


## Article

# Examination of a Short-Term, Prognostic Predictive Method for Terminal Cancer Patients Using the Barthel Index

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**Abstract:** For the estimation of short-term prognosis in terminal cancer patients, it is important to establish a prognostic index that does not involve blood tests. We compared the prognostic ability of the Barthel Index (BI) with the Glasgow Prognostic Score (GPS). Ninety-seven inpatients with terminal cancer at Onomichi Municipal Hospital who died between 2018 and 2019 were retrospectively analyzed. The sensitivity, specificity, accuracy, and area under the receiver operating characteristic curve (AUROC) were compared between the BI and GPS. For predicting the 15 day prognosis, the BI showed higher specificity, accuracy, and AUROC than the GPS. For predicting the 30 day prognosis, the BI showed higher sensitivity, accuracy, and AUROC than the GPS. The BI can predict the 15 or 30 day prognosis in terminal cancer patients. As the BI does not require blood tests, it may be an option for prognostic prediction in terminal cancer patients.

**Keywords:** Barthel Index (BI); terminal cancer patients; Glasgow Prognostic Score (GPS); Activities of Daily Living (ADL)

## 1. Introduction

Short-term prognostic prediction is important for terminal cancer patients and medical staff in palliative care. For patients, a prognosis of 30 days or fewer represents the last chance for them to make final decisions. For example, Steinhäuser et al. reported that patients want to know how much time they have left, and they want to receive their treatment preferences in writing [1]. For medical staff, short-term prognostic prediction is useful to determine appropriate medical interventions [1]. Niki et al. reported that if depressed patients are unlikely to survive for several weeks, antidepressants would rarely be prescribed because they take at least two weeks to bring about improvement and could cause unpleasant anticholinergic side effects [2]. Similarly, Morita et al. reported that although midazolam is frequently used in palliative care settings, tolerance can develop, and thus, midazolam should be used for patients with an estimated short prognosis, such as a few weeks [3]. Currently, there are several short-term, prognostic predictive methods, but most require subjective medical staff

judgment, so predictions still depend on staff experience [4–7]. Therefore, a method that can objectively predict prognosis is required.

The Glasgow Prognostic Score (GPS), the combination of C-Reactive Protein (CRP) and Albumin (Alb), has been an objective method for predicting survival rates in patients with inoperable non-small cell lung cancer [8]. Miura et al. reported that the GPS [8] can predict three week prognosis with higher sensitivity than the Palliative Prognostic Index (PPI) [9,10]. However, GPS assessment requires blood tests, and Chow et al. reported that routine blood tests should be avoided if not directly related to the control of symptoms [11]. Therefore, there is a need for a method of predicting the prognosis without blood tests.

On the other hand, Bennett et al. reported the relevance of the Barthel Index (BI) [12], which is a typical Activities of Daily Living (ADL) index, to the prognosis of terminally ill patients in a hospice [13]. Godfrey et al. reported the same in palliative care patients [14]. The BI [12] was originally established to assess ADL in stroke patients and is now widely used as a simple method to assess ADL for various diseases.

In this study, we focus on the BI [12], without the use of blood tests, and compare the characteristics of the BI with GPS as a short-term prognostic indicator for terminal cancer patients. To the best of our knowledge, there are no reports that compare the short-term prognostic ability of the BI with other indicators.

## 2. Materials and Methods

### 2.1. Study Participants and Data Collection

Patients with major diseases, including cancer, who died during their hospitalization at Onomichi Municipal Hospital in Japan from January 2018 to December 2019 were identified from the Diagnosis Procedure Combination (DPC) claims database and retrospectively analyzed. Initially, one-hundred thirty patients were enrolled, and ninety-seven were selected after exclusion of 33 patients with missing data on the BI and GPS (a combination of CRP and Alb) from the 2 days before and after admission. Age, gender, primary cancer, BI, CRP, and Alb values were recorded at admission. All test results from within 2 days before and after admission were extracted. The duration between admission and death was also investigated.

### 2.2. BI and GPS Evaluation Methods

The BI [12] was developed to measure disability and is one of the most commonly used ADL scales. The BI includes 10 personal activities: feeding, moving from a wheelchair to the bed and returning, personal toilet, getting on and off the toilet, bathing one's self, walking on a level surface, ascending and descend stairs, dressing, controlling bowels, and controlling bladder. The BI scale measures patients' actual performance in basic ADLs by inquiry and/or observation, and the 10 items are scored using arbitrary weightings (0, 5, 10, or 15) to arrive at a total possible score range of 0 to 100. Patients were grouped into three ADL groups by individual BI scores as follows: "BI 0–35", "BI 40–75", and "BI 80–100" [15].

The GPS [8] was constructed as previously described. Patients with both an elevated CRP ( $>1.0$  mg/dL) and Alb ( $<3.5$  g/dL) were allocated a score of 2. Patients in whom only one of these biochemical abnormalities was present were allocated a score of 1. Patients in whom neither of these abnormalities was present were allocated a score of 0.

### 2.3. Predictive Performance

Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), accuracy, and Area Under the Receiver Operating Characteristic curve (AUROC) for predicting 15 or 30 day prognosis were calculated for the BI and GPS.

## 2.4. Statistical Analysis

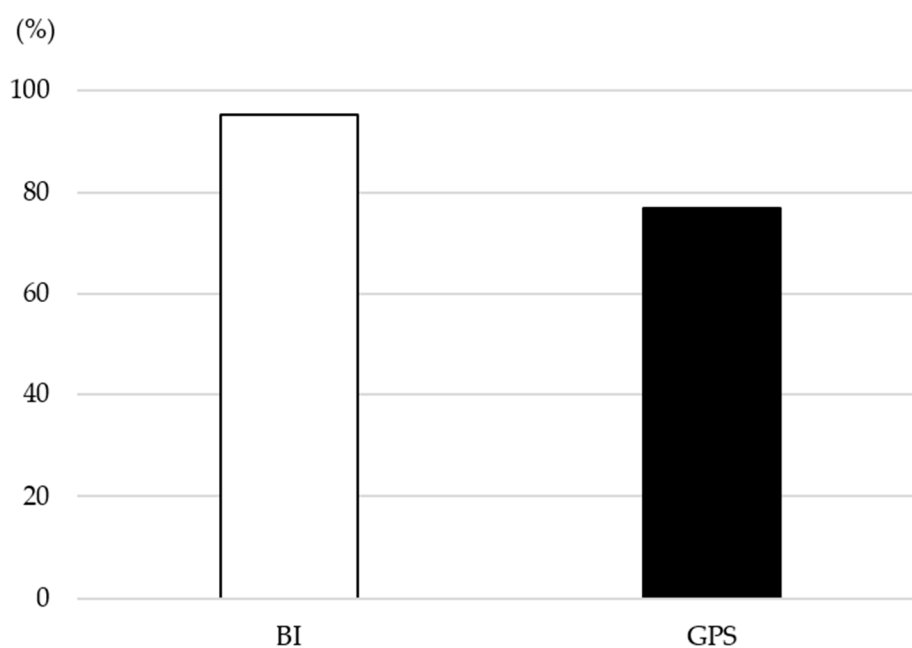
Cutoff values predicting prognosis and AUROC were determined by plotting a Receiver Operating Characteristic curve (ROC) for the BI and GPS. Survival or death within 15 or 30 days after admission were defined as dependent variables, and the BI and GPS were defined as independent variables. The Kaplan–Meier method and the log-rank test were performed by the three groups of BI (BI 0–35, BI 40–75, BI 80–100). Patients who were alive 60 days after admission were censored for analysis. For calculating the sample size, we assumed that at least 97 patients with all examination results were needed to calculate accuracy within a 20% width in 95% confidence intervals for a 50% value. A *p*-value less than 0.05 was considered statistically significant for all tests. All statistical analyses were performed with EZR Version 1.40 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [16]. Continuous or ordinal variables are presented as the median (25–75% Interquartile Range (IQR)). Categorical variables are expressed as numbers and percentages.

## 2.5. Ethical Considerations

The study protocol was designed to adhere to ethical guidelines for medical and health research involving human subjects and was approved by the research ethics committee of Onomichi Municipal Hospital (Approval Number 20-7, 1 May 2020). The collected data were anonymized so that it was not possible for third parties to easily identify specific individuals.

## 3. Results

BI screening was carried out on 95.4% of patients, and the GPS screening was carried out on 76.9% of patients (Figure 1). In other words, the rate of administration of BI was higher than that of the GPS.



**Figure 1.** Screening rates according to the BI and GPS. BI: Barthel Index, GPS: Glasgow Prognostic Score.

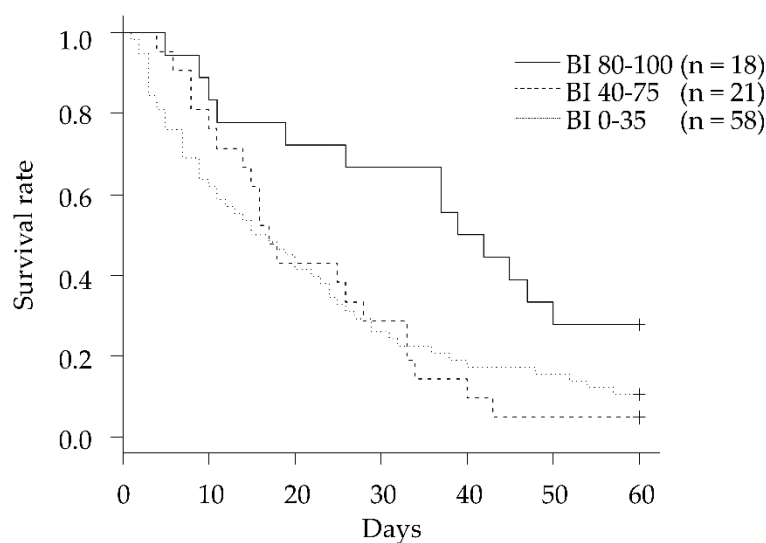
Patient backgrounds are presented in Table 1. The median (IQR) age was 80 (72–86) years. The percentage of males was 64.9%. The median (IQR) duration between admission and death was 19 (9–38) days.

**Table 1.** Baseline characteristics of the study population.

Characteristic	Finding
N	97
Age (years), median (IQR)	80 (72–86)
Gender (male), n (%)	63 (64.9)
Primary cancer, n (%)	
Gastric	15 (15.5)
Lung malignant mesothelioma	12 (12.4)
Blood	12 (12.4)
Pancreatic	11 (11.3)
Colon and rectum	10 (10.3)
Biliary tract	10 (10.3)
Liver	8 (8.2)
Brain	6 (6.2)
Prostate	4 (4.1)
Bladder	2 (2.1)
Others	7 (7.2)
Duration between admission and death (days), median (IQR)	19 (9–38)

IQR: Interquartile Range.

The percentage of deaths according to the BI and Kaplan–Meier survival curves for the three groups are presented in Figure 2. The BI 0–35 group was 58 patients; the BI 40–75 group was 21 patients; and the BI 80–100 group was 18 patients. The Kaplan–Meier survival curves showed that survival rates differed among them (log-rank test,  $p = 0.02$ ). Table 2 shows the sensitivity, specificity, PPV, NPV, accuracy, and AUROC of each prognostic method calculated using the cutoff values from the ROC and survival analyses. The BI values with the highest Youden index for the ROC curve were 0–35 within 15 days after admission and 0–75 within 30 days after admission. The GPS values with the highest Youden index for the ROC curve were both two within 15 and 30 days after admission. For predicting 15 day prognosis, using a cutoff of BI 40–100/0–35 showed higher specificity (0.474), PPV (0.466), NPV (0.718), accuracy (0.567), and AUROC (0.593) than the GPS. Furthermore, for predicting 30 day prognosis, using a cutoff of BI 80–100/0–75 showed higher sensitivity (0.906), PPV (0.734), NPV (0.667), accuracy (0.722), and AUROC (0.635) than the GPS.



**Figure 2.** Survival analysis. The Kaplan–Meier method and the log-rank test were performed by classifying the BI (BI 0–35, BI 40–75, BI 80–100). The BI 0–35 group was 58 patients; the BI 40–75 group was 21 patients; and the BI 80–100 group was 18 patients. BI: Barthel Index.

**Table 2.** Sensitivity, specificity, positive and negative predictive values, accuracy, and area under the receiver operating characteristic curves of the Barthel Index and Glasgow Prognostic Score.

Variable	Predictive Period (Days)	Cutoff Value	Sensitivity	Specificity	PPV	NPV	Accuracy	AUROC
BI	15	40–100/0–35	0.711	0.474	0.466	0.718	0.567	0.593
BI	15	80–100/0–75	0.895	0.237	0.430	0.778	0.495	0.566
GPS	15	0,1/2	0.816	0.288	0.425	0.708	0.495	0.552
GPS	15	0/1,2	0.947	0.102	0.404	0.750	0.433	0.525
BI	30	40–100/0–35	0.672	0.545	0.741	0.462	0.629	0.609
BI	30	80–100/0–75	0.906	0.364	0.734	0.667	0.722	0.635
GPS	30	0,1/2	0.813	0.364	0.712	0.500	0.660	0.588
GPS	30	0/1,2	0.953	0.152	0.685	0.625	0.680	0.552

AUROC, Area Under the Receiver Operating Characteristic Curve; BI, Barthel Index; GPS, Glasgow Prognostic Score; NPV, Negative Predictive Value; PPV, Positive Predictive Value.

## 4. Discussion

The purpose of this study was to compare the characteristics of the BI as a short-term prognostic indicator with the GPS for terminal cancer patients. The rate of BI administration was higher than that of the GPS. For predicting 15 day prognosis, a cutoff of BI 40–100/0–35 showed higher specificity, PPV, NPV, accuracy, and AUROC than the GPS. For predicting 30 day prognosis, a cutoff of BI 80–100/0–75 showed higher sensitivity, PPV, NPV, accuracy, and AUROC than those of the GPS. These results suggest that the BI can predict 15 or 30 day prognosis for terminal cancer patients better than GPS.

Doctors need to judge the start or continuation of treatment according to the prognosis of each terminal cancer patient. Steinhauser et al. reported that the prognosis of dying patients is very important to doctors and health care providers in terms of determining treatment options [1].

Bennett et al. reported the change rates of the BI were more important indicators of prognosis than absolute measures in terminally ill patients in a hospice [13]. Additionally, Godfrey et al. reported that length of prognosis could be informed by the BI on admission and change rates of the BI in palliative care patients [14]. From the above reports, the change rates of the BI may also be important in short-term prognosis [14].

This study had some limitations. First, in this study, we did not investigate the effects of variables such as gender on the results, and thus, further studies are needed on this effect. Second, because this study was a retrospective study, the BI could not be directly compared with existing prognostic methods used to predict short-term prognosis, such as the PPI and Prognosis in Palliative care Study predictor models [17]. Third, the findings cannot be generalized because verification was performed at a single facility. Therefore, a multicenter validation study is required in the future.

**Author Contributions:** M.O. and K.O. conceived of and designed this study. M.O. and K.O. collected the data, and M.O. and K.B. analyzed the data. F.M., S.O., K.B., H.S., T.O., E.T., S.T., and N.S. supervised the conducting of this study. M.O. and K.O. drafted the manuscript, and all authors contributed substantially to its revision. All authors have read and agreed to the published version of the manuscript.

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**Conflicts of Interest:** The authors declare no conflict of interest.

## References

- Steinhauser, K.E.; Christakis, N.A.; Clipp, E.C.; McNeilly, M.; Grambow, S.; Parker, J.; Tulskey, J.A. Preparing for the end of life: Preferences of patients, families, physicians, and other care providers. *J. Pain Symptom Manag.* **2001**, *22*, 727–737. [\[CrossRef\]](#)
- Niki, K.; Okamoto, Y.; Matano, Y.; Ishii, R.; Matsuda, Y.; Takagi, T.; Uejima, E. Validation of a short-term, objective, prognostic predictive method for terminal cancer patients in a palliative care unit using a combination of six laboratory test items. *J. Palliat. Med.* **2019**, *22*, 685–690. [\[CrossRef\]](#) [\[PubMed\]](#)

3. Morita, T.; Tei, Y.; Inoue, S. Correlation of the dose of midazolam for symptom control with administration periods: The possibility of tolerance. *J. Pain Symptom Manag.* **2003**, *25*, 369–375. [[CrossRef](#)]
4. Gripp, S.; Moeller, S.; Bölke, E.; Schmitt, G.; Matuschek, C.; Asgari, S.; Asgharzadeh, F.; Roth, S.; Budach, W.; Franz, M.; et al. Survival prediction in terminally ill cancer patients by clinical estimates, laboratory tests, and self-rated anxiety and depression. *J. Clin. Oncol.* **2007**, *25*, 3313–3320. [[CrossRef](#)] [[PubMed](#)]
5. Hui, D.; Park, M.; Liu, D.; Paiva, C.E.; Suh, S.Y.; Morita, T.; Bruera, E. Clinician Prediction of Survival Versus the Palliative Prognostic Score: Which Approach Is More Accurate? *Eur. J. Cancer* **2016**, *64*, 89–95. [[CrossRef](#)] [[PubMed](#)]
6. Christakis, N.A.; Lamont, E.B. Extent and determinants of error in doctors' prognoses in terminally ill patients: Prospective cohort study. *BMJ* **2000**, *320*, 469–472. [[CrossRef](#)] [[PubMed](#)]
7. Glare, P.; Virik, K.; Jones, M.; Hudson, M.; Eychmuller, S.; Simes, J.; Christakis, N. A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ* **2003**, *327*, 195–198. [[CrossRef](#)] [[PubMed](#)]
8. Forrest, L.M.; McMillan, D.C.; McArdle, C.S.; Angerson, W.J.; Dunlop, D.J. Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. *Br. J. Cancer* **2003**, *89*, 1028–1030. [[CrossRef](#)] [[PubMed](#)]
9. Morita, T.; Tsunoda, J.; Inoue, S.; Chihara, S. The Palliative Prognostic Index: A scoring system for survival prediction of terminally ill cancer patients. *Support. Care Cancer* **1999**, *7*, 128–133. [[CrossRef](#)] [[PubMed](#)]
10. Miura, T.; Matsumoto, Y.; Hama, T.; Amano, K.; Tei, Y.; Kikuchi, A.; Suga, A.; Hisanaga, T.; Ishihara, T.; Abe, M.; et al. Glasgow prognostic score predicts prognosis for cancer patients in palliative settings: A subanalysis of the Japan-prognostic assessment tools validation (J-Pro Val) study. *Support. Care Cancer* **2015**, *23*, 3149–3156. [[CrossRef](#)] [[PubMed](#)]
11. Chow, E.; Harth, T.; Hruby, G.; Finkelstein, J.; Wu, J.; Danjoux, C. How accurate are physicians' clinical predictions of survival and the available prognostic tools in estimating survival times in terminally ill cancer patients?—A systematic review. *Clin. Oncol.* **2001**, *13*, 209–218. [[CrossRef](#)]
12. Mahoney, F.I.; Barthel, D.W. Functional Evaluation: The Barthel Index. *Md. State Med. J.* **1965**, *14*, 61–65. [[PubMed](#)]
13. Bennett, M.; Ryall, N. Using the modified Barthel index to estimate survival in cancer patients in hospice: Observational study. *BMJ* **2000**, *321*, 1381–1382. [[CrossRef](#)] [[PubMed](#)]
14. Godfrey, J.; Poole, L. An audit of the use of the Barthel Index in palliative care. *Int. J. Palliat. Nurs.* **2007**, *13*, 543–548. [[CrossRef](#)] [[PubMed](#)]
15. Sinoff, G.; Ore, L. The Barthel activities of daily living index: Self-reporting versus actual performance in the old-old (> or =75 years). *J. Am. Geriatr. Soc.* **1997**, *45*, 832–836. [[CrossRef](#)] [[PubMed](#)]
16. Kanda, Y. Investigation of the freely available easy-to-use software 'EZ' for medical statistics. *Bone Marrow Transplant.* **2013**, *48*, 452–458. [[CrossRef](#)] [[PubMed](#)]
17. Gwilliam, B.; Keeley, V.; Todd, C.; Gittins, M.; Roberts, C.; Kelly, L.; Barclay, S.; Stone, P.C. Development of Prognosis in Palliative care Study (PiPS) predictor models to improve prognostication in advanced cancer: Prospective cohort study. *BMJ Support. Palliat. Care* **2012**, *2*, 63–71. [[CrossRef](#)] [[PubMed](#)]

