Mini Nutritional Assessment as a useful method to predict the development of pressure ulcer among elderly inpatients

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Disclosure summary:

All authors have nothing to disclose.

Related paper presentation: 4th Congress of the World Union of Wound Healing Societies

Running head: Effectiveness of MNA for pressure ulcer prediction

Abbreviations:

PU, pressure ulcer; MNA, Mini Nutritional Assessment; SGA, Subjective Global Assessment; BMI, body mass index; ROC, receiver operating characteristic; AUC, area under the curve; TP, total protein; ChE, cholinesterase

Abstract:

OBJECTIVES: Malnutrition is a major risk factor of pressure ulcers (PU). However, the best method of nutritional assessment to prevent PU is still unclear. This study was designed to determine the usefulness of Mini Nutritional Assessment (MNA) and plasma amino acid analysis to predict the formation of PU among inpatients.

DESIGN: This was a prospective, observational cohort study with a mean observation period of 62.2±86.4 days.

SETTING: Intermediate and acute care wards of a hospital in rural Japan.

PARTICIPANTS: The 422 patients analyzed had an average age of 85.0±7.6 years.

MEASUREMENTS: MNA, Subjective Global Assessment (SGA), Braden Scale (PU prognostic score), pressure ulcer formation, and biochemical analysis including plasma amino acid concentrations.

RESULTS: PU developed in 7.1% of the patients. A MNA score of less than 8 was more sensitive than a rating of moderate or severe malnourishment on the SGA combined with a Braden Scale score of <15 in predicting future PU. Area under the receiver operating characteristic curve (AUC) of MNA was superior to that of the Braden Scale. Braden Scale nutrition subscore had the lowest AUC among the six Braden Scale subscores. The PU group showed significantly lower plasma arginine concentrations than the No PU group.

CONCLUSION: MNA was able to predict the development of PU. A MNA of <8 performed better than the SGA, Braden Scale, and plasma arginine levels in predicting PU development. Although lower plasma arginine concentration at time of admission was associated with PU development, the area under the ROC curve was not significant. The findings from this prospective study support the use of nutritional assessment among inpatients in order to predict PU risk and target appropriate interventions.

Key Words: Pressure ulcers, MNA, Braden Scale, arginine

INTRODUCTION

Protein-energy malnutrition is recognized as a major risk factor of pressure ulcers (PU). The European Pressure Ulcer Advisory Panel (EPUAP) and National Pressure Ulcer Advisory Panel (NPUAP) strongly recommend high-protein mixed oral nutritional supplements and/or tube feeding, in addition to the usual diet, to individuals with significant nutritional risk and PU risk[1]. Also, the latest guidelines from the Japanese Society for Parenteral and Enteral Nutrition support the efficacy of nutritional assessment and intervention to prevent and treat PU[2]. There are many methods for general nutritional assessment, one of which is the Mini Nutritional Assessment (MNA) that was developed in the 1990s and has been suggested as a tool to predict future development of PU[3]. However, the best method of nutritional assessment to prevent PU remains controversial, and the MNA also has not yet been tested for its ability to predict pressure ulcer development.

An ideal nutritional assessment should include dietetic, anthropometric and functional parameters,[4] and this is especially true for inpatients who face high PU risk and have access to resources in order to perform the assessment. MNA includes these parameters.

The Braden Scale for Predicting Pressure Sore Risk (Braden Scale)[5] is adopted widely for the risk assessment of PU development, and the use of the Braden Scale is recommended by the Japanese guidelines for prevention and management of pressure ulcers[6]. The Braden Scale consists of 6 subscales, “friction and shear,” “sensory perception,” “moisture,” “activity,” “mobility” and “nutrition.” According to a recent report, a total Braden Scale score has a sensitivity of 65% and specificity of 70% in predicting PU formation in acutely ill adult veterans[7]. The Braden Scale is easy to implement, however the nutrition category on the scale only assesses usual food intake, which is largely subjective.

Furthermore, we have previously reported that plasma arginine levels were significantly

lower in percutaneous endoscopic gastrostomy patients with PU[8]. As arginine supplementation improved PU healing in these patients[8, 9], depletion of plasma arginine may have a crucial role in the pathophysiology of PU development. However, it is still unclear whether arginine deficiency is a predisposing factor of PU.

Therefore, this study was primarily designed to determine the usefulness of MNA and the Braden Scale to predict the onset of PU among Japanese inpatients in a prospective fashion. Secondly, plasma amino acid analysis was also performed to see whether low plasma arginine at the time of admission correlates with PU development during hospitalization.

METHODS

Subjects

All subjects admitted consecutively to the intermediate and acute care wards of Takada Welfare Hospital during the study period (March, 2010 - March, 2011) were eligible for enrollment regardless of the primary disease. All 438 eligible patients consented to participate. Of those, 9 patients were excluded for incomplete data and 7 patients were excluded for pre-existing pressure ulcers. The remaining 422 patients (age: range 61-102 years, 85.0±7.6 years) were analyzed. The study was approved by the Institutional Review Board of Takada Welfare Hospital (Fukushima, Japan). Study protocol was explained and written informed consent was obtained from the patients or their relatives.

Scoring MNA, SGA and Braden Scale

Two trained nutritionists assessed the nutritional status of inpatients using MNA, formerly called the Mini Nutritional Assessment-Short Form (MNA-SF). MNA is a clinical tool that can be used to identify geriatric patients at risk of malnutrition. The MNA consists of six questions, including food intake, weight loss, mobility, psychological stress or acute disease,

neuropsychological problems and body mass index (BMI) or calf circumference. These items yield 0-2 points or 0-3 points, where 1 indicates poor function and 2 or 3 indicate normal functions[10, 11]. Scores from 12 to 14 points correspond to "normal nutritional status," those from 8 to 11 points are "at risk of malnutrition," and those from 0 to 7 points are designated "malnourished."

Another nutritional status assessment tool is the Subjective Global Assessment (SGA) outlined by Detsky and colleagues[12]. The SGA classification employs historical data on weight change, dietary intake, gastrointestinal symptoms and functional impairment. Physical examination is also performed to detect clinical characteristics of undernutrition, such as loss of subcutaneous fat and muscle wasting. The SGA rates patients into "well nourished," "moderately malnourished," and "severely malnourished" groups, and was conventionally used in the study hospital before MNA was adopted.

Braden Scale total scores were assessed by trained nurses in the study ward to estimate the risk of pressure sore development. One registered nurse with a Wound, Ostomy and Continence Nurse certification received formal training in Braden Scale scoring, and trained other nurses by holding seminars as well as assessing the Braden Scale in volunteer patients. The Braden Scale scoring was performed only for patients rated as "moderately" or "severely malnourished" by SGA. The lowest and highest possible scores on the Braden Scale are 6 and 23, respectively, and patients with scores of <15 were defined as harboring a more than moderate risk of PU development. Many studies have suggested that a score of <19 is the cutoff point for risk of pressure ulcer development[13], however the cutoff point with the best predictive accuracy may depend on age and race[14]. The Japanese guidelines state that the cutoff point ranges between 14 to 20[6], and a cutoff of <15 is generally applied in Japan for inpatients. This cutoff of <15 was adopted for this study. Those who scored <15 on the Braden Scale went through an

additional assessment for plasma amino acids, vitamins and trace elements.

Determination of pressure ulcer development

Ward nurses checked the skin status of patients daily to note the date of PU formation, and new incidence of PU development was judged at biweekly rounds of pressure ulcer assessment panel independent from this study. Pressure ulcer with depth of d2 or greater in DESIGN-R, which is equivalent of Stage II or greater in NPUAP and Grade II or greater in EPUAP, was judged as PU development. DESIGN-R is a pressure ulcer scale developed by the Japanese Society of Pressure Ulcers. DESIGN-R d2 does not include skin redness, which is a sign of deep tissue injury. Screening for deep tissue injury by skin ultrasound was not performed in this study, and therefore deep tissue injuries may not have been judged as PU formation. In this study, repeated admissions of the same patient were counted as one stay, and only newly-developed open pressure ulcer sores that developed in the facility or between admissions were counted in the study.

Laboratory Testing

Total protein, albumin, C-reactive protein (CRP), aspartate amino transferase (AST), alanine amino transferase (ALT), cholinesterase (ChE), blood urea nitrogen (BUN), creatinine, triglyceride (TG), and fasting plasma glucose (FPG) were measured in the hospital laboratory with the Hitachi Autoanalyzer 7070 (Hitachi High-Technologies Corporation, Tokyo, Japan) and complete blood count was measured by XT-1800i (Sysmex, Kobe, Japan) as routine admission tests in most of the patients. Plasma amino acid analysis was performed using high-performance liquid chromatography. Amino acid analysis and measurements of phosphorus, copper, zinc, vitamin A, B1, E and insulin were performed only in those who were rated moderately or severely malnourished by the SGA and scored <15 on the Braden Scale. These measurements were performed by SRL Inc. (Tokyo, Japan). Blood for biochemical

analyses was drawn from patients upon admission after overnight fast.

Statistical Analysis

Only research doctors who were not directly involved in the data collection performed statistical analyses. Statistical differences between the PU group and the No PU group at the time of enrollment were analyzed by unpaired t-test. Data are given as mean ± SD. Pair wise test and area under the ROC curve analysis were performed by GraphPad Prism version 5 (GraphPad Software Inc., La Jolla, CA), and multiple regression analyses were performed using IBM SPSS Statistics 17 (IBM corporation, Armonk, NY). Significance was denoted at $P<0.05$.

RESULTS

Basic characteristics and outcome

The average age of all patients was 85.0±7.6 years (Table 1). Of the 422 patients enrolled, 30 (7.1%) developed PU during a mean follow-up period of 62.2±86.4 days. The BMI of the patients who developed PU were significantly lower than that of those who did not, but there was no significant difference in age between the groups (Table 1). Also, there were significant differences in the total days of hospital stay (PU: 111±108 days vs. No PU: 42±65 days, $P=0.002$) and the lengths of follow up (PU: 129±119 days vs. No PU: 57±81 days, $P=0.003$).

The Braden Scale was assessed in 239 subjects who were determined by SGA to face moderate or high nutritional risk. Of those, 104 patients scored less than 15 and were determined as being at high risk by the Braden Scale, and from this group, 17 developed PU during hospitalization. However, 3 out of the 183 subjects who were determined by SGA to be "well-nourished" and 10 out of the 135 patients who scored 15 or above on the Braden Scale also developed PU. Therefore, a SGA rating of moderately or severely malnourished combined with

a Braden Scale score of less than 15 had a sensitivity of 57% and a specificity of 78% to detect future PU in this population (Table 2). In contrast, using MNA, only 5 patients in the whole study population were determined as "well-nourished." Twenty-nine out of 30 patients who developed PU scored <8 on the MNA and belonged to the "malnourished" group and the remaining one patient was determined as being "at a risk of malnutrition." Therefore, MNA with a cut-off of <8 showed a very high sensitivity of 97% but low specificity of 42% to predict the onset of PU (Table 2). The negative predictive value of the MNA (<8) was also better than that of the SGA (moderately or severely malnourished) combined with the Braden Scale (<15). However, the specificity and positive predictive values of the MNA were lower than those of the combined SGA and Braden Scale (Table 2). The ROC curve of MNA in all patients was superior to that of the Braden Scale among those who were rated moderately or severely malnourished by the SGA (Figure 1).

Multiple logistic regression model for the prediction of pressure ulcer development using MNA

Multiple logistic regression model analysis showed that MNA independently and significantly associated with PU development in all subjects after adjusting for age, sex, and BMI (Table 3). When TP, albumin, ChE, and TG were also adjusted, only the MNA was significantly associated with PU development (odds ratio 0.715, 95% confidence interval: 0.546-0.937, P=0.015, n=252).

Subscore analysis in Braden Scale

To assess the association and prediction accuracy of each query, subscores of the Braden Scale were individually analyzed by pair-wise t-test and ROC analysis (Table 4). There was a significant difference in the total score and the sensory perception, activity, mobility, and friction/shear subscores between the PU and No PU groups. The nutrition and moisture

subscores were not significantly different between the PU and No PU groups, and the ROC analyses were not significant for these subscores. However, the nutrition subscore showed the lowest AUC, signifying a weakness of the Braden Scale in nutritional assessment.

Biochemical profile of patients who developed PU

In routine laboratory testing, TP, albumin, ChE, and TG were significantly lower in the PU group than in the No PU group (Table 5). More detailed screenings for biochemical analysis were performed in patients who were rated moderately or severely malnourished by the SGA and scored <15 on the Braden Scale. Total amino acid, essential amino acid and branched-chain amino acid levels were not significantly different between the patients who developed PU and those who did not (data not shown). However, plasma arginine concentrations were significantly lower in the PU group compared to the No PU group (Table 5). For vitamins and minerals, the PU group showed significantly lower serum vitamin A (Table 5) than the No PU group, with no significant differences in the levels of phosphorus, copper, vitamins B1 and E and zinc (data not shown).

DISCUSSION

This study showed a significant benefit of nutritional assessment for the prediction of future PU development. The major findings include; the effectiveness of the MNA; insufficient power of the Braden Scale in the nutrition subscore; and the possible utility of serum arginine concentration as an index of PU risk.

The current report, for the first time, shows that the MNA has a sufficient capability to assess future risk of PU among aged inpatients. The usefulness of the Braden Scale has been reported in many previous studies[15, 16]. However, in this study, an MNA rating of less than 8 had better sensitivity and negative predictive value than a SGA rating of moderately or severely

malnourished combined with a Braden Scale score of less than 15, and the area under the ROC curve of MNA in all patients was superior to that of the Braden Scale in patients rated moderately or severely malnourished by SGA. Among our test subjects, use of the Braden Scale led to an increase in false negatives that may benefit from more aggressive intervention.

Nutritional status is considered one of the most important factors influencing the pathophysiology of PU. For example, Lahmann et al. reported that nutrition is the second strongest predictor of PU in long-term care residents in Germany[17]. Furthermore, among patients with PU, simple accumulation of caloric intake helped PU healing[18]. The MNA has been validated by many researchers for its effectiveness to identify geriatric patients who are malnourished or at risk of malnutrition[19]. By our study showing the usefulness of the MNA in assessing PU risk, the importance of nutritional status in the formation of PU was reinforced.

In fact, the weakest aspect of the Braden Scale may be in its nutrition assessment. Our study showed that of the 6 Braden Scale subscales, the nutrition subscale was not a significant predictor of PU by ROC analysis and did not show any significant differences between the PU and No PU groups. Also, it has been reported that the modified Braden Scale excluding nutrition subscore was more predictive of PU development than the conventional Braden Scale[20]. The Braden Scale nutrition subscale gives scores of 1 (very poor) to 4 (excellent) based on usual food intake pattern. A questionnaire-based assessment such as the Braden Scale is easy to adopt in a domestic setting, but can be very subjective. In medical facilities where advanced physical assessment is possible and the formation of PU is frequent, more detailed and quantitative methods such as measurement of BMI may be suitable[21]. Since the MNA adopts BMI or calf circumference to assess current nourishment, malnutrition predisposing to PU development may be detected more effectively than the corresponding questionnaire in the Braden Scale.

A possible problem of adopting the MNA over the Braden Scale for inpatients is its low specificity and low positive predictive value. This may increase the number of patients requiring nutritional intervention. PU formation occurs in only a minor subset of patients, but the morbidity, its damage to the quality of life, and the cost of PU can be great. Among inpatients, the incidence of PU formation is higher than in other populations, and if nutritional risk for PU is found, there are more possible interventions to prevent PU in a hospital compared to other settings. In addition, nutritional improvement has been shown to improve general condition of the patients including the healing of primary disease. As such, the use of screening measures with high sensitivity may be justified, even if they have somewhat lower specificity. However, the effectiveness of specific interventions needs to be tested in the future.

Another notable finding from this prospective observational study is that the patients who developed PU during hospital observation showed lower plasma concentrations of arginine at admission than those who did not develop PU. We have previously reported that inpatients with PU showed significantly lower plasma arginine concentrations than those without PU[8]. Also, we and others have shown that oral arginine supplementation may improve PU healing[8 9]. However, the question remains as to whether chronic arginine deficiency leads to PU formation. Research to date has shown that arginine metabolism produces nitric oxide, which is essential in wound healing[22]. Arginine is also reported to be beneficial in maintaining tissue integrity and facilitating wound healing [23]. Moreover, it has been demonstrated that orally administered arginine can be effectively absorbed and utilized[24]. In this prospective study, arginine depletion correlated with PU development however the ROC curve analysis for arginine was not significant. As such, plasma arginine concentration by itself may not sufficiently predict PU development, but whether arginine supplementation in patients with low plasma arginine has a preventive effect on PU formation remains to be investigated.

Besides arginine, lower plasma concentrations of vitamin A correlated with PU development. Vitamin A deficiency is reported to inhibit wound healing through decreased collagen reconstruction and impaired re-epithelialization[25]. In a previous report, inpatients with PU showed lower serum vitamin A concentration compared to those without PU[8]. We have also reported that L-arginine- and zinc-rich formula increased plasma arginine concentration and improved the rate of PU healing in patients on tube feeding.[8] To determine the efficacy and efficiency of nutrient-specific supplementation to prevent PU, a prospective, randomized, controlled intervention trial will be necessary.

In addition to arginine and vitamin A, concentrations of total protein, albumin, cholinesterase and triglycerides were significantly lower in those who developed PU than those who did not. These plasma proteins and lipids have been reported to significantly correlate with nutritional status[26]. The result of this study is reasonable as those who developed PU had lower nutritional status, as determined by significantly lower MNA scores, compared to those who did not develop PU. In this study, the average lengths of hospital stays were significantly different between the PU and No PU groups. The length of hospital stay is suggested as a predisposing factor of PU development, and a poor nutritional status may also be a predisposing factor for longer hospital stay. This may be investigated as a topic for future research.

One of the limitations of this study was that Braden Scores and detailed biochemical analyses including plasma amino acid concentrations were assayed only in those rated moderately or severely malnourished by the SGA. This method makes it difficult to compare the MNA and Braden Scale directly, but was applied due to personnel and financial constraints. Another limitation of the study is that inter-rater reliability was not assessed for the MNA, SGA and Braden Scale scoring, although the benefit of the MNA is that it does not require formal training, and its inter-rater reliability has been validated in a previous report[27]. Also, this study

used a Braden Scale cutoff point of <15 as opposed to <19, which is used in many other studies. This was done according to the recommendation of the Japanese Society of Pressure Ulcers, but it limits the comparison of data with other studies.

CONCLUSION

Geriatric inpatients with malnutrition as assessed by MNA were more likely to develop PU, and those who developed PU showed lower plasma arginine concentrations than those who did not. An MNA rating of <8 performed better than the SGA, Braden Scale, or arginine levels in predicting PU development. Although lower plasma arginine concentration at time of admission was associated with PU development, the area under the ROC curve was not significant. Supplementation of arginine based on amino acid profiling may be useful for the prevention of PU.

ACKNOWLEDGMENTS

Author Contributions: MSY is the corresponding author and designed the study JY. FT, II and AS helped with data collection. TK provided nutritional consultation. SU provided authorization for this study and aided the acquisition of subjects. Kozue Takano built the patient data registry. TW and HS provided advice for this study. JY performed analysis and interpretation of the data and prepared the manuscript with MSY.

Sponsor's Role: None

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Tables

Table 1. Basic characteristics

	Scores	All	No PU (392)	PU (30)
Age (years)		85.0±7.6	86.8±7.5	84.8±7.5
Female ratio (%)		61.4	62.5	46.7
BMI (kg/m^2)		21.5±4.1	21.7±4.2	19.6±3.1*
SGA + Braden Scale (persons)	Low risk	318	305	13
	High risk	104	87	17
MNA (persons)	12-14	5	5	0
	8-11	160	159	1
	0-7	257	228	29

PU: pressure ulcer, BMI; body mass index, SGA: Subjective Global Assessment, MNA: Mini Nutritional Assessment. High risk by SGA + Braden Scale denotes SGA at moderate or high risk and Braden Scale below 15. *P<0.05, No PU vs. PU. Chi-square test for sex, t-test for age and BMI.

Table 2. Predictive values of the Braden Scale and MNA

Cut-off	Sensitivity	Specificity	PPV	NPV
SGA + Braden Scale (Moderate/severe + <15)	0.57	0.78	0.16	0.96
MNA (<8)	0.97	0.42	0.11	0.99

SGA: Subjective Global Assessment, MNA: Mini Nutritional Assessment, PPV: positive predictive value, NPV: negative predictive value.

405 Table 3. Multiple logistic regression model for pressure ulcer development

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variables	β	SE	Wald	P value	Odds ratio	95 % CI
intercept	-0.79	2.7				
age	0.09	0.029	0.094	0.759	1.009	0.953-1.069
Sex (female)	-1.116	0.433	6.644	0.010	0.328	0.140-0.765
BMI	0.017	0.062	0.072	0.788	1.017	0.900-1.149
MNA	-0.423	0.105	16.113	<0.001	0.655	0.533-0.805

407 N = 422. CI: confidence intervals, BMI: body mass index, MNA: Mini Nutritional Assessment

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Table 4. Braden Scale subscore analysis

	No PU (n=212)	PU (n=27)	P value (t-test)	AUC	P value (ROC)
Sensory perception	3.5±0.7	3.1±0.8	0.03	0.634	0.02
Moisture	3.0±1.1	2.7±1.0	0.1	0.606	0.07
Activity	2.5±1.1	1.7±0.8	<0.001	0.702	<0.001
Mobility	3.0±1.0	2.4±1.0	0.007	0.658	0.007
Nutrition	2.4±1.1	2.1±1.2	0.2	0.572	0.2
Friction and shear	2.1±0.8	1.3±0.6	<0.001	0.713	<0.001
total score	16.5±4.8	13.4±3.9	<0.001	0.689	0.001

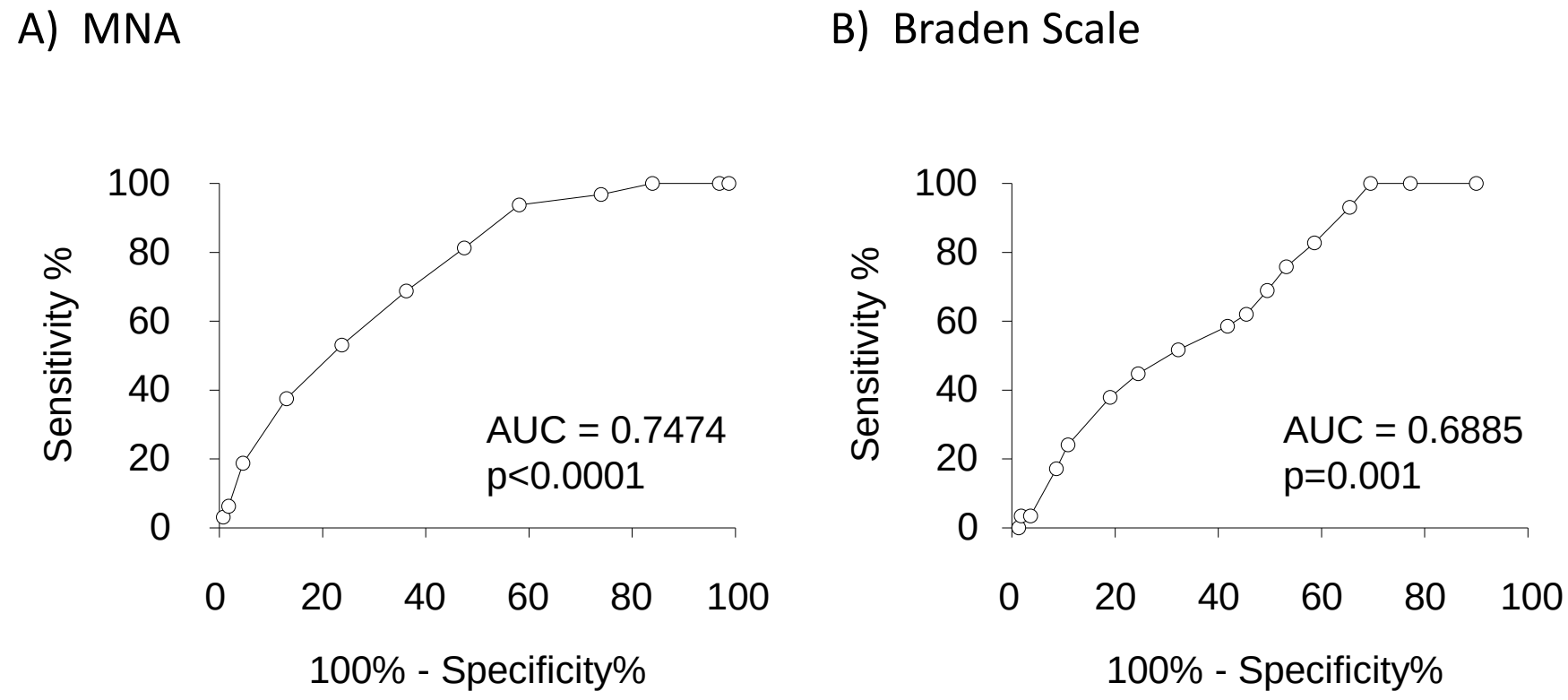
PU: pressure ulcer. Mean±SD. AUC: area under the receiver-operator characteristic curve. P value for ROC analysis was evaluated by testing the null hypothesis that the area under the curve really equals 0.50.

Table 5. Laboratory tests with significant differences between No PU and PU patient groups

		No PU	PU	P value
Total protein	g/dl	6.6±0.7 (334)	6.1±0.8 (26)	0.01
Albumin	g/dl	3.5±0.6 (325)	3.0±0.6 (27)	0.001
ChE	U/l	216±76 (314)	169±50 (24)	<0.001
Triglyceride	mg/dl	88.9±39.5 (303)	70.9±18.2 (21)	<0.001
Vitamin A	IU/dl	79.0±43.1 (99)	58.4±32.5 (17)	0.02
Arginine	nmol/ml	82.6±23.7 (99)	71.6±16.8 (17)	0.04

PU: pressure ulcer, ChE: cholinesterase. Mean±SD. Numbers of patients are shown in parentheses. Vitamin A, and arginine concentrations were measured only in those who were rated moderately or severely malnourished by SGA and scored <15 on the Braden Scale. The normal serum concentration range is 97 to 316 IU/dl for vitamin A. The normal plasma concentration range of arginine is 53.6 to 133.6 nmol/ml.

Figure 1


A) MNA
Sensitivity %
100
80
60
40
20
0
0
20
40
60
80
100
100% - Specificity%
AUC = 0.7474
p<0.0001
B) Braden Scale
Sensitivity %
100
80
60
40
20
0
0
20
40
60
80
100
100% - Specificity%
AUC = 0.6885
p=0.001