A new predictive indicator for development of pressure ulcers in bedridden patients based on common laboratory tests results

N Hatanaka,1,4 Y Yamamoto,1 K Ichihara,2 S Mastuo,1 Y Nakamura,3 M Watanabe,4 Y Iwatani4

ABSTRACT

Background: Various scales have been devised to predict development of pressure ulcers on the basis of clinical and laboratory data, such as the Braden Scale (Braden score), which is used to monitor activity and skin conditions of bedridden patients. However, none of these scales facilitates clinically reliable prediction.

Aims: To develop a clinical laboratory data-based predictive equation for the development of pressure ulcers.

Methods: Subjects were 149 hospitalised patients with respiratory disorders who were monitored for the development of pressure ulcers over a 3-month period. The proportional hazards model (Cox regression) was used to analyse the results of 12 basic laboratory tests on the day of hospitalisation in comparison with Braden score.

Results: Pressure ulcers developed in 38 patients within the study period. A Cox regression model consisting solely of Braden scale items showed that none of these items contributed to significantly predicting pressure ulcers. Rather, a combination of haemoglobin (Hb), C-reactive protein (CRP), albumin (Alb), age, and gender produced the best model for prediction. Using the set of explanatory variables, we created a new indicator based on a multiple logistic regression equation. The new indicator showed high sensitivity (0.73) and specificity (0.70), and its diagnostic power was higher than that of Alb, Hb, CRP, or the Braden score alone.

Conclusions: The new indicator may become a more useful clinical tool for predicting pressure ulcers than Braden score. The new indicator warrants verification studies to facilitate its clinical implementation in the future.

Pressure ulcers result from prolonged bed rest. They are painful, slow to heal, and difficult to manage, and they result in increased healthcare costs and prolonged hospitalisation. Early identification of patients at risk for pressure ulcers is critical to prevent development of such ulcers. It is generally thought that pressure ulcers occur as a result of a combination of extrinsic and intrinsic factors. The extrinsic factors and the mechanisms by which they cause pressure damage are well known. Pressure, shear, force, and friction are three factors that, either singly or in combination, are responsible for development of pressure ulcers. Patients at increased risk for pressure ulcers are bedridden, especially unconscious, patients.

Common factors used to assess the risk of pressure ulcers are patient mobility, skin condition, skin moisture, nutrition, and activity. Various risk assessment scales have been developed by Braden,3 Norton,4 and others5-7 that are intended to predict the development of pressure ulcers through identification of specific risk factors. The Braden Scale is the most widely used instrument in Japan, and we use it routinely in our hospital. The Braden Scale comprises six subscales: sensory function, skin moisture, mental activity, mobility, nutrition, shear force, and friction. Each factor is rated on a 3- or 4-point scale, for a total score of 6-23. The lower the overall score, the greater the risk for development of pressure ulcers. However, according to our clinical experience, prediction on the basis of the Braden score is not always satisfactory. In addition to malnutrition, a low albumin (Alb) level has been implicated as a risk factor for pressure ulcers,8-10 and there have been reported attempts include serum Alb as an additional factor to existing clinical scales.11-14

We feel it is necessary to include more laboratory data to improve the accuracy of prediction. We therefore carried out a prospective study to identify risk factors among common laboratory variables in addition to the clinical variables conventionally used in scales that predict the risk of pressure ulcer development.

METHODS

Subjects
A total of 149 bedridden patients (104 men, 45 women; mean age 71.6 (11.3) years) who were hospitalised at Tenri Hospital for a respiratory disorder, and required constant attentive care or needed a considerable amount of assisted care were enrolled in the study. These patients were hospitalised between December 2003 and May 2004 and were followed over a 3-month period. Pressure ulcers developed in 38 patients within the observation period. Primary diagnoses in these 38 patients were lung cancer (n = 24), pneumonia (n = 7), chronic obstructive pulmonary disease (n = 4), and interstitial pneumonia (n = 3). Primary diagnoses in the 111 patients in whom pressure ulcers did not develop were lung cancer (n = 54), pneumonia (n = 35), chronic obstructive pulmonary disease (n = 16), and interstitial pneumonia (n = 6).

Study
Only patients without pressure ulcers at the time of hospitalisation were enrolled in the study. On
the day of hospitalisation, each patient’s Braden score was determined and common laboratory tests were performed: erythrocyte count (RBC), leucocyte count (WBC), lymphocyte count (Lym), platelet count (Plt), haemoglobin (Hb), albumin (Alb), cholesterol (Cho), total bilirubin (T-Bil), aspartate aminotransferase (AST), C-reactive protein (CRP), urea nitrogen (Urea), and creatinine (Cre) levels. At our hospital, we have 5 grades of mattress: daily mattress (grade 1), preventive mattress (grade 2), standard pressure-relieving mattress (grade 3), qualified air mattress (grade 4), and highly qualified air mattress (grade 5). As a preventive measure, all patients were given a grade 3 mattress during hospitalisation.

We closely observed development of pressure ulcers in these patients up to 3 months after hospitalisation: observations were discontinued after 3 months or hospital discharge or development of pressure ulcer. We assessed ulcers in 5 grades, and defined more than grade 1 (closed-persistent erythema) as development of a pressure ulcer. The average observation in patients who developed pressure ulcers was 21.6 (17.8) days (range 5–79 days); in patients who did not develop pressure ulcer, it was 37.4 (28.3) days (range 5–79 days). Twelve laboratory tests were performed every 3–4 days during the study period.

The study protocol was approved by the ethics committee and patients provided informed consent for their participation in the study.

**Analytical procedures**

The proportional hazards model (Cox regression) was used to identify variables that were independently associated with development of pressure ulcers. Cox regression analysis was performed with the following predictive variables: age, gender (male: 1, female: 0), Braden score, and 12 different laboratory tests. Table 1 shows characteristics (age, Braden score, and 12 laboratory tests on hospitalisation) of the 111 patients in whom pressure ulcers did not develop and of the 38 patients in whom pressure ulcers did develop. We calculated correlation coefficients among the potential predictor variables. A strong correlation was found between Hb and RBC (r = 0.90) and between Cre and Urea (r = 0.78). These variables were not included together in the regression model to avoid multicollinearity. Each variable was tested for normality by the \( x^2 \) goodness of fit test and skewness-kurtosis statistics. The CRP, AST, and T-Bil values were transformed by base 10 logarithm to produce normal distributions (following each log CRP, log AST, and log T-Bil). Elements out of range of 3 SD were omitted for each variable. Data were expressed as arithmetic mean (SD) (table 1).

After relevant explanatory variables were identified by Cox regression analysis, we created a predictor equation for pressure ulcer development by multiple logistic regression analysis using the same explanatory variables. The laboratory test results used in creating the equation were those obtained 3–5 days prior to the development of pressure ulcer, not those obtained upon

### Table 1

<table>
<thead>
<tr>
<th>Item</th>
<th>Partial regression coefficient</th>
<th>p Value</th>
<th>Relative risk (two-sided 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory function</td>
<td>0.112</td>
<td>0.658</td>
<td>1.12 (0.68 to 1.83)</td>
</tr>
<tr>
<td>Skin moisture</td>
<td>-0.048</td>
<td>0.827</td>
<td>0.95 (0.62 to 1.47)</td>
</tr>
<tr>
<td>Mental activity</td>
<td>0.147</td>
<td>0.545</td>
<td>1.16 (0.72 to 1.86)</td>
</tr>
<tr>
<td>Mobility</td>
<td>0.131</td>
<td>0.590</td>
<td>1.14 (0.71 to 1.83)</td>
</tr>
<tr>
<td>Nutrition</td>
<td>-0.126</td>
<td>0.521</td>
<td>0.88 (0.60 to 1.30)</td>
</tr>
<tr>
<td>Shearing force and friction</td>
<td>-0.218</td>
<td>0.457</td>
<td>0.80 (0.45 to 1.43)</td>
</tr>
</tbody>
</table>
hospitalisation. To avoid multicollinearity, all variables were tested for normality, and correlation coefficients were calculated between each two variables. The correlation between Alb and logCRP was 0.43, while other correlations were lower.

To evaluate the utility of the new predictor equation in comparison to that of other predictors, we performed receiver operating characteristic (ROC) curves analysis. To check the practicality of the new predictor, we also investigated serial changes in the new indicator in the 38 patients over the course of pressure ulcer development.

All statistical analyses were performed with general purpose statistical software (SPSS II for Windows, V.11.01.J and STAT Flex for Windows, V.5.0).

**Laboratory analysis**

RBC (10^7/l), WBC (10^9/l), Lym (10^6/l), Plt (10^10/l), and Hb (g/l) were measured using a Sysmex model XE automatic analyser (Sysmex Products, Kobe City, Japan). Alb (g/l), Cho (mg/l), T-Bil (mg/l), AST (U/l), CRP (mg/l), and Cre (mg/l) was measured using a Hitachi model 7600 automatic analyser (Hitachi Products, Hitachi City, Japan). Reagent kits for Alb, Cho, T-Bil, AST, Urea, and Cre were obtained from Wako (Osaka City, Japan) and a reagent kit for CRP was obtained from Denkaseiken (Goizumi City, Japan).

**RESULTS**

Table 2 shows results of Cox regression analysis performed on the six sub-scores constituting sub-scores of the Braden score as explanatory variables. None of the six factors, i.e. sensory function, skin moisture, mental activity, mobility, nutrition, shear force, or friction was shown to have a significant discriminatory ability in predicting pressure ulcers (table 2).

However, a Cox regression model with a combination of Hb, logCRP, Alb, age, and gender, which were identified by adequate prospective or prognostic studies. The new indicator based on logistic regression analysis using age, gender, Alb, Hb, and logCRP as explanatory variables.

Table 4 shows the results of multiple logistic regression analysis; the following regression model was used to compute a predictive value $P$ for pressure ulcer development:

$$P = 1/1 + e^{-0.67 + 0.022\times Hb + 1.51\times \log_{10} CRP + 0.064\times Alb - 0.01 \times Age - 0.91 \times gender}.$$  

$P$ (new indicator) takes a value between 0 and 1. The higher the $P$ value, the greater the risk of pressure ulcer development, whereas the closer the $P$ value to 0, the lower the risk.

We then compared the diagnostic power of the new indicator in comparison to that of other predictive variables. Figure 1 shows ROC curves for the new indicator, Alb, Hb, CRP, and the Braden score. The new indicator had higher sensitivity and specificity than other variables judging from the areas under the curves (table 5). The Braden score was shown to have almost no ability to predict pressure ulcers. The cut-off value of the new indicator was derived as the point of the new indicator where the ROC curve intersects with line $y = 1 - x$, where $y$ denotes sensitivity and $x$ denotes the false positive rate. Thus, the cut-off value was determined to be 0.28. Sensitivity and specificity of the new indicator were 0.73 and 0.70, respectively, when the cut-off value of 0.28 was used.

Figure 2 shows serial changes of the new indicator among the 38 patients who developed pressure ulcers. The median value of the new indicator increased gradually; it surpassed the cut-off value at 9–11 days before the onset of pressure ulcer. Sensitivity increased steeply to 0.38 at 9–11 days, and subsequently increased further.

**DISCUSSION**

There are many risk assessment scales for prediction of pressure ulcers. The three scales most commonly used are the Norton, Braden, and Waterlow Scales. However, none of these scales satisfactorily predicts pressure ulcer development in hospitalised patients. Defloor and Grypdonck\(^{21}\) are of the opinion that the effectiveness of the Norton and Braden Scales is very low and that much needless work is done and resources are wrongly allocated. This may be because the risk assessment scales are based simply on clinical observation of patients’ appearance, physical ability, and nutritional status and not on factors identified by adequate prospective or prognostic studies.

Our study clearly indicated that the Braden score, although it was originally meant to predict pressure ulcers, is of no practical value for that purpose. The new indicator based on logistic regression analysis requires age, gender, Hb, Alb, and CRP for derivation. Age and gender were introduced into the regression model as control variables to avoid the confounding influences of age and gender related differences in Hb, Alb, and CRP. The significance levels of regression coefficients showed that contribution to prediction of pressure ulcer is highest for Hb, then for Alb and CRP, in that order.

There have been epidemiological surveys on risk factors associated with pressure ulcers. Pieper et al reported older age, prolonged hospital stay, multiple co-morbid conditions, lower blood Hb, decreased serum Alb, increased WBC, and low Braden scores to be risk factors for pressure ulcers.\(^{19}\) However, they used simple single-variable analysis of factors (two-sample t test) in comparing patients with and without pressure ulcers. William et al, Bresloa et al, Verier et al, Gengebacher et al, Burr et al and Matsuyama et al also reported the importance of low serum Alb, high CRP, and low Hb as risk factors.\(^{20,21}\) Unfortunately, their results are not statistically appropriate because they did not adjust for possible differences in demographic factors between patients with and without pressure ulcers. It is essential to adjust for the confounding effects of age and gender, at least, by multivariate analysis, such as Cox regression or multiple logistic regression.
regression analysis. There is no such study reported in the literature; we believe ours is the first.

Association between a low Alb level and risk for development of pressure ulcers was suggested in previous studies, and our study confirmed this risk multivariately.

The importance of Hb is unclear. Results of previous studies have indicated that decreased Hb is associated with pressure ulcer development, whereas both our Cox regression analysis and logistic regression analysis indicated that increased Hb is related to the occurrence of pressure ulcers. The reason for the discrepancy is not clear. However, we presume that the increased Hb level may reflect decreasing oxygen-carrying capacity in peripheral tissue.

Generally malnutrition, chronic inflammation, and the acute phase response can result in anaemia. Anaemia may trigger development of pressure ulcers because decreased oxygen-carrying capacity impairs tissue metabolism, resulting in poor wound healing. The relation between increased Hb and the occurrence of pressure ulcers that we observed may be particular to patients with respiratory disorders. Raised Hb might be related to compensation of chronic respiratory failure, and chronic respiratory failure might mean decreased oxygen-carrying capacity similar to that associated with anaemia. Our results regarding nutritional markers Alb and acute-phase protein CRP were similar to other reported results. Raised CRP suggests inflammation, and some inflammatory diseases produce fever, sweating, weakness, and a decline in the patient’s general medical condition. Lowering of Alb level was assumed to be due to leakage from capillaries caused by inflammation. Nutritionally-depleted patients with inflammation would be expected to have a lower Alb level. Chronic respiratory failure might be a risk factor for pressure ulcers; inflammation and malnutrition might increase the risk even further.

The Braden score is the most widely used routine risk assessment, but was shown in our study to have no significance. We evaluated diagnostic performance of the new indicator using Hb, logCRP, and Alb values. The ROC curve showed that the new indicator was more useful for predicting the risk of pressure ulcers than any of the other indicators (Braden score, Alb, Hb, or CRP) used alone (fig 1).

We considered the new indicator more useful, for the following reasons. The value of the new indicator increases 9–11 days before the onset of pressure ulcers. The new indicator was more useful, probably because our patients were only high-risk, bedridden patients, and some were unconscious. In addition, they were given pressure-relieving mattresses on hospitalisation. We believe the predictive indicator derived from Hb, CRP, and Alb values is more clinically useful for assessment of the risk of pressure ulcers than the Braden score.

We evaluated diagnostic performance of the new indicator using Hb, logCRP, and Alb values. The ROC curve showed that the new indicator was more useful for predicting the risk of pressure ulcers than any of the other indicators (Braden score, Alb, Hb, or CRP) used alone (fig 1). We could not compare Braden score and the new indicator simply, because determination of the Braden score and laboratory tests were different. However, the new indicator had a sufficiently high area of under the ROC curve. We considered the new indicator more useful, for the following reasons. The value of the new indicator increases 9–11 days before the onset of pressure ulcers.

Table 5 Areas under the receiver operating characteristic curves

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Areas under the curves</th>
<th>Standard error</th>
<th>z Value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>New indicator</td>
<td>0.79</td>
<td>0.055</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alb</td>
<td>0.58</td>
<td>0.065</td>
<td>3.28</td>
<td>0.011</td>
</tr>
<tr>
<td>Hb</td>
<td>0.61</td>
<td>0.059</td>
<td>2.72</td>
<td>0.006</td>
</tr>
<tr>
<td>CRP</td>
<td>0.62</td>
<td>0.059</td>
<td>2.75</td>
<td>0.006</td>
</tr>
<tr>
<td>Braden score</td>
<td>0.56</td>
<td>0.067</td>
<td>3.07</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Alb, albumin; Hb, haemoglobin; CRP, C-reactive protein.
Various scales have been devised to predict development of pressure ulcers; however, none of these scales facilitates clinically reliable prediction.

A new predictive indicator for the development of pressure ulcers has been created, based on a multiple logistic regression equation using the combination of haemoglobin (Hb), C-reactive protein (CRP), albumin (Alb), age, and gender.

The new indicator showed high sensitivity (0.73) and specificity (0.70), and its diagnostic power was higher than that of Alb, Hb, CRP, or the Braden Scale alone.

The new indicator may become a more useful clinical tool for predicting pressure ulcers than the Braden Scale.
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