



A Retrospective Cohort Study of 4,739 Patients with Pancreatic Neuroendocrine Tumors Identifies Prolonged Survival After Surgical Resection Even in Advanced Stages

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ABSTRACT

- 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 and undifferentiated 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 stages I, II/III, 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
- Poorly or undifferentiated neuroendocrine tumors and carcinomas, patients who received treatment at a site other than the reporting center, patients with multiple cancers, and patients with incomplete staging data were excluded
- This identified 4,739 patients
- 8th edition staging for based on clinical TNM data was used for univariate and multivariate logistic regression models to evaluate clinicodemographic factors associated with receipt of surgery
- 8th edition staging for based on pathological TNM data was used for univariate and multivariate Cox regression models to evaluate clinicodemographic factors associated with overall survival

RESULTS: PREDICTORS OF SURGERY

- 3,866 patients (81.6%) underwent surgical resection
- 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 and less likely for patients age ≥ 70
- For stage II/III patients, age ≥ 70 , Black race, and community facility type were associated with decreased odds of surgery. Patients with body or tail tumors were more likely to receive surgery
- For stage IV patients, surgery was less likely for age ≥ 70 , Black race, other tumor location, uninsured/Medicaid/unknown patients and community facility type

Table 1: Relative Odds of Surgery by Clinical Stage at Diagnosis: Multivariate Logistic Regression

	Odds Ratios [95% CI]		
	Stage I (n=1,202)	Stage II/III (n=1,853)	Stage IV (n=1,084)
≥ 70 age at diagnosis, y (reference: <70 y)	0.31 [0.16-0.58]	0.26 [0.17-0.40]	0.63 [0.42-0.96]
Race (reference: White)			
Black	1.59 [0.61-4.13]	0.57 [0.36-0.89]	0.65 [0.44-0.96]
Other / unknown	0.68 [0.26-1.81]	1.26 [0.58-2.72]	1.03 [0.58-1.84]
Tumor location (reference: head)			
Body/tail	2.30 [1.34-3.97]	2.83 [1.90-4.21]	1.09 [0.81-1.46]
Other	2.33 [1.10-4.94]	0.86 [0.56-1.30]	0.58 [0.41-0.83]
Charlson-Devo Score (reference: 0)			
1+	0.75 [0.44-1.26]	1.35 [0.92-1.99]	1.63 [1.21-2.21]
Insurance (reference: private)			
Medicare	0.74 [0.38-1.41]	0.94 [0.60-1.46]	0.72 [0.50-1.04]
Uninsured / Medicaid / unknown	1.64 [0.56-4.89]	1.07 [0.61-1.86]	0.70 [0.49-0.99]
Facility type (reference: academic)			
Community	0.65 [0.27-1.56]	0.66 [0.46-0.93]	0.41 [0.31-0.55]
Unknown	0.55 [0.11-2.84]	1.18 [0.57-2.46]	0.98 [0.63-1.53]



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RESULTS: PREDICTORS OF SURVIVAL

- 3,551 patients had survival time data; the total number of deaths was 705
- Predictors of overall survival varied by stage
- For stage I patients, surgery and tumor location did not predict improved survival; male sex and increased comorbidity were associated with increased hazard of death
- For stage II/III patients, surgery and tumor of the body/tail were associated with decreased hazard of death. Male sex, age ≥ 70, and community facility type were associated with increased hazard of death
- For stage IV patients, age ≥ 70 and increased comorbidities were associated with increased hazard of death. Surgery decreased the hazard of death

CONCLUSIONS

- 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
- Receipt of surgery for stage I tumors is associated with age ≥ 70 and tumor location in the body/tail though these factors are not predictive of survival in this cohort
- After adjustment for other variables, receipt of surgery for stage IV patients showed a 71% decreased hazard of death
- 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 2: Relative Hazard of Death: Multivariate Cox Proportional Hazards Models (Adjusted HR [95% CI])

	Stage I	Stage II/III	Stage IV
Male sex (reference: female)	2.10 [1.01-4.35]	1.63 [1.24-2.13]	
≥70 age at diagnosis, y (reference: <70y)	2.05 [0.88-4.81]	1.36 [0.97-1.89]	1.96 [1.12-1.70]
Surgical resection (reference: none)		0.23 [0.17-0.31]	0.29 [0.23-0.38]
Tumor location (reference: head)			
Body/tail		0.63 [0.47-0.85]	0.87 [0.69-1.10]
Other		0.81 [0.57-1.16]	0.77 [0.59-1.01]
Charlson-Deyo score 1+ (reference: 0)	2.00 [1.02-3.91]	1.40 [1.07-1.84]	1.45 [1.15-1.84]
Community facility type (reference: academic)	1.86 [0.92-3.76]	1.56 [1.20-2.03]	1.14 [0.93-1.40]