious disease, n (%)		12 (4.1)	24 (5.3)	0.486
Dementia, n (%)		92 (31.7)	127 (27.9)	0.258
Diabetes, n (%)		35 (12.1)	80 (17.5)	0.044
Living alone, n (%)[a]		7 (2.8)	14 (3.1)	0.822
Older family caregiver, n (%)[a]		146 (58.2)	252 (56.5)	0.659
Using air-cell mattress, n (%)		101 (46.8)	168 (44.9)	0.666

PU, pressure ulcer.
[a] Two data were missing for care-need certification. Forty-two data were missing for living alone, and 51 were missing for family caregiver's age.

3.3. The association of nutritional status and related factors with PU development

Table 3 displays data regarding nutritional status and nutrition-related factors for PU development. There were significantly more malnourished patients in the PU group than in the non-PU group (58.7% vs. 32.6%, $p < 0.001$). Family caregivers in the PU group had significantly less knowledge about nutritional prevention for PU than in non-PU group (23.3% vs. 41.7%, $p < 0.001$). Patients in the PU group tended to have lower energy intake ($p = 0.055$) and fewer patients in PU group received an adequate diet than in the non-PU group ($p < 0.001$).

Twenty-one patients in the PU group and seven patients in the non-PU group had not received nutritional intervention; this difference was significant ($p < 0.001$). The majority of patients received oral or enteral nutrition (99.2% in the PU group vs. 99.3% in the non-PU group). For PU group, significantly fewer nurses had conducted assessments of the patients' nutritional status and adequacy of dietary intake ($p < 0.001$ for both) and even fewer nurses had tended to assess the caregiver's nutritional knowledge ($p = 0.088$).

Table 2
Pressure ulcer status.

		n (%)
Depth, n (%)	Superficial ulcer	157 (54.1)
	Full-thickness ulcer	133 (45.9)
Site, n (%)	Sacrum	135 (46.6)
	Greater trochanter	32 (11.0)
	Heel	28 (9.7)
	Coccyx	20 (6.9)
	Iliac crest	12 (4.1)
	Ischial tuberosity	9 (3.1)
	Others	54 (18.6)
Number of home-acquired PUs, n (%)	1	194 (66.9)
	2	58 (20.0)
	3	21 (7.2)
	4	17 (5.9)

PU, pressure ulcer.

Table 3
Nutritional risk factors for pressure ulcer development.

	With PU (N = 290)		Without PU (N = 456)		p-value
	n	Value	n	Value	
Patient status[a]					
Malnutrition, n (%)	223	131 (58.7)	411	134 (32.6)	<0.001
Patient and caregiver factors[a]					
Caregiver knowledge about nutrition, n (%)	219	51 (23.3)	369	153 (41.7)	<0.001
Mean energy intake in kcal (SD)	108	1031 (326.3)	194	1105 (316.6)	0.055
Adequate diet three times a day, n (%)	238	168 (70.6)	422	372 (88.2)	<0.001
Nutritional management[b]					
Nutritional intervention, n (%)					
None	279	21 (7.5)	454	6 (1.3)	<0.001
By any route		258 (92.5)		448 (98.7)	
(Oral)	258	199 (77.1)	448	344 (76.8)	
(Enteral)		57 (22.1)		101 (22.5)	
(Parenteral)		2 (0.8)		3 (0.7)	
Nutritional assessment, n (%)					
Patient's nutritional status	290	223 (76.9)	453	411 (90.7)	<0.001
Caregiver's knowledge	289	219 (75.8)	453	367 (81.0)	0.088
Energy intake	289	108 (37.4)	452	194 (42.9)	0.134
Adequate diet three times per day	288	238 (82.6)	454	422 (93.0)	<0.001
Consultation with dietitian, n (%)	287	5 (1.7)	455	10 (2.2)	0.668

PU, pressure ulcer.
[a] Whether do patients or caregivers have following statuses?
[b] Whether do the health professionals conduct following nutritional interventions and assessments?

3.4. Multivariate analysis of nutritional status and related factors with PU development

Table 4 shows the results of multivariate analysis of risk factors for PU development. Malnutrition was significantly associated with PU development and showed the highest odds ratio after adjusting for other risk factors (OR, 2.29; 95% CI, 1.53–3.44).

Then, the more detailed nutritional factors were investigated. Table 5 shows the results of multivariate analysis of nutrition-related factors associated with PU development using the stepwise method. Of factors other than nutrition, immobility in bed, immobility in a chair, extreme bony prominence, joint contracture, excess moisture on skin, edema, and caregiver's knowledge about mattress use were significantly associated with PU development by univariate analysis. These variables were adjusted for in Model 2. Caregiver's knowledge and adequate dietary intake were

Table 4
Multivariate analysis of risk factors for pressure ulcer development.

Variables	Reference	Category	Odds ratio	95% CI
Malnutrition	Absence	Presence	2.29	1.53–3.44
Age	–	–	0.99	0.97–1.02
Sex	Male	Female	0.95	0.63–1.44
Care-need certification	Care level 3-5	Not certified	0.76	0.18–3.10
		Support level	1.31	0.44–3.89
		Care level 1-2	1.30	0.60–2.80
Cerebrovascular disease	Absence	Presence	0.54	0.36–0.80
Diabetes	Absence	Presence	1.20	0.70–2.05
Immobility on bed	Absence	Presence	1.91	1.14–3.22
Immobility on chair	Absence	Presence	1.18	0.76–1.83
Extreme bony prominence	Absence	Presence	1.43	0.95–2.16
Joint contracture	Absence	Presence	1.18	0.72–1.93
Excess moisture on skin	Absence	Presence	1.66	1.08–2.53
Edema	Absence	Presence	1.28	0.86–1.91

Hosmer–Lemeshow test: $p = 0.93$.
CI, confidence interval.

Table 5
Stepwise multivariate analysis of nutrition-related factors for pressure ulcer development.

	Model 1		Model 2	
	Odds ratio	95% CI	Odds ratio	95% CI
Patient's and caregivers factors				
Caregivers knowledge about nutrition	0.45	0.30–0.67	0.74	0.47–1.18
Adequate diet three times a day	0.41	0.26–0.66	0.53	0.31–0.90
Nutritional assessment				
Patient's nutritional status	0.43	0.27–0.68	–	–
Adequate diet three times a day	0.47	0.28–0.79	–	–

Hosmer–Lemeshow test: $p = 0.69$ for Model 1, and $p = 0.17$ for Model 2 in patient and caregiver factors model, and $p = 0.73$ for Model 1 in nutritional assessment factors model.
Model 1 was adjusted for age, sex, care level, cerebrovascular disease, and diabetes. Model 2 was additionally adjusted for immobility on bed, immobility on chair, extreme bony prominence, joint contracture, excess moisture on skin, edema, and caregiver knowledge about mattress.
CI, confidence interval.

significantly associated with lower odds in Model 1, but only the latter was significant in Model 2 after adjusting for other risk factors (OR, 0.53; 95% CI, 0.31–0.90).

For nutritional management, assessment of the patient's nutritional status and adequate dietary intake were significantly associated with lower odds for PU development (OR, 0.43, 0.47; 95% CI, 0.27–0.68, 0.28–0.79, respectively).

3.5. *Association between nutritional status and related factors with PU severity*

Next, we examined the influence of malnutrition and nutrition-related factors on PU severity. Table 6 shows the results of univariate analysis. Patients with full-thickness PUs were more likely to be malnourished; this association was also significant and the strongest in the multivariate model (OR, 1.88; 95% CI, 1.03–3.45; Table 7)

Nutrition-related patient and caregiver factors were not significantly different between the two groups. On the other hand, nutritional intervention and assessment of the patient's nutritional status, caregiver's knowledge and adequate dietary intake were significantly associated with PU severity in the univariate analysis. In the multivariate analysis, only assessment of caregiver's knowledge about nutrition was associated with lower odds of having a full-thickness PU (OR, 0.48; 95% CI, 0.27–0.83). Other variables regarding nutritional management were not included in the stepwise model.

4. Discussion

To the best of our knowledge, this is the first study to reveal the impact of patient's nutritional status on the development and severity of home-acquired PUs in older patients receiving home care. In addition, this study evaluated detailed nutrition-related factors of caregivers and health professionals for PU prevention, which may provide practical information in daily home care practice for PU and nutritional management.

Surprisingly, malnutrition had the highest odds ratio of all PU risk factors even after adjusting for other well-known risk factors. It was reported that malnutrition was a risk factor for PU in hospitals and nursing homes[7,8]; our results revealed that this can be true even in the home care setting. Contrary to our results, Bergquist previously reported that nutritional risk was not significantly associated with PU development in home care setting.[10] This discrepancy might be explained by the facts that the relative influences of risk factors for PU development are changing due to the improved quality of care. In our study, a larger proportion of the patients used an air-cell mattress than in the previous studies of patients with PUs (8.6–21.8%)[4,11]; therefore, our populations were receiving sufficient pressure redistribution management. This is probably because that the quality improvement of care for pressure redistribution is promoted by the long-term care insurance in Japan. On the other hand, more than half of the patients with PUs were malnourished in our study consistent with a previous research,[9] indicating our study population remained a poor nutritional status. These data suggest that nutritional aspects are growing in importance as the care for other risk factors for pressure ulcers is improving.

Furthermore, malnutrition was independently and most strongly associated with the development of full-thickness PUs. In the population evaluated in this study, almost half of the patients with PUs had full-thickness PUs which is a higher proportion than in hospitals or institutions.[1,19] These results indicated that severe

Table 6
Differences in nutritional risk factors between patients with superficial and full-thickness pressure ulcers.

	Superficial ulcer ($N = 157$)		Full-thickness ulcer ($N = 133$)		*p*-value
	n	Value	*n*	Value	
Patient status					
Malnutrition, *n* (%)	128	67 (52.3)	95	64 (67.4)	0.024
Patient and caregiver factors					
Caregiver knowledge about nutrition, *n* (%)	128	27 (21.1)	91	24 (26.4)	0.362
Adequate diet three times per day, *n* (%)	136	100 (73.5)	102	68 (66.7)	0.250
Mean energy intake in kcal (SD)	56	1071 (353.7)	52	988 (291.3)	0.189
Nutritional management					
Nutritional intervention, *n* (%)					
None	152	7 (4.6)	127	14 (11.0)	0.045
By any route		145 (95.4)		113 (89.0)	
(Oral)	145	116 (80.0)	127	83 (73.5)	
(Enteral)		27 (18.6)		30 (26.5)	
(Parenteral)		2 (1.4)		0 (0.0)	
Nutritional assessment, *n* (%)					
Patient nutritional status	157	128 (81.5)	133	95 (70.9)	0.042
Caregiver knowledge	157	128 (81.5)	132	91 (68.9)	0.013
Adequate diet three times per day	156	136 (87.2)	132	102 (77.2)	0.027
Energy intake	157	56 (35.7)	132	52 (39.4)	0.514
Consultation with dietitian, *n* (%)	155	3 (1.9)	132	2 (1.5)	0.786

Table 7
Multivariate analysis of risk factors for full-thickness pressure ulcer development.

Variable	Reference	Category	Odds ratio	95% CI
Malnutrition	Absence	Presence	1.88	1.03–3.45
Age	–	–	1.00	0.96–1.03
Sex	Male	Female	0.81	0.42–1.55
Care-need certification	Care level 3-5	Not certified	1.85	0.18–19.51
		Support level	0.81	0.13–5.19
		Care level 1-2	0.47	0.12–1.78
Immobility on bed	Absence	Presence	1.51	0.69–3.26
Immobility on chair	Absence	Presence	1.13	0.59–2.19
Joint contracture	Absence	Presence	1.64	0.80–3.38

Hosmer–Lemeshow test: $p = 0.28$.
CI, confidence interval.

PUs are serious problems in the home care. Malnutrition causes reduction of the connective tissue that protects the skin from damage by external pressure, resulting in weakened tissue tolerance[20] and probably leading to more severe PUs. Once a severe PU develops in a malnourished patient, wound healing is delayed. Therefore, these results also suggested that nutritional management is important for preventing severe PUs in the home care setting.

Adequate dietary intake and assessment of dietary intake by a health professional were significant preventive factors for PU development. Protein intake has been shown to be related to PU development in the long-term care setting.[8] Therefore, dietary intake will be the key factor in the home care setting as well. It was useful to learn that subjective dietary assessment can be sufficient for detecting PU risk in the home care setting.

This study revealed that only one-fifth of caregivers had knowledge about nutritional management for PU prevention, which was significantly associated with PU development although not significant in the multivariate model. In the home care setting, health professionals have a limited amount of time to care for patients. Also, because nutritional care is largely related to daily dietary habits, family caregivers spend a greater amount of time caring for these patients than do health care professionals; therefore, caregiver's requirements for knowledge or training are great.[21] Furthermore, this study found that assessment of the caregiver's nutritional knowledge was a significant preventive factor for PU severity after adjusting for demographic characteristics, indicating that nutritional assessment in the home care setting should include an assessment of the caregiver's knowledge as well as the patient's nutritional status which is generally recommended in other settings.[22,23] A previous study reported that the participation of health professionals in PU management reduced the incidence of hospital-acquired PU.[24] Therefore, the collaborations of health care professionals with family caregivers may be indispensable to prevent the severe PUs in the home care setting.

This study also revealed that the assessment of the patient's nutritional status by a health professional was a significant preventive factor for PU in the home care setting. However, only a few of the health professionals consulted with a dietitian or performed an objective assessment of energy intake. It has been reported that only half of the home care agencies obtained a dietary consultation; still, this was a much higher proportion than found in this study.[25] The associations between consultation or objective assessments and PU development were not necessarily significant; however, it may be necessary to improve insufficient quality of nutritional management by health professionals in the home care system for PU prevention.

There were several limitations in this study. First, although the participating offices were randomly selected from throughout the country, it may be necessary to cross-validate the results because only about 40% of all offices participated in this study. Second, some data about nutritional management were missing. This could have been due to the methodology of the mailed questionnaire survey and/or the limitations of collecting the objective data in the home care setting. In this setting, standardized nutritional assessment is not required by the our long-term care insurance, resulting in the low response rate for objective energy intake. Therefore, participating nurses comprehensively evaluated malnutrition, which may include various types of nutritional status. Further research using available standardized tools will be needed to evaluate each different nutritional criterion separately. Finally, the multivariate analyses for the performance of nutritional assessment adjusting other PU risk assessments could not be conducted due to multicolinearity. This is because PU risk assessment was a comprehensive process that included nutritional assessment. It may be necessary in a future study to examine each contribution of the performance of different risk assessments.

In conclusion, malnutrition was the most important of the factors associated with the development and severity of PUs in the home care setting. Ensuring adequate dietary intake was a significant preventive factor for PU development, as was the performance of a nutritional assessment by a health professional. Because the management of pressure distribution has improved greatly in recent years, nutritional management represents the next important point for PU prevention in home care.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgements

This work was supported by research grants from the Ministry of Health, Labor, and Welfare, 2007, Japan. The authors would like to acknowledge that I.S. was responsible for design, statistical analysis, results interpretation, and the writing of the manuscript. O.M. contributed to data collection and data management. S.J. and S.H. contributed to study conception, design, results interpretation, and review of the manuscript.

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Estimation of Protein Requirements According to Nitrogen Balance for Older Hospitalized Adults with Pressure Ulcers According to Wound Severity in Japan

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OBJECTIVES: To estimate protein requirements in older hospitalized adults with pressure ulcers (PrU) according to systemic conditions and wound severity.

DESIGN: Secondary nitrogen balance study over 3 days.

SETTING: Long-term care facility.

PARTICIPANTS: Twenty-eight older adults with PrU using a urinary catheter.

MEASUREMENTS: Nitrogen balance over 3 days was evaluated from habitual nitrogen intake measured using a food weighing record and nitrogen excretion from urine, feces and wound exudate. Nitrogen intake required to maintain nitrogen equilibrium was estimated as an average protein requirement using a linear mixed model.

RESULTS: Nitrogen intake at nitrogen equilibrium was 0.151 gN/kg per day (95% confidence interval = 0.127–0.175 gN/kg per day) for all participants. The amount of protein loss from wound exudate contributed little to total nitrogen excretion. A Charlson comorbidity index of 4 or greater (the median value) was related to lower nitrogen intake at nitrogen equilibrium ($P = .005$). Severe PrU with heavy exudate amounts and measured wound areas of 7.9 cm^2 or greater (the median value) were related to higher nitrogen intake at nitrogen equilibrium in individuals with a Charlson comorbidity index of 3 or less (both $P = .04$). Larger wound area (correlation coefficient (r) = 0.55, $P = .003$) and heavier exudate volume ($r = 0.53$, $P = .004$) were associated with muscle protein hypercatabolism measured according to 3-methylhistidine/creatinine ratio.

CONCLUSION: The average protein requirement is 0.95 g/kg per day for older hospitalized Japanese adults with PrU, but protein requirements depend on an individual's condition and wound severity and range from 0.75 to 1.30 g/kg per day. Severe PrU can require higher protein intakes because of muscle protein hypercatabolism rather than direct loss of protein from wound exudate. **J Am Geriatr Soc 60:2027–2034, 2012.**

Key words: aged; dermatology; nutrition; nursing; wound care

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DOI: 10.1111/j.1532-5415.2012.04202.x

Pressure ulcers (PrU) and malnutrition are two major concerns for hospitalized older adults.[1,2] Malnutrition often coexists with PrU in older adults and is a critical factor in delayed healing of PrU.[3–5] Meeting requirements for protein intake is of particular importance for preservation of body muscle mass and rapid healing of PrU.[6,7] According to international guidelines,[8,9] the current recommended protein intake for individuals with PrU is generally 1.25 to 1.5 g/kg per day,[8,9] but there are three concerns regarding this recommendation.

First, this recommendation is mostly based on expert opinions or the extrapolation of a few indirect studies, which originally aimed to reveal the effect of oral nutritional supplements on PrU healing without a clear definition of the requirement.[6,8–11] According to the dietary reference intakes for healthy people,[12–14] protein requirements are generally determined to minimize the risk of nutritional deficiency. Because individuals have different requirements, the estimated average requirement is defined to meet requirements for 50% and the recommended dietary allowance for 97.5% of the population, based on the distribution of individual requirements. For this purpose, the nitrogen

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0002-8614/12/$15.00

balance method is regarded as the standard method.[12–15] Many nitrogen balance studies have been conducted for healthy older adults (average requirements are 0.58–0.85 g/kg per day)[12,13,15–17] and older hospitalized adults (1.06 g/kg per day),[18] but there have been no studies measuring nitrogen balance for older adults with PrU.

In nitrogen balance studies, complete calculation of nitrogen loss across all routes is essential to avoid underestimation of protein requirements.[12,13] A concern regarding PrU is nitrogen loss from wound exudate. A previous study revealed that the amount of protein loss from PrU exudation was 0.2 g/d on average, increasing to a maximum of approximately 2.0 g/d with increasing PrU severity in the exudate.[19] Although it was still lower than that in acute wounds,[20,21] the influence of this route on systemic nitrogen balance remains unclear.

The second concern is a lack of adequate data on the influence of comorbidities on differences in protein requirements in older adults with PrU. Restriction of protein intake will be required in some systemic conditions such as renal insufficiency for individuals with PrU to avoid detrimental effects on systemic conditions, because they are often severely ill with various comorbidities.[8,22–24]

The third concern is that the current recommendation was determined independently of variation in PrU severity. Previous studies have reported that greater stress caused by surgery, acute wounds, or chronic wounds resulted in a greater degree of muscle protein breakdown, negative nitrogen balance, and thus greater dietary protein requirement.[20,25–27] Although the current guidelines for PrU mention the need to increase the amount of protein intake in individuals with PrU with extreme levels of exudate based on expert opinion,[8,9] no clinical studies have been performed to comprehensively evaluate protein metabolism and then protein requirements according to PrU severity. Because nitrogen balance is methodologically limited in the direct evaluation of protein synthesis or breakdown,[12,13] urinary excretion of 3-methylhistidine (3MeH) is frequently measured as an indicator of muscle protein catabolism.[28]

PURPOSES

The purposes of this study were to estimate the average protein requirement for maintenance of nitrogen balance and to examine the effects of systemic and wound conditions on protein requirements for older hospitalized adults with PrU.

METHODS

Study Design

A cross-sectional, 3-day secondary nitrogen balance survey was conducted between August 2009 and August 2011. There are two methods to determine nitrogen balance.[15–18] Although the primary method can estimate individual protein requirements by experimentally providing several levels of protein intake for a individual, it is usually not used for hospitalized individuals, who cannot tolerate radical changes in intake level. Therefore, the secondary method was selected,[18] whereby nitrogen balances are evaluated under habitual nutritional intake in an observational survey and protein requirements can be obtained for a group.

The ethical committee of the Graduate School of Medicine, University of Tokyo approved the survey protocol. Written informed consent was obtained from participants or their proxies.

Participants

Older adults with PrU were recruited from a long-term care hospital in Japan. A long-term care hospital is a specialized facility for older adults who require chronic medical care for long periods. It was selected because many patients received a dietary plan during their hospital stay that was long enough to ensure steady periods of nutritional intake. Individuals who had at least one PrU, were aged 65 and older, used a urinary catheter as usual care to complete 24-hour urine collection, and had been on a nutritional plan for at least 1 week to assume a nutritionally steady state were included.

Procedures

Dietary assessment under habitual intake and 24-hour urine collection were conducted for 3 consecutive days after at least 1 week after admission to ensure repeatability. Evaluations for nutritional status and wound status were conducted on 1 of these 3 days. Blood sampling was performed within 1 week of urine collection. During the study period, each participant received standardized care for PrU based on the Japanese guidelines.[29] Participants received an individualized nutritional plan determined by a local doctor and a dietitian based on the participant's condition or disease type.

Data Collection

Demographic Data

Information on age, sex, independence level determined according to the Japanese Ministry of Health, Labor, and Welfare, and comorbidities evaluated using the Charlson comorbidity index[30] was collected from medical charts.

Nutritional Status and Systemic Condition Data

Current body weight was collected from the medical chart from the preceding 2 weeks. To calculate body mass index (BMI), height was estimated from knee height measured by a trained researcher using a formula validated for elderly Japanese individuals.[31] Serum levels of albumin, prealbumin, C-reactive protein, blood urea nitrogen, and creatinine were measured according to the laboratory's standard procedures (SRL Inc., Ishikawa, Japan). Estimated glomerular filtration rate (eGFR) was calculated according to the formula recommended by the Japanese Society of Nephrology.[32] Renal insufficiency was defined as an eGFR of less than 60 mL/min per 1.73 m^2.

Wound Status

A researcher determined wound locations, measured wound area, and amount of protein loss from wound exudation and used the DESIGN-R tool to evaluate PrU severity.[33,34]

The DESIGN-R tool was developed to evaluate PrU severity using seven items: depth, exudate, size, inflammation and infection, granulation tissue, necrotic tissue, and pocket (undermining).[33,34] A total DESIGN-R score ranging from 0 (healed) to 66 (greatest severity) was calculated from six items excluding depth to determine the overall severity of the PrU and was classified into three categories: slight (a total score of ≤ 9), moderate (10–18) and severe (≥ 19).[33,34] Depth score was independently classified into two groups. Superficial PrU included persistent redness and dermal wounds, and deep PrU included wounds extending to the subcutaneous tissue, muscle, or bone and unstageable wounds. The predictive validity and interrater reliability of the DESIGN-R tool have been confirmed in previous studies.[33,34] The standardized protocol to evaluate DESIGN-R was developed based on the Japanese guideline.[29] Another researcher independently checked the DESIGN-R score of the primary researcher.

The wound area was measured by tracing the wound margin using a commercially available measurement system (VISITRAK; Smith & Nephew Wound Management, Tokyo, Japan).[35] The wound area was calculated for the total area including undermining.

Protein loss from wound exudation (g/d) was calculated by multiplying exudate volume and total protein level.[19] Exudate was collected under a transparent occlusive dressing covering the wound surface (OpSite Wound Dressing; Smith & Nephew Wound Management). After several hours, the retained fluid within the film was collected. The collected samples were centrifuged to remove cell debris (8,000 × *g* for 5 minutes). The volume was measured using a micropipette to the nearest 10 μL and was converted to volume per day (mL/d). When exudate was difficult to collect, its volume was estimated using a equation validated from a previous study that included some of the same population.[36] The total protein level in the exudate was measured using the Biuret method (SRL Inc.). If the total protein level was not measurable because of a small sample volume, the level was estimated as 70% of the serum level.[37]

To analyze nitrogen balance statistically according to wound severity for individuals with multiple PrU, the subscores for exudate, size, granulation tissue, and pocket of the DESIGN-R tool; total wound area; and measured exudate volume were summed for each wound in a participant, whereas the highest score was selected for other subscores of the DESIGN-R tool.

Nutritional Intake

Nutritional intake was assessed using a 3-day food weighing record. Researchers weighed all foods using a digital scale to the nearest 1 g before and after meals and calculated the proportion of dietary intake. A dietitian in the hospital calculated the nutritional composition of all menus using the Standard Tables of Food Composition in Japan (Fifth Revised and Enlarged Edition). For participants who received nutrients enterally and parenterally, the content and volume of all supplements and infusions were recorded. For nutrients administered orally and enterally, the digestion and absorption efficiency for protein was assumed to be 90% based on the dietary reference intake for Japanese,[14] whereas that for amino acids administered parenterally was 100% to adjust for the differences in nutritional routes. Daily protein intake was divided by 6.25 and converted to nitrogen intake (gN). Energy and nitrogen intake were expressed per 1 kg of body weight. The nonprotein calorie:nitrogen ratio (NPC:N) was calculated to evaluate the energy–protein balance.

Nitrogen Excretion

Nitrogen excretion through urinary, fecal, miscellaneous including sweat or skin, and wound exudate loss was calculated. A 24-hour urine collection was performed for 3 days using a plastic bag connected to a urinary catheter. On each day, duplicate samples (each approximately 10 mL) were collected from pooled urine after stirring adequately and stored at −80°C for later use. The mean value of duplicates was used for further analysis to reduce measurement errors. The concentration of urinary urea nitrogen was measured using the urease method (SRL Inc.). Total urinary nitrogen excretion (gN) was calculated as urinary urea nitrogen excretion (gN) times 1.25. Urinary creatinine was measured to evaluate the accuracy of the 24-hour urine collection. Because most participants were bedridden and had functional fecal incontinence, nitrogen excretion from the fecal and miscellaneous sources such as sweat were estimated at 0.018 and 0.008 gN/kg per day, respectively.[12,18] Nitrogen loss from wound exudation (g/N) was calculated as protein loss from exudate (g) divided by 6.25. Total nitrogen excretion from the above routes were expressed as gN/kg of body weight per day.

Nitrogen Balance

Nitrogen balance was calculated for each day as follows: nitrogen balance (gN/kg) = nitrogen intake (gN/kg) − total nitrogen excretion (gN/kg). The nitrogen intake required to maintain nitrogen equilibrium was regarded as the average requirement of protein intake in this population.

Muscle Protein Catabolism

The concentration of 3MeH was measured using high-performance liquid chromatography according to the laboratory's protocol (SRL Inc.) on the second day of a 3-day urine collection. Urinary excretion of 3MeH were normalized according to creatinine excretion (3MeH/Cr) to standardize differences in muscle mass.[28,38]

Statistical Analysis

Descriptive data were expressed as mean ± standard deviation or n (%). All analyses were conducted using SAS version 9.2 (SAS Institute, Inc., Cary, NC). Interday reliability was evaluated for dietary and urinary nitrogen using intraclass correlation coefficients (ICC) between 3 days.

Nitrogen intake to achieve nitrogen equilibrium was estimated from a linear mixed model with evaluation days as a repeated variable (SAS MIXED procedure). Nitrogen balance parameters including obligatory nitrogen loss (ONL, gN/kg per day), utilization efficiency, and nitrogen intake at nitrogen equilibrium with their 95% confidence intervals (95% CIs) were estimated as the absolute values of the *y*-intercept, slope, and *x*-intercept, respectively, using the ESTIMATE statement. The model included a dichotomized variable of systemic conditions or wound severity to explore the differences in parameters. The cut-off point was set at the median value in this survey unless there was a clinical reference value.

The associations between 3MeH/Cr and variables of wound severity were evaluated using Pearson correlation coefficients (r) and partial correlations adjusted for systemic conditions.

RESULTS

Twenty-eight participants with 36 PrU were recruited and entered into analysis. The length of stay was more than 30 days for 20 of 28 participants. Mean age was 86.0 ± 8.2, 18 were female (Table 1), and 26 were bedridden. Twenty-eight ulcers were deep, and mean DESIGN-R total score was 18.3 ± 10.0.

Table 1. Demographic Characteristics and Nutritional Status (N = 28 Participants; N = 36 Pressure Ulcers)

Variable	Value
Age, mean ± SD	86.0 ± 8.2
Sex, n	
Female	18
Male	10
Independence level, n	
Chair-bound	2
Bedridden	26
Charlson comorbidity index (range 0–30), mean ± SD	4.2 ± 2.5
Height, cm, mean ± SD	143.6 ± 11.9
Weight, kg, mean ± SD	38.6 ± 8.5
Body mass index, kg/m^2, mean ± SD	18.7 ± 3.2
Serum albumin level, g/dL, mean ± SD	2.7 ± .5
Serum prealbumin level, mg/dL, mean ± SD	13.3 ± 5.0
Serum C-reactive protein level, mg/dL, mean ± SD	3.4 ± 4.3
Serum blood urea nitrogen level, mg/dL, mean ± SD	24.7 ± 23.5
Serum creatinine level, mg/dL, mean ± SD	.7 ± .5
Estimated glomerular filtration rate, mL/min per 1.73 m^2, mean ± SD	104.5 ± 54.8
Nutritional route, n	
Orally alone	7
Enterally alone	10
Parenterally alone	11
Location, n[a]	
Sacrum	23
Greater trochanter or ischial tuberosity	6
Lower extremity	2
Coccyx	1
Other	4
Depth, n[a]	
Deep	28
Superficial	8
Wound variable, mean ± SD[a]	
DESIGN-R total score (range 0–66)	18.3 ± 10.0
Measured area, cm^2	12.4 ± 20.8
Measured exudate volume, mL	1.7 ± 6.3

SD = standard deviation.

[a] Wound variables were evaluated for all wounds in a participant.

Mean energy intake was approximately 24.5 kcal/kg per day, and mean protein intake was approximately 0.95 g/kg per day, corresponding to 0.150 gN/kg per day of nitrogen intake (Table 2). Average protein intake over 3 days was strongly correlated with energy intake ($r = 0.91$, $P < .001$). Mean total nitrogen excretion was approximately 0.150 gN/kg per day. Mean nitrogen balances were almost neutral over 3 days, ranging from −0.003 to 0.001 gN/kg per day. The ICCs of all dietary intakes and urine samples over 3 days were greater than 0.9, indicating almost perfect interday reliability. Almost half of participants had a positive nitrogen balance (n = 13 for days 1 and 3, and 14 for day 2). Average nitrogen balance over 3 days was correlated with average protein intake ($r = 0.65$, $P < .001$), energy intake ($r = 0.45$, $P = .02$) and NPC:N ($r = -0.54$, $P = .003$).

In Figure 1A, the estimated ONL was 0.095 gN/kg per day (95% CI = 0.061–0.128 gN/kg per day), utilization efficiency was 0.629 (95% CI = 0.439–0.818), and nitrogen intake at nitrogen equilibrium was 0.150 gN/kg per day (95% CI = 0.126–0.174 gN/kg per day) when the nitrogen balance did not include loss from exudation for all participants. When loss from wound exudation was added, nitrogen intake at nitrogen equilibrium was 0.151 gN/kg per day (95% CI = 0.127–0.175 gN/kg per day) (Figure 1B). Table 3 shows the parameters of the scatter plots for nitrogen balance according to systemic conditions. Nitrogen intake at nitrogen equilibrium was 0.186 gN/kg per day (95% CI = 0.154–0.217 gN/kg per day) in participants with a Charlson comorbidity index of 3 or less, which was significantly higher than the 0.122 gN/kg per day (95% CI = 0.092–0.151 gN/kg per day) in those with a score of 4 or greater (the median value) ($P = .005$). Moreover, nitrogen intake at nitrogen equilibrium tended to be higher in participants with an eGFR of 60 mL/min per 1.73 m^2 or greater than in those with an eGFR of less than 60 mL/min per 1.73 m^2 ($P = .09$).

The parameters for nitrogen balance according to wound severity were then evaluated. To avoid confounding with systemic condition, the analysis was performed only for participants in good condition in terms of comorbidity and renal function (Table 4). For participants with a Charlson comorbidity index of 3 or less, nitrogen intake at nitrogen equilibrium was higher for PrU with a heavy exudate amount ($P = .04$) or wound areas of 7.9 cm^2 or larger ($P = .04$) than for PrU with none to a moderate amount of exudate or wound areas less than 7.9 cm^2, respectively. Similar results were obtained for participants with normal renal function ($P = .004$ for exudate amounts and $P = .007$ for wound areas). There were no significant differences in ONL or slope between any groups.

The 3MeH/Cr was positively associated with DESIGN-R exudate score ($r = 0.41$, $P = .03$), size score ($r = 0.36$, $P = .06$), pocket score ($r = 0.39$, $P = .04$), and total score ($r = 0.46$, $P = .01$); measured wound area ($r = 0.55$, $P = .003$); measured exudate volume ($r = 0.53$, $P = .004$), and the amount of protein loss from exudation ($r = 0.56$, $P = .002$). These associations were unchanged when comorbidity or inflammatory status was adjusted.

Table 2. Daily Nutritional Intake and Nitrogen Excretion and Interday Reliability

Variable	Day 1	Day 2	Day 3	Intraclass Correlation Coefficient
	Mean ± Standard Deviation			
Intake				
Energy				
kcal	917.0 ± 319.0	913.9 ± 351.0	922.3 ± 323.2	.963
kcal/kg	24.5 ± 9.1	24.4 ± 9.9	24.5 ± 9.1	–
Protein				
g	35.7 ± 16.7	35.4 ± 17.6	34.9 ± 16.1	.960
g/kg	.95 ± .47	.94 ± .49	.92 ± .44	–
Nitrogen				
gN	5.72 ± 2.66	5.66 ± 2.82	5.59 ± 2.58	–
gN/kg	.152 ± .075	.151 ± .078	.148 ± .071	–
Nonprotein calorie:nitrogen ratio	156.4 ± 86.8	157.8 ± 86.5	163.2 ± 89.0	–
Excretion				
Urinary nitrogen, gN	3.87 ± 1.76	3.76 ± 1.81	3.63 ± 1.80	.982
Fecal nitrogen, gN	.70 ± .15	.70 ± .15	.70 ± .15	–
Miscellaneous nitrogen, gN	.31 ± .07	.31 ± .07	.31 ± .07	–
Nitrogen loss from wound exudate, gN	.02 ± .06	.02 ± .06	.02 ± .06	–
Total nitrogen				
gN	5.86 ± 2.26	5.73 ± 2.34	5.56 ± 2.31	–
gN/kg	.155 ± .060	.151 ± .057	.147 ± .058	–
Nitrogen balance, gN/kg	–.003 ± .060	.000 ± .056	.001 ± .051	–
Urinary creatinine, g	.30 ± .12	.30 ± .11	.29 ± .11	.975

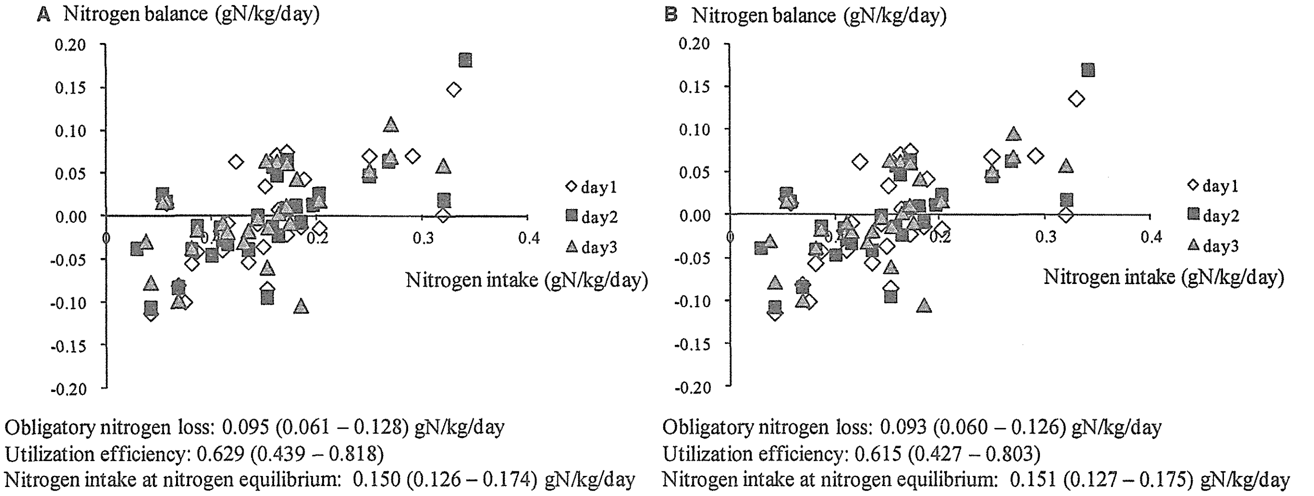

Figure 1. Scatter plots of nitrogen balance and nitrogen intake at baseline over 3 days for all participants with pressure ulcers (N = 28). (A) Nitrogen balance without nitrogen loss from wound exudate. (B) Nitrogen balance with nitrogen loss from wound exudate. Values represent estimates (95% confidence intervals).

DISCUSSION

This is the first survey to determine protein requirements for maintenance of nitrogen balance in older hospitalized Japanese adults with PrU in a long-term care setting despite small sample size. The purpose of nutritional care for PrU is to maintain nutritional status according to catabolic status caused by PrU and to promote wound healing through the supply of adequate nutrients to local site. The data using secondary and short-term nitrogen balance method will contribute especially to the first purpose.

The crude average protein requirement for all participants corresponds to 0.94 g/kg per day (95% CI = 0.79–1.09 g/kg per day). Because interindividual variance cannot be directly determined in the secondary design, safe protein intake would be 1.18 g/kg per day with assumed interindividual variance of 25% (2 standard deviations in previous reports).[14] When these data are rounded for clinical use, average and safe protein requirements for older adults with PrU are 0.95 and 1.20 g/kg per day, respectively. Safe intake was similar to the lower limit of the current recommendation for PrU treatment.[8] Compared with the average requirements of 0.56 to 0.85 g/kg per day for healthy older people,[14–17] it seems that the influence of PrU on nitrogen balance can increase protein requirements, although the value was lower than

Table 3. Parameters from a Linear Mixed Model of Nitrogen Balance According to Systemic Conditions

		Obligatory Nitrogen Loss, gN/kg per Day		Utilization Efficiency		Intake at Nitrogen Equilibrium, gN/kg per Day	
Variable	n	Estimate (95% CI)	*P*-value	Estimate (95% CI)	*P*-value	Estimate (95% CI)	*P*-value
Age							
<85	13	.098 (.036–.159)	.89	.640 (.308–.972)	.91	.163 (.127–.198)	.39
≥85	15	.093 (.052–.134)		.617 (.375–.859)		.142 (.110–.175)	
Sex							
Female	18	.088 (.048–.128)	.68	.604 (.398–.811)	.83	.155 (.125–.185)	.40
Male	10	.106 (.025–.188)		.689 (.102–1.234)		.134 (.093–.175)	
Comorbidity score[a]							
≤3	13	.125 (.064–.186)	.32	.710 (.394–.984)	.87	.186 (.154–.217)	.005
≥4	15	.090 (.050–.129)		.726 (.452–.990)		.122 (.092–.151)	
Estimated glomerular filtration rate, mL/min per 1.73 m^2							
≥60	20	.101 (.051–.152)	.70	.640 (.367–.912)	.92	.164 (.136–.192)	.09
<60	8	.088 (.041–.135)		.659 (.361–.956)		.119 (.075–.164)	

CI = confidence interval.
[a] Variables classified according to median value.

Table 4. Nitrogen Intake at Nitrogen Equilibrium According to Wound-Related Characteristics for Participants in Good Systemic Condition

	Charlson Comorbidity Score ≤3 Points			Normal Renal Function (eGFR ≥60 mL/min per 1.73 m^2)		
Variable	n	Estimate (95% CI)[a]	*P*-value	n	Estimate (95% CI)[a]	*P*-value
Depth[b]						
Superficial	3	.153 (.080–.226)	.32	4	.130 (.071–.188)	.19
Deep	10	.192 (.152–.232)		16	.172 (.143–.202)	
Exudate amount[b]						
None to moderate	9	.158 (.119–.196)	.04	15	.142 (.117–.167)	.004
Heavy	4	.231 (.172–.289)		5	.222 (.178–.266)	
Inflammation or infection[b]						
None	11	.176 (.134–.218)	.89	13	.168 (.135–.201)	.36
≥Slight	2	.183 (.083–.283)		7	.143 (.098–.188)	
DESIGN-R total score						
≤18	5	.176 (.117–.236)	.70	8	.146 (.104–.189)	.27
≥19	8	.190 (.143–.237)		12	.176 (.141–.211)	
Measured area						
<7.9 cm^2	6	.143 (.095–.191)	.04	9	.125 (.091–.159)	.007
≥7.9	7	.211 (.167–.256)		11	.192 (.161–.223)	

CI = confidence interval.
[a] Estimated nitrogen intake at nitrogen equilibrium (gN/kg per day).
[b] Subcategories of DESIGN-R tool.

that of 1.06 g/kg per day for hospitalized older adults in rehabilitation units[18] and for critically ill individuals (>2.00 g/kg per day).[39] Moreover, half of participants in the current survey had a positive nitrogen balance, whereas most postsurgical individuals have a serious negative nitrogen balance.[20,25] In addition to differences in race, age, participant physical condition, and settings, wound type may influence these results; a lower protein requirement than that needed for individuals with critical illnesses may adequately neutralize the influence of PrU, which is generally localized damage.[8]

Poor systemic conditions, including high burden of comorbidity and renal insufficiency, were related to lower protein requirements of approximately 0.12 gN/kg per day, corresponding to 0.75 g/kg per day of protein. The average requirement for participants in good condition was approximately 0.17 gN/kg per day of nitrogen, corresponding to 1.10 g/kg per day of protein. A high burden of comorbidity was an unexpected factor in lower protein requirements for PrU because higher protein requirements usually accompany similar conditions such as critical illness or cachexia.[40] Conversely, one study reported the disadvantage of high protein intake in terms of greater mortality in severely edematous malnourished people affected by famine,[41] partly because excessive nitrogen intake may not be effectively used for endogenous protein synthesis and may be harmful.[42] Anorexia, which may further decrease nitrogen excretion and protein requirements through the accommodation process, provides a survival advantage in combination with this condition.[42–44] A recent study also reported that feeding tubes are not beneficial for PrU healing in nursing home residents with advanced cognitive impairment, although the amount of nutritional intake was unclear. This study may indirectly support the results of the current study and provide an opportunity to reconsider nutritional support for people with PrU who are severely ill.[45] Impaired renal function, although not clearly significant, was an expected factor in lower protein requirement. This condition increases nitrogen retention and decreases urinary nitrogen excretion due to low eGFR, resulting in an apparent positive nitrogen balance and lower protein requirement. High protein intake increased the risk of renal function deterioration in individuals with renal insufficiency.[24,29,44] Assessment of the systemic condition should take priority when protein requirements are determined for older adults, even those with PrU.

Heavy amounts of exudate and large wound areas were factors associated with greater protein requirements for people in good conditions. Because the nitrogen intake required to maintain nitrogen equilibrium ranged from 0.192 to 0.231 gN/kg per day, the average protein requirement was 1.30 g/kg per day for people with severe PrU. The amount of protein loss from exudate itself did not directly contribute to greater protein requirement, as a previous study indicated.[19] Conversely, heavy exudate amounts and large wound areas may be related to muscle protein hypercatabolism independently from systemic inflammatory conditions. Therefore, protein requirements for severe PrU will be greater because of high muscle protein catabolism rather than the compensation of direct loss from exudation. Although the details of protein turnover are not clear, severe PrU will cause muscle protein hypercatabolism, which provides adequate amino acids at wound sites to promote protein synthesis for wound healing.[46] The average protein requirement is 0.85 g/kg per day for individuals with less-severe PrU, which is similar to that for healthy older people.[14] Because an adequate protein supply would attenuate protein breakdown,[38] setting a higher average requirement for severe PrU is reasonable for individuals in relatively good systemic conditions.

A limitation of this study was the small sample size, which may have decreased the statistical power in stratified analyses. In addition, this survey was conducted in a convenient long-term medical setting. Further studies involving other settings such as nursing homes or acute care hospitals are required. Second, estimated values were used for nitrogen loss from fecal, miscellaneous, and part of exudate loss because of difficulty in measurement. Also, resting energy expenditure could not be measured, although energy balance has an influence on nitrogen use.[12–14] The results revealed that NPC:N ratio and energy intake influenced nitrogen balance, indicating that the balance between energy and protein intake is another factor in maintaining nitrogen balance, although the effect of protein intake could not be clearly differentiated from that of energy intake because of their strong correlation. Furthermore, differences in nutritional routes may influence the outcomes independent of amount of nutritional intake.[45] Finally, average protein requirements may not be equivalent to the optimal level to promote PrU healing because nitrogen balance reflects protein mass in the whole body and, in this study, was evaluated over a short period of time. Further studies will be required to prospectively evaluate the role of protein requirements for wound healing.

CONCLUSION

Based on the sample of 28 older hospitalized Japanese adults, the average protein requirement for PrU is 0.95 g/kg per day. The average requirements depended on participant condition and wound severity; a high burden of comorbidity and renal insufficiency decreased them, whereas severe PrU increased them, possibly because of muscle protein hypercatabolism. With these data, even though there are several limitations, protein requirements can be objectively and flexibly determined for older hospitalized adults with various PrU severities.

ACKNOWLEDGMENTS

The authors greatly appreciate Ms. Keiko Tabata, RN, the clinical staff, and dietitians at Sengi Hospital; Dr. Mayumi Okuwa, RN, PhD, and Ms. Yosie Shigeta, RN, MHS, at Kanazawa University; and Ms. Hiroe Koyanagi, RN, MHS, Ms. Sanae Sasaki, RN, and members of the team for PrU management at University of Tokyo Hospital.

Conflict of Interest: This study was funded by a grant from the Japanese Society of Pressure Ulcers and a Grant-in-Aid for Fellows of Japan Society for the Promotion of Science (#22–2766). None of the authors have any financial or any other kind of personal conflicts

Author Contributions: Shinji Iizaka: Study design, obtaining research funds, data collection and analysis, and preparation of first draft and final manuscript. Junko Matsuo, Chizuko Konya, Junko Sugama: Study design, supervision of data collection, interpretation of data, and comment on drafts. Rie Sekine: Data collection, interpretation of data, and comment on drafts. Hiromi Sanada: Study design, supervision of data collection, interpretation of data, and preparation of first draft and final manuscript.

Sponsor's Role: The funding organizations had no roles in research design, data collection, analysis, preparation of draft, or approval of final manuscript.

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