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Factors Associated with Dying from Pancreatic Neuroendocrine Tumor

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BACKGROUND: Survival outcomes in patients with pancreatic neuroendocrine tumors (PNETs) are dichotomous; some experience rapid disease progression and death, others a more indolent course. The purpose of this study is to identify clinicopathologic factors that predict death from disease (DOD) in patients undergoing curative resection of PNET.

METHODS: We performed a retrospective review of patients undergoing curative resection for PNET at our institution over 10 years to determine factors associated with death from disease. Patients undergoing palliative resection were excluded.

RESULTS: 125 patients met inclusion criteria. Median follow-up was 41 months (IQR 23-67). 11 patients (8.8%) died from disease with a median overall survival (OS) of 30 mos (IQR 8-41] versus 47 mos (IQR 24-70) in those still alive. DOD patients were younger (52 yrs vs. 57 yrs, p= 0.05) and more likely to present with metastatic disease at diagnosis (54% v. 23%, p=0.02); have positive final margin resection (27% vs. 7%, p=0.03); have poorly-differentiated histology (22% v. 3%, p=0.02); and have high grade disease (33% v. 4%, p<0.001). DOD patients had shorter RFS with 12 mos (IQR 4-29) vs 37 mos (IQR 19-65), p= 0.018. On univariable analysis, metastatic disease at diagnosis with HR 3.151 (95%CI 0.950-10.456, p=0.061); positive final margin status with HR 4.917 (95%CI 1.269-19.050, p=0.021); Ki-67 (%) with HR 1.045 (95%CI 1.019-1.071, p=0.001); and mitotic rate with HR 1.058 (95%CI 1.006-1.113, p=0.028) were significantly associated with OS to p < 0.10. On multivariable analysis including these variables, positive final

margins remained independently associated with OS with HR 5.346 (95% CI 1.071-26.693, p=0.041) to p<0.05.

CONCLUSION: Patients with PNET have favorable prognosis when compared to other pancreatic malignancy. While most have an indolent course, inability to achieve negative margins, early disease recurrence after curative resection, and high grade or poorly differentiated tumors confer higher risk of dying from disease.

Table 1. Comparison of clinicopathologic factors among patients undergoing surgical resection of PNET who remain alive versus died from disease

	Alive	Dead	p value
Variable	n=114 (%)	n=11 (%)	
Median Age, yr (IQR)	57 (48-65)	52 (42-55)	0.051
Female Sex	54 (47%)	4 (46%)	0.485
Functional Endocrine Tumor			
Nonfunctional	86 (75%)	8 (73%)	0.842
Insulinoma	15 (13%)	1 (9%)	0.700
Gastrinoma	11 (10%)	2 (18%)	0.376
Glucagonoma	1 (1%)	0	N/A
Other	1 (1%)	0	N/A
Metastases Present at Diagnosis	26 (23%)	6 (54%)	0.021
Type of Resection			
Distal Pancreatectomy	55 (52%)	4 (40%)	0.454
Pancreaticoduodenectomy	31 (30%)	5 (50%)	0.182
Enucleation	5 (5%)	1 (10%)	0.477
Total Pancreatectomy	13 (12%)	0	N/A
Central Pancreatectomy	1 (1%)	0	N/A
Positive Pathologic Margin Status	8 (7%)	3 (27%)	0.028
Positive Nodal Status	44 (42%)	8 (73%)	0.051
WHO 2017 Grade			
G1-NET	59 (55%)	3 (33%)	0.218
G2-NET	46 (43%)	3 (33%)	0.589
G3-NET	0	1 (11%)	N/A
NEC	3 (3%)	2 (22%)	0.015