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*Session: What Does the Future Hold? Prognostication in Advanced Cancer and Clinical Decision Making*

# Development and initial validation of a prognostic nomogram for ambulatory patients with advanced cancer

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# Background

✓ Oncologists frequently face the difficult task of estimating prognosis in patients with incurable malignancies.

✓ Their prediction of prognosis informs decision making ranging from recommendations of cancer treatments to hospice enrollment

Krishnan et al. J Support Oncol, 2013; 11(2):68-74

✓ CPS is often inaccurate and usually too optimistic, which may result in overly aggressive cancer treatment

White et al. PLoS One 11:e0161407
Amano et al. J Pain Symptom Manage 50:139–146

# Background

✓ Most of the studies describe a sample of patients with advanced disease, a low functional performance, and a short life expectancy.

Simmons et al. J Pain Symptom Manage 53:962–970

✓ Few studies have evaluated the prognosis of outpatients with advanced cancer who are receiving anticancer treatment and concomitantly undergoing PC.

# Aim

✓ To develop and test a new prognostic tool in ACP when they were first referred to PC.

# Methods

**Design:** prospective, observational study

**Setting:** Barretos Cancer Hospital (Barretos-SP, Brazil)

## Development Phase

from Mar/2011 to Apr/2012
Sample size: a ratio of at least 1:10 between the number of events vs the number of predictors in the multivariate model (150 events)

## Validation Phase

from Apr/2014 to Oct/2014
Sample size: proportion of correct answers of 80%; an absolute error = 5%, and a level of significance of 5% n = 246; 10% rate of lack of information, minimum of 270 pts

# Methods (data collection)

## Development sample

**35 initial putative prognostic variables**

- ✓Patient characteristics (age, gender)
- ✓Tumor characteristics (type , metastasis, treatment)
- ✓Nutritional aspects (BMI, edema, ascitis, feeding tubes)
- ✓KPS
- ✓HRQOL indices (EORTC QLQ-C30)
- ✓Cancer symptoms (ESAS),
- ✓Blood samples (CBC, Calcium, LDH, Albumin, CRP)

**Cox regression analyses**

**Nomogram**

## Validation sample

Data regarding patient characteristics, KPS, and blood samples (complete blood count and serum albumin levels) were collected by the research nurses during the initial evaluation

# Methods (statistical analysis)

- Patients were followed until death.
- Follow-up was terminated after reaching a predefined rate of at least 70% of deaths (development phase =155 from 221; validation phase = 194 from 276)

## Development sample

- ✓ Univariate and multivariate Cox regression survival analyses.
- ✓ All variables with p <0.2 were entered in the multivariate model (stepwise method).
- ✓ The final prognostic model was used to develop the BPN
- ✓ Nomogram function (rms package version 4.0) and the coxph function (Survival package version 2.37-4) of R statistical software version 2.15.1.

# Methods (statistical analysis)

## Validation sample

| Validation | Analysis | Expected values |
|---|---|---|
| **Discrimination** | Survival analysis | Kaplan-Meier survival curves were constructed to compare survival according with BPN category |
| | ROC curve calculation | The BPN scores were used as continuous variables and the occurrence of death (yes/no) as a categorical variable in ROC curve analyses |
| | C-index | >0.5 = no discrimination; 1.0 = perfect discrimination between the expected and the observed outcomes |
| | Kolmogorov- Smirnov (K-S) goodness of fit | Measure the ability of BPN to discriminate between groups (alive vs death). According to the sample size, a value > 0.081 was expected |
| **Calibration** | Hosmer-Lemeshow goodness of fit | It evaluates the quality of fit of the model; adequate results should be nonstatistically significant (*P > .05).* |

# Results (construction of nomogram)

**35 initial putative prognostic variables**

**14 variables (univariate analysis; p<0.2)**

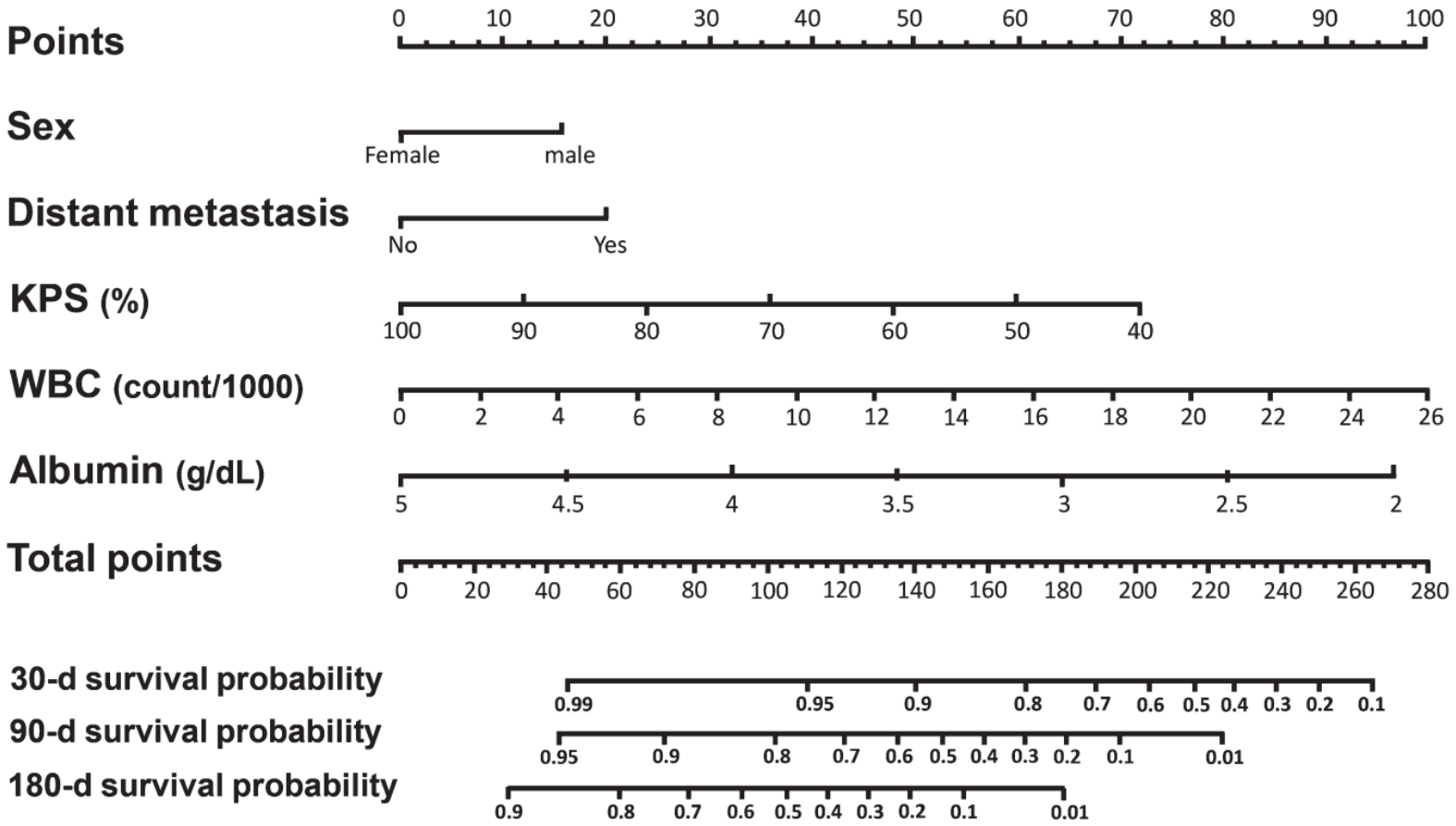
**Final model**

| Variables | B (SE) | Exp (B) | 95% CI | *P*-value |
|---|---|---|---|---|
| Female | −0.373 (0.176) | 0.689 | 0.488-0.972 | .034 |
| KPS | −0.030 (0.006) | 0.971 | 0.959-0.982 | <.001 |
| Albumin | −0.966 (0.162) | 0.380 | 0.277-0.522 | <.001 |
| Distant metastasis | 0.587 (0.208) | 1.799 | 1.196-2.706 | .005 |
| WBC count | 0.086 (0.023) | 1.089 | 1.042-1.139 | <.001 |

# Characteristics of patients in the training and validation cohorts

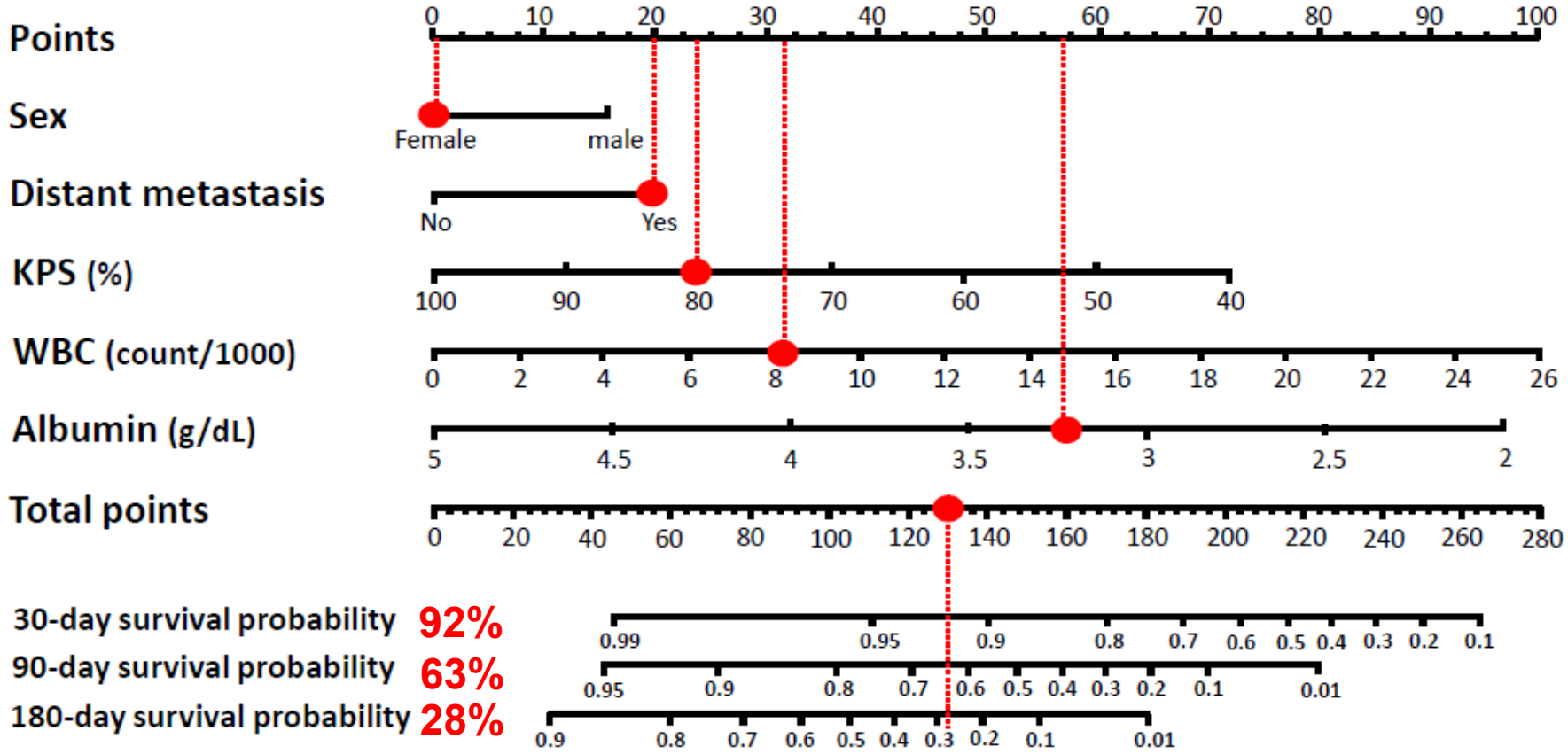
| Characteristics | Training set (n=221) | | Validation set (n=276) | |
|---|---|---|---|---|
| | N | % | N | % |
| Age (years) | | | | |
| median (p25-p75) | 61.0 | 52-70.5 | 60.2 | 52.6-69.4 |
| Gender | | | | |
| Woman | 109 | 49.3 | 164 | 59.4 |
| Man | 112 | 50.7 | 112 | 40.6 |
| Site of metastasis | | | | |
| Lung (Yes) | 59 | 26.7 | 92 | 33.3 |
| Hepatic (Yes) | 41 | 18.6 | 93 | 33.7 |
| Bone (Yes) | 62 | 28.1 | 102 | 37.0 |
| Central nervous system (Yes) | 15 | 6.8 | 26 | 9.4 |
| KPS (score) | | | | |
| median (p25-p75) | 80 | 60-90 | 60 | 50-70 |

# Results (construction of nomogram)



# Case example

female (0 points), breast cancer with bone and lung metastasis (20 points), KPS=80% (24 points), WBC=8,125 (31,5 points), serum albumin=3.25 (57 points); total points =132.5.

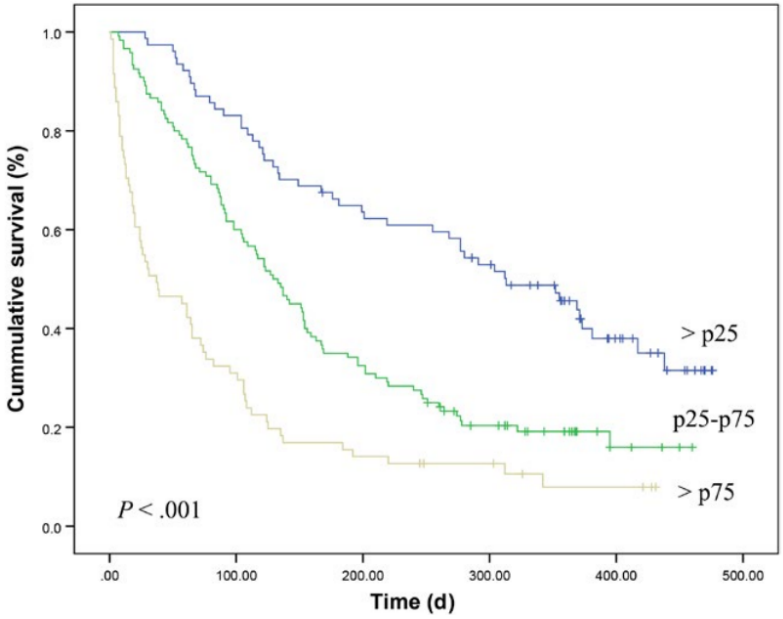


# Results (construction of nomogram)

**Calibration and discrimination results of BPN**

| Characteristics | 30 d | 90 d | 180 d |
|---|---|---|---|
| Cutoff scores | 162 | 150 | 142 |
| Area under the ROC curve | 0.840 | 0.743 | 0.741 |
| Sensitivity | 78.4% | 66.3% | 66.7% |
| Specificity | 74.9% | 65.2% | 69.4% |
| NPV | 93.6% | 75.3% | 55.7% |
| PPV | 42.5% | 54.7% | 78.3% |
| K-S | 0.537 | 0.342 | 0.383 |
| C-index | 0.71[a] | 0.71[a] | 0.71[a] |
| Hosmer-Lemeshow | $P = .538$ | $P = .580$ | $P = .756$ |

**Overall survival curves according to BPN scores in validation sample.**




## Median survival times:

< 25th percentile = **313 days**

25th-75th percentile = **129 days**

> 75th percentile = **37 days**

# Conclusions

✓The BPN is a new prognostic tool with adequate calibration and discrimination properties.

✓Although it should be considered a valid tool to be used in the prognostication of adult patients with advanced solid tumors, its prognostic capacity is not ideal.

✓Further strategies of prognostication and improvements in the BPN should be tested in future studies.

# Research Perspectives

**Future prospective studies are needed to:**

- ✓ Compare the BPN with the other prognostic tools
- ✓ Test the feasibility of BPN in other clinical settings
- ✓ To create an online tool with results with probabilities of survival and survivals in best and worst case scenarios