

Prognostic Relevance of a Novel AJCC Staging Classification for Neuroendocrine Tumors of the Pancreas

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Abstract:

Background: The AJCC Cancer Staging Manual (7th edition, 2010) has introduced a novel TNM staging classification for pancreatic neuroendocrine tumors which is derived from the staging system for exocrine pancreatic adenocarcinomas. This classification has not yet been validated.

Methods: Patients with pancreatic neuroendocrine tumors treated at the H. Lee Moffitt Cancer Center between 1999 and 2010 were assigned a stage (I-IV) based on the new AJCC classification. Overall survival from time of initial diagnosis was measured and statistical significance calculated using the log-rank test. The prognostic relevance of the AJCC staging classification was compared to the relevance of a staging classification proposed recently by the European Neuroendocrine Tumor Society (ENETS).

Results: 425 patients with histologically proven pancreatic neuroendocrine tumors were identified. Both the novel AJCC classification and the ENETS classification were highly prognostic for survival ($p < 0.00001$).

Conclusions: The novel AJCC 7th Edition TNM classification for pancreatic neuroendocrine tumors is highly prognostic for overall survival and should be adopted in clinical practice.

Introduction:

- In 2010, the American Joint Committee introduced a formal TNM staging classification for pancreatic neuroendocrine tumors (table 1)
- This staging classification is derived from the TNM staging of exocrine pancreatic adenocarcinomas.
- The prognostic relevance of this staging classification has not been tested.

Methods:

- A databased consisting of all histologically proven cases of pancreatic neuroendocrine tumors seen at the Moffitt Cancer Center between 1999 and 2010 was created
- Tumors were clinically or pathologically classified by stage based on the novel AJCC staging system. Tumors were also classified according to the European Neuroendocrine Tumor Society (ENETS) TNM staging classification.
- Tumors were assigned a histologic grade (low, intermediate, high) based on pathology reports. Both descriptive terms (well differentiated, moderately differentiated, poorly differentiated), and numerical terms (mitotic rate, Ki-67 index) were used for assignment of grade.
- Overall survival (OS) was measured for each patient from time of initial diagnosis to time of death, or last contact. Kaplan Meier methodology with log-rank testing was used to compare survival by stage and by grade.

Results:

- 425 patients with pancreatic neuroendocrine tumors were identified.
- Median and 5-year survival rates correlated closely with tumor stage, according to both the AJCC and the ENETS staging classifications (figures 1A and 1B, table 2)
- Tumor grade (low, intermediate, high) was highly prognostic for survival, independent of stage (figure 2).

Table 1: AJCC TNM classification

T1 Tumor limited to the pancreas, ≤ 2 cm
T2 Tumor limited to the pancreas > 2 cm
T3 Tumor extends beyond the pancreas but no involvement of the celiac axis or the SMA
T4 Tumor involves the celiac axis or the SMA (unresectable)

N0 No regional LN metastasis
N1 Regional LN metastasis
M0 No distant metastasis
M1 Distant metastasis

Stage	T	N	M
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T3	N0	M0
IIB	T1-3	N1	M0
III	T4	Any N	M0
IV	Any T	Any N	M1

Figure 1A and 1B: Overall survival by AJCC and ENETS classifications

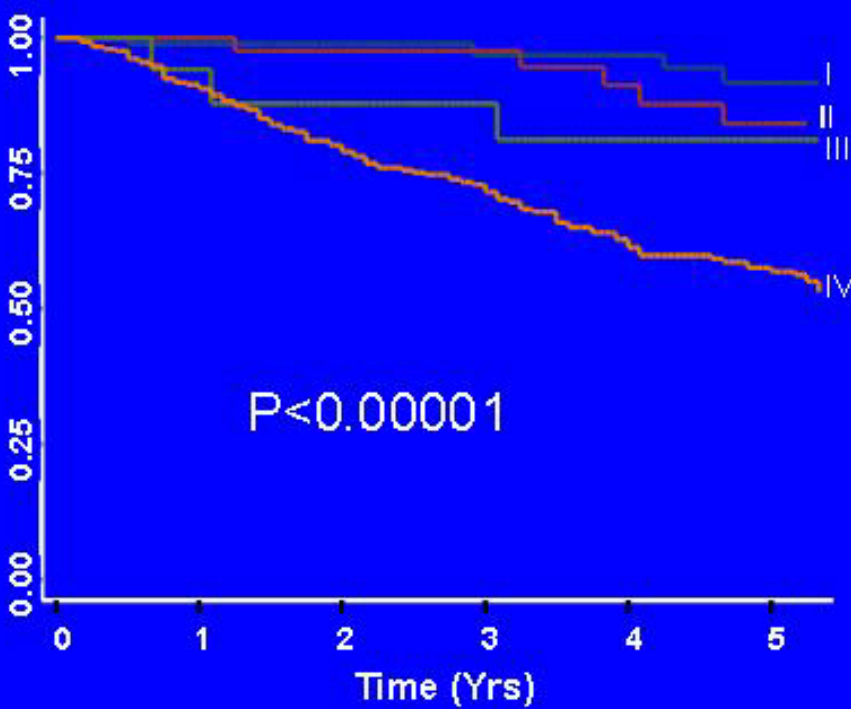


Fig. 1A

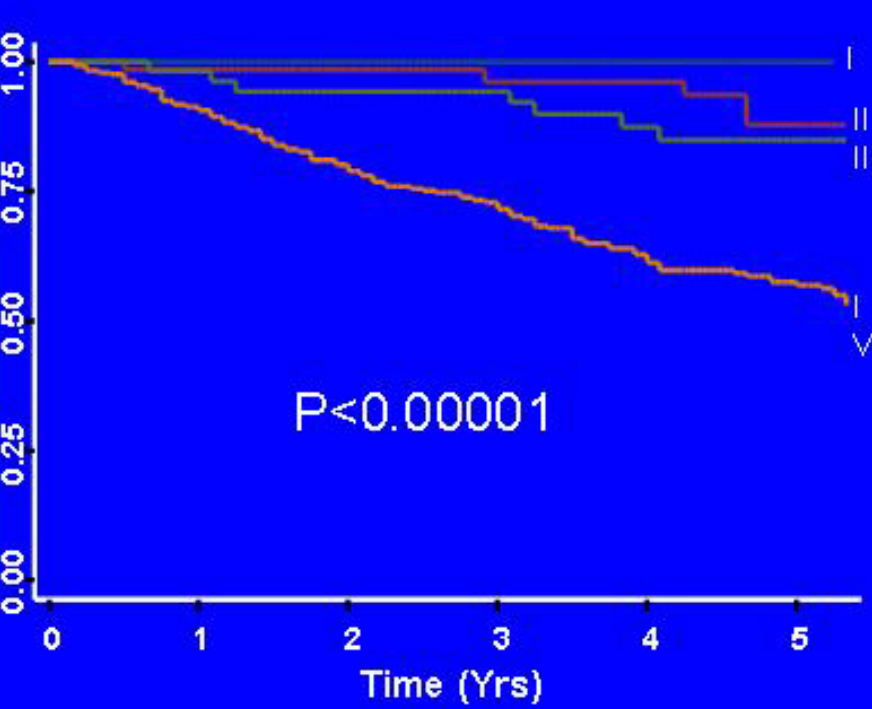
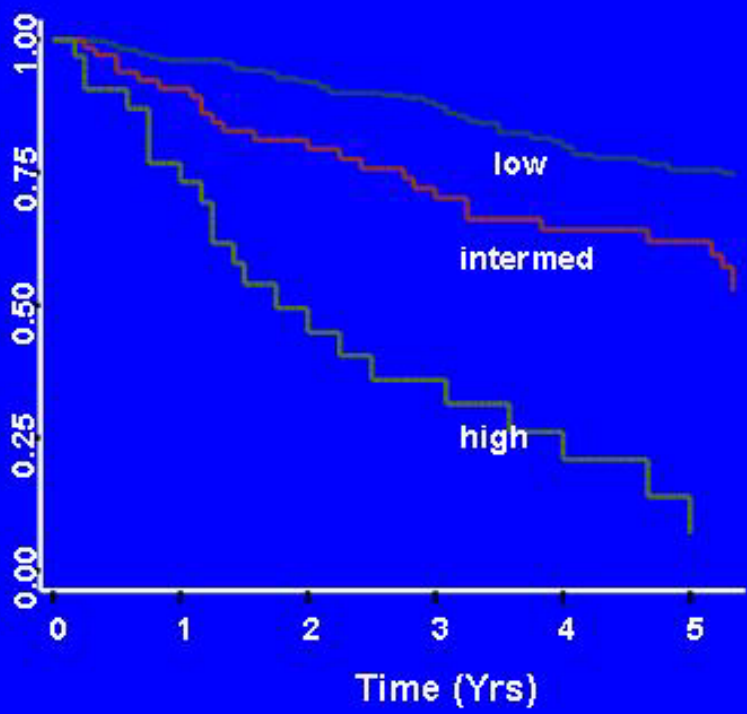


Fig. 1B

Table 2: 5-year survival rates of patients classified by the AJCC vs. ENETS TNM staging systems

Stage	No. of patients (AJCC)	5-year survival rate (AJCC)	No. of patients (ENETS)	5-year survival rate (ENETS)
I	64	92%	25	100%
II	41	84%	63	88%
III	18	81%	55	85%
IV	282	57%	282	57%

Figure 2: OS stratified by tumor grade



Conclusions:

- The novel AJCC TNM classification for pancreatic neuroendocrine tumors is highly prognostic for overall survival
- A three-tiered tumor grading system is also highly prognostic for survival and should be combined with stage for estimation of prognosis
- Both the AJCC and ENETS staging classifications can be adopted in clinical practice.

