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A Retrospective Cohort Study of 1,301 Patients with Pancreatic Neuroendocrine Tumors Identifies Prolonged Survival After Surgical Resection Even in Advanced Stages

Benjamin D. Powers[1,1]; *Ambuj Kumal[2]; Jason B. Fleming[1]; Jonathan Strosberg[1]; Daniel A. Anaya[1]*

[1]Moffitt Cancer Center; [2]USF Morsani College of Medicine

BACKGROUND: The management of patients with PNETs according to clinical stage and tumor grade remains controversial. The new AJCC Staging Manual attempts to address this through a new staging system for PNETs that excludes poorly-differentiated tumors (neuroendocrine carcinoma). In this study, we assess surgical utilization and impact on survival in patients with well- and moderately-differentiated PNETs using AJCC 8th criteria and measure outcomes for stage I and IV disease.

METHODS: Using data from the NCDB (2004-2013) we included patients 18 years or older with pancreatic tumors (C25.0 to 25.9); tumor histology codes for PNETs; and well-differentiated and moderately-differentiated tumors (n=1,301). Poorly or undifferentiated and neuroendocrine carcinomas were excluded. Univariate and multivariate logistic and Cox regression models were used to examine predictors of surgery and overall survival.

RESULTS: 1,151 patients (88.5%) underwent surgical resection. In multivariate logistic regression, age ≥ 70 was associated with a lower likelihood of surgery for all stages ($p<0.05$). Beyond this, drivers of surgical utilization varied significantly by stage; for clinical stage I patients, surgery was more likely for patients with body or tail tumors relative to pancreatic head tumors while for stage IV patients,

surgery was driven by treatment at an academic facility. On multivariate Cox regression, surgical utilization was associated with increased survival for the whole cohort as well as stage II/III and stage IV patients specifically, and was not associated with survival for stage I patients (data in Table 1).

CONCLUSION: When staged according to the 8th Edition of the AJCC Manual, surgical resection the PNET was associated with improved survival in patients of all stages except stage I. This observation suggests that local control of the primary PNET through surgical resection drives outcomes even in patients with advanced stage and should be considered in the multidisciplinary management of PNETs.

Table 1:

Predictors of Receipt of Surgery and Survival for Well- and Moderately-Differentiated PNETs

Relative Odds of Surgery	All Stages	Stage I	Stage IV
Age ≥ 70 years (reference: <70y)	0.31 [0.18-0.54]	0.04 [0.01-0.20]	0.24 [0.06-0.89]
Body/tail tumor (reference: head)	1.60 [1.00-2.56]	3.50 [1.45-8.44]	1.02 [0.41-2.57]
Charlson-Deyo Score 1+ (reference: 0)	1.23 [0.79-1.94]	0.92 [0.33-2.56]	1.43 [0.55-3.72]
Community Facility (reference: academic)	0.38 [0.25-0.59]	0.65 [0.27-1.56]	0.17 [0.06-0.44]
Relative Hazard of Death			
Surgical Resection (reference: none)	0.28 [0.17-0.49]	0.58 [0.17-2.00]	0.25 [0.10-0.65]
Age ≥ 70 years (reference: <70y)	2.48 [1.43-4.31]	2.12 [0.89-5.04]	4.86 [2.24-10.53]
Charlson-Deyo Score 1+ (reference: 0)	2.01 [1.30-3.11]	2.32 [1.03-5.22]	1.52 [0.72-3.24]
Community Facility (reference: academic)	1.02 [0.63-1.66]	2.54 [1.10-5.83]	0.66 [0.29-1.48]

Relative Odds of Surgery: Multivariate Logistic Regression (Adjusted OR [95% CI]) and Relative Hazard of Death: Cox Proportional Hazards Models (Adjusted HR [95% CI]). Additional covariates assessed and/or included in models were sex, race, year of diagnosis, TNM, grade, functional status and insurance status.