A Nomogram Predicting the Benefit of Adjuvant Therapy in Resected Pancreatic Ductal Adenocarcinoma

P. J. Worth, C. Bicquart, R. El Youssef, A. R. Wissel, E. W. Gilbert, B. C. Sheppard, K. G. Billingsley, C. R. Thomas, S. Y. Wang
Oregon Health & Science University (OHSU), Portland, OR

Background:
Pancreatic ductal adenocarcinoma (PDA) remains a cancer that poses significant clinical challenges. Five year survival rates remain below 20% despite significant advances in our understanding and treatment. Surgery remains the only potentially curative treatment, however only about 10-20% of tumors are detected at a resectable stage, and even then outcomes remain poor. There is a role for adjuvant chemo- and radio-therapy in improving survival and loco-regional control, however no clear consensus exists as to the optimal treatment. Currently, radiotherapy is aimed at improving local margins and resection bed recurrence rates whereas chemotherapy addresses occult systemic disease. Treatment is generally based on patient- and pathology-specific factors. Identifying which patients will benefit most from a course of adjuvant therapy and the magnitude of that benefit remains a challenge. The aims of this investigation were to review our center's experience and create a tool for clinicians to utilize in estimating survival benefit from chemotherapy or chemoradiotherapy (CRT).

Materials and Methods:
We retrospectively reviewed charts of patients who underwent pancreatectomy with curative intention for PDA from 1996-2010. Primary endpoints included overall survival after surgery alone, surgery with adjuvant chemotherapy, or surgery with adjuvant chemoradiotherapy. Potential covariates including age, sex, lymphadenectomy, lymph node status, histologic grade, margin status, lyphovascular space involvement (LVSI), and perineural invasion (PNI) were collected. Several types of multivariate survival regression models –including Cox proportional hazards, Weibull, exponential, log-logistic, and log-normal—were constructed and compared. Forward stepwise variable selection was used to select the final covariates included in the model. Model performance was compared using the Akaike Information Criterion (AIC). The best performing model was internally-validated for both discrimination (concordance index) and calibration (calibration curve) using bootstrap resampling.

Results:
A total of 179 patients were included in the study. At the time of analysis, 146 patients had expired (82%). For the entire cohort, median survival was 16.4 months. Subdivided into treatment groups, median survival for surgery alone was 15.2 months; surgery with chemotherapy 12.6, and surgery with chemoradiotherapy 20.8 months. In comparing regression models with the AIC, log-logistic and log-normal methods were found to have the least information loss and best performance. We found that nodal involvement, margins, and PNI had the most effect on outcome estimates. Patients with positive nodes, margins, or PNI also derived the most benefit from adjuvant chemoradiotherapy in our model. We selected the log-normal model for incorporation into a web-based application to estimate survival benefit following surgical resection of PDA with and without chemotherapy or CRT. The model was found to have a concordance index of 0.66.

Conclusions:
The model generated from our institution's experience is a parametric model which allows clinicians to estimate the benefit an patient with a particular tumor and resection may gain from adjuvant therapy. This allows for improved clinical guidance and may serve to aid in decision making on the part of patients and their families.

Disclosures: none.