**Development of a cachexia integrated nomogram to predict survival for inpatients with advanced cancer.**

Author(s)
Zhimeng Jia, MD CCFP
University of Alberta

**Background:** For palliative care consultants, robust, validated prognostic tools are necessary in guiding treatment decisions, goals of care discussions, and disposition planning. Nomograms have been widely accepted as practical prognostic tools.[1,2,3] Our objective was to develop a prognostic nomogram to predict overall survival (OS) in advanced cancer inpatients with a focus on demographic, disease and cachexia features.
Methods: 292 adult, advanced cancer inpatients seen by an acute care palliative care consult team from August 2008 to August 2009 were included in this study. Computed tomography images were assessed for total area and radiodensity of skeletal muscle and subcutaneous adipose tissue.[4] Univariate and multivariate Cox proportional hazard modelling with forward selection was used to evaluate covariates for inclusion in the final OS model. To model non-linear, mortality-related threshold(s) in continuous variables, restricted cubic splines were used. The final Cox multivariate analyses were used to formulate a nomogram.

**Results:** Patients were 97% deceased, 57% male, 67 ± 13 years of age, mean ECOG of 2.4 [95%CI 1.6-2.3], and median OS of 74 days [95%CI 58-90d]. Factors unrelated to OS at the univariate level ($p > 0.05$) included dyspnea, brain metastasis, and recent (< 4 weeks) venous thromboembolic events. Covariates eliminated in the multivariate analysis ($p > 0.05$) included lymphocyte count, neutrophil count, delirium, dysphagia, anorexia, and recent (< 4 weeks) ICU stay, sepsis, and infection. Cachexia features related to OS at the univariate level ($p < 0.000$) include oral intake (3 categories: severely reduced, moderately reduced, and normal), fat depletion (2 categories: radiodensity ≥ -81 and < -81 Hounsfield units), and reduced muscle mass (3 categories: very low, low, and normal). A 4-category index of these features provided survival discrimination (Log-rank test $p < 0.000$) with median OS of 149d [117-181d], 90d [70-110d], 43d [33-53d] and 16d [0-32d]. Next, three cancer diagnosis groups also provided median OS discrimination ($p<0.000$): Central nervous system and breast (126d [80-172d]); Gastrointestinal, lung, hematologic, gynecological, and urinary tract (73d [58-88d]); Primary unknown and head and neck (43d [32-54d]). ECOG ($p < 0.000$) and aspiration ($p < 0.000$) were also significant at univariate level. In the final multivariable model: three categories of cancer diagnosis ($p=0.032$), ECOG ($p=0.002$), aspiration ($p=0.004$), and the 4-category cachexia index ($p=0.001$) were independent predictors of OS; age ($p=0.534$), and sex ($p=0.112$) were not. The nomogram formulated from the multivariate analysis with survival probabilities at 14, 30, 90 and 180 days, can be accessed
here: https://www.dropbox.com/s/5f0j8eg3383rlbe/Nomographs%2020March2019.docx?dl=0

**Discussion:** We identified clinically accessible information in advanced cancer inpatients and rigorously evaluated their prognostic values. The results suggest that the prognostic value of cachexia may supersede other commonly accepted clinical (e.g. delirium) and laboratory variables (e.g. lymphocyte count). Next, CT imaging data is shown to be a readily available objective measurement for cachexia severity with survival discrimination in this population. Finally, we were able to transform the results of the multivariate analysis into a practical prognostic tool to aid palliative care consultants in the care of advanced cancer inpatients. External validation of the nomogram to evaluate its accuracy and applicability across different care settings is in progress.

**References**

1. Touijer K, and Scardino PT. Nomograms for staging, prognosis, and predicting treatment outcomes. *Cancer*. 2009;115:3107-3111. doi:10.1002/cncr.24352

2. Yap W, Shih M, Kuo C, et al. Development and Validation of a Nomogram for Assessing Survival in Patients With Metastatic Lung Cancer Referred for Radiotherapy for Bone Metastases. *JAMA Netw Open.*2018;1(6):e183242. doi:10.1001/jamanetworkopen.2018.3242

3. Miao DL, Song W, Qian J, et al. Development and Validation of a Nomogram for Predicting Overall Survival in Pancreatic NeuroendocrineTumors. *Transl Oncol*. 2018;11(5):1097–1103. doi:10.1016/j.tranon.2018.06.012

4. Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. *Appl Physiol Nutr Metab*. 2008;33:997–1006