

# Risk of Metastatic Spread in Patients with Early-Stage, Surgically Resected Pancreatic Neuroendocrine Tumors

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## Abstract:

**Background:** The risk of metastatic spread among patients with early-stage surgically resected pancreatic neuroendocrine tumors has not been well established.

**Methods:** Patients with surgically resected localized or locally advanced pancreatic neuroendocrine tumors treated at the H. Lee Moffitt Cancer Center between 1999 and 2010 were assigned a stage (I-III) based on the new AJCC classification. Recurrence-free survival was measured for each stage. A separate analysis was performed excluding patients who had been referred to Moffitt Cancer Center after metastatic recurrence.

**Results:** 123 patients with non-metastatic, surgically-resected pancreatic NETs were identified. 5-year recurrence-free survival correlated with AJCC stage (p=0.01).

**Conclusions:** The novel AJCC 7<sup>th</sup> Edition TNM classification for pancreatic neuroendocrine tumors is highly prognostic for recurrence in patients with surgically resected, non-metastatic tumors.

## 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 for metastatic recurrence after surgical resection of stage I-III tumors has not been tested.

## Methods:

- A database 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. Patients with stage I-III surgically-resected tumors were identified (figure 1).

- Overall survival (OS) was measured for each patient from time of initial diagnosis to time of death, or last contact.

- Recurrence-free survival (RFS) was measured from time of surgical resection until death or cancer recurrence, or last follow-up. Kaplan Meier methodology with log-rank testing was used to compare RFS by stage.

- In order to minimize referral bias causing overestimation of recurrence, a separate analysis of RFS was performed excluding patients who had only been referred to Moffitt Cancer Center after metastatic recurrence.

## Results:

- 123 patients were identified who had non-metastatic, surgically resected tumors (figure 1).
- 5-year recurrence-free survival rates correlated closely with AJCC tumor stage (figure 2).
- Excluding patients who were only referred after recurrence, the absolute 5-year risk of recurrence for stages I and II was 10% and 27% respectively (figure 3).
- 5-year recurrence rate for tumors <2cm (stage IA) was 0% (figure 2).
- RFS curves do not plateau at 5-years. Longer follow-up is needed to determine the lifetime recurrence rates after resection of non-metastatic pNETs.

Table 1: AJCC TNM classification

	Stage	T	N	M
T1 Tumor limited to the pancreas, <2cm	IA	T1	N0	M0
T2 Tumor limited to the pancreas >2cm	IB	T2	N0	M0
T3 Tumor extends beyond the pancreas but no involvement of the celiac axis or the SMA	IIA	T3	N0	M0
T4 Tumor involves the celiac axis or the SMA (unresectable)	IIB	T1-3	N1	M0
N0 No regional LN metastasis	III	T4	Any N	M0
N1 Regional LN metastasis	IV	Any T	Any N	M1
M0 No distant metastasis				
M1 Distant metastasis				

Figure 1: Number of Resected Cases

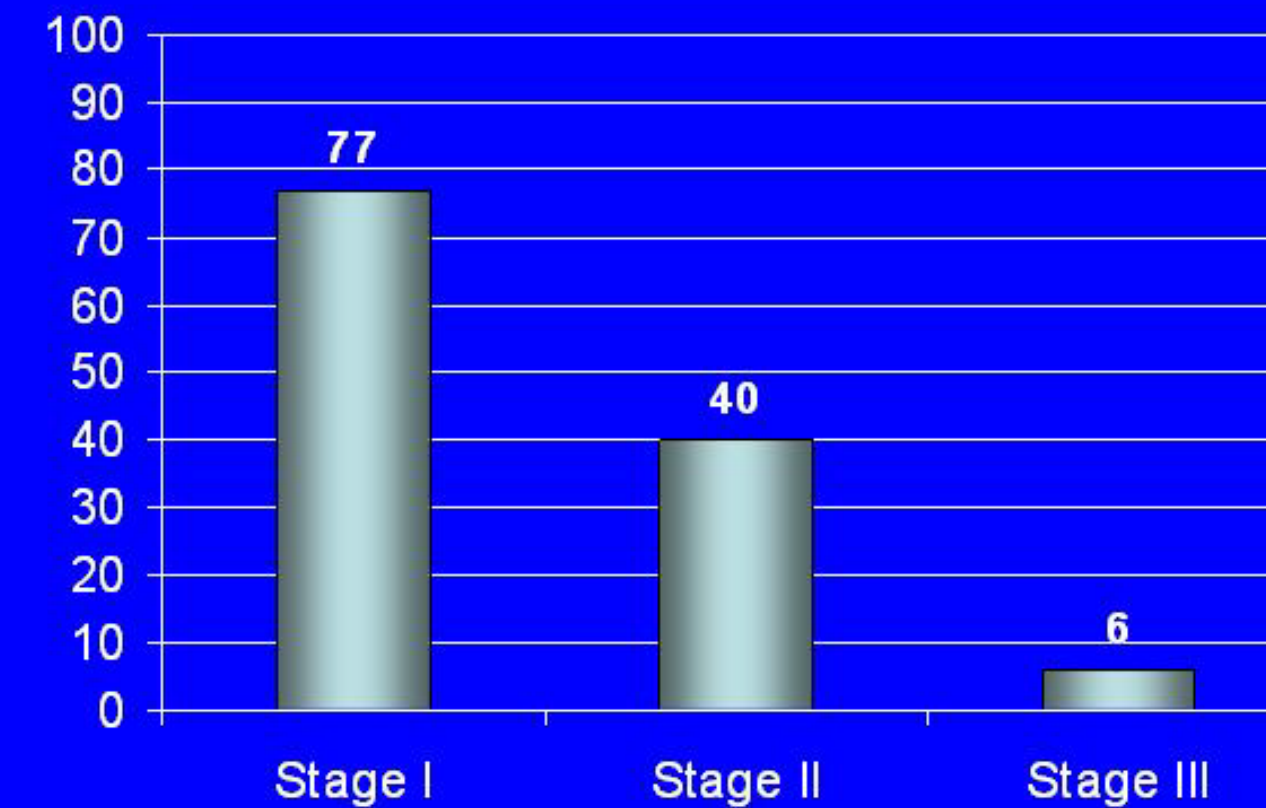


Figure 3: Recurrence-free Survival by AJCC Stage (excluding patients who presented after recurrence)

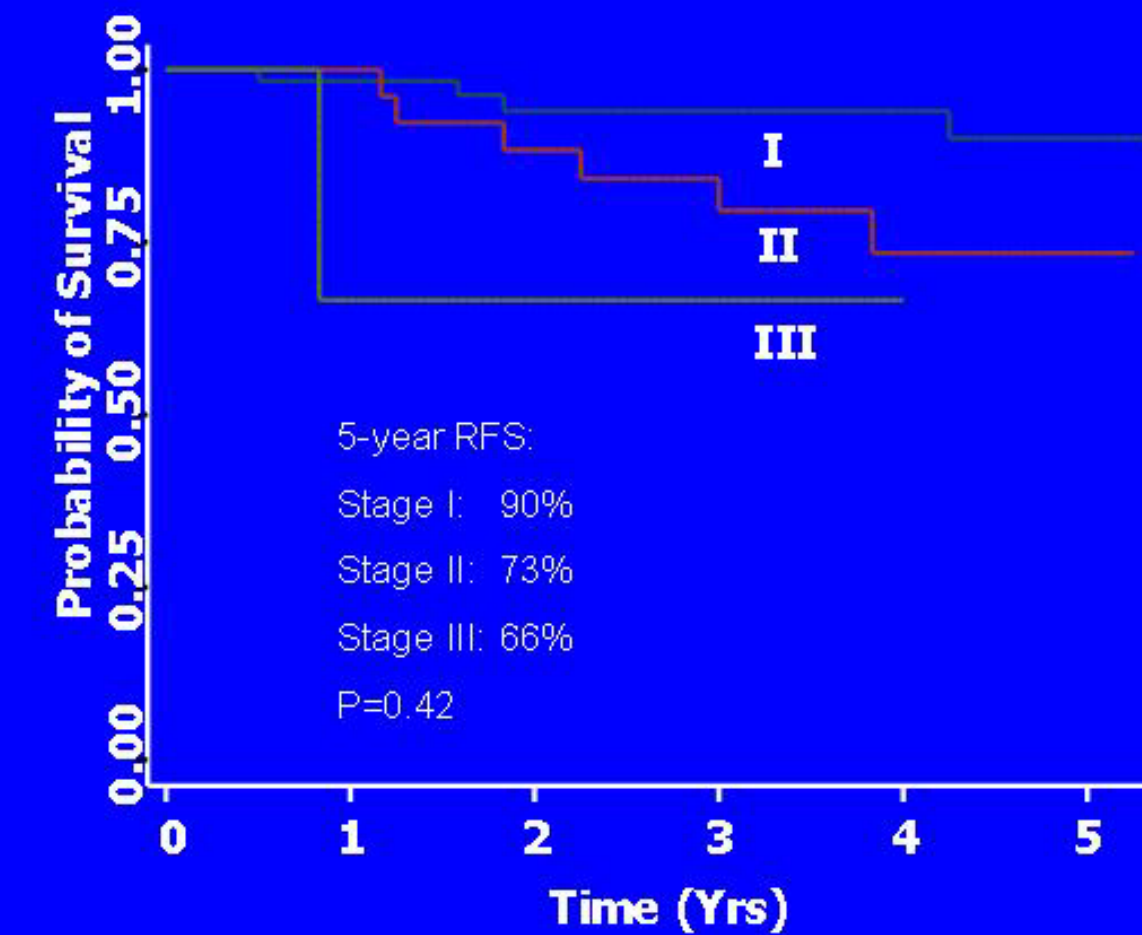
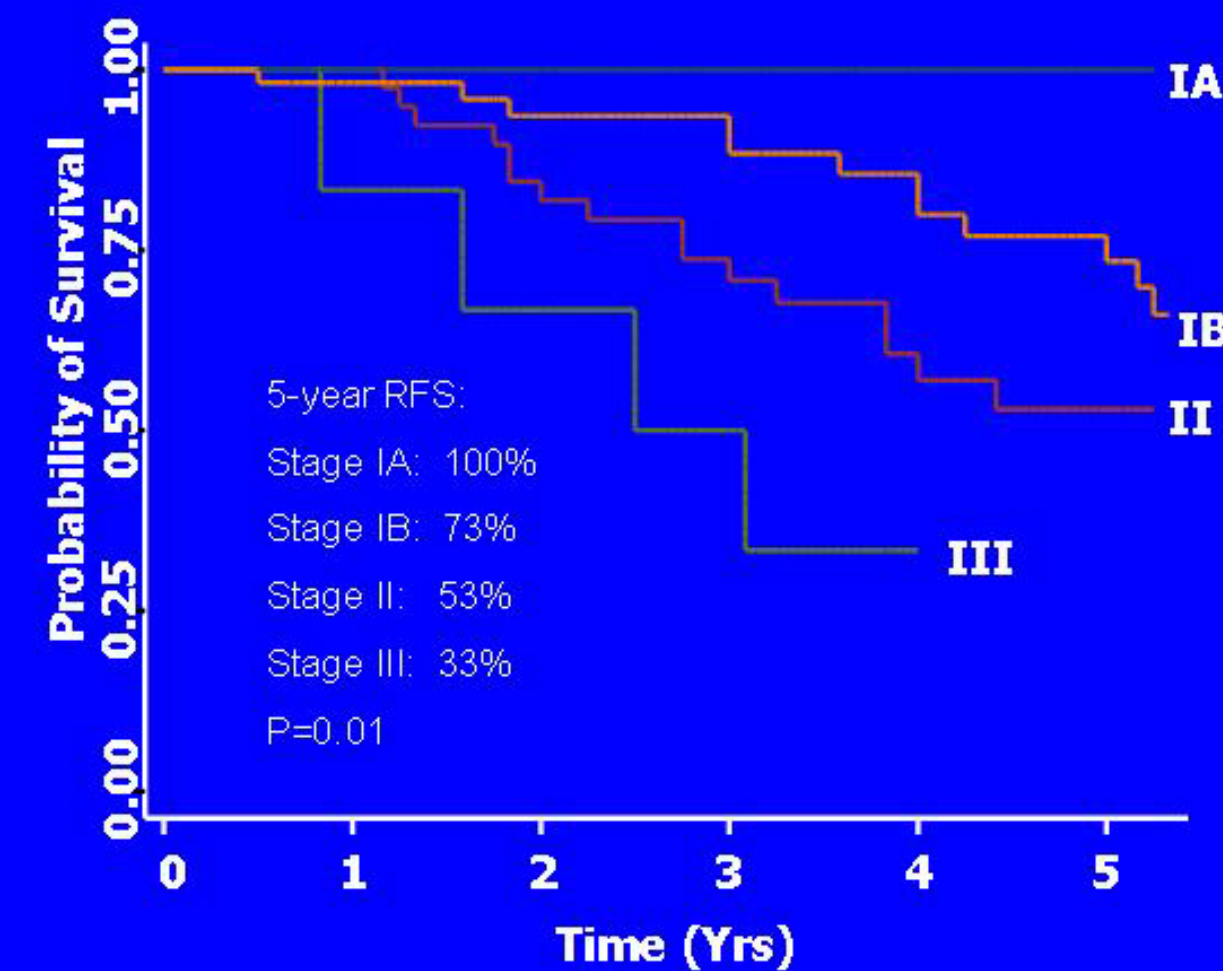


Figure 2: Recurrence-free Survival by AJCC Stage



## Conclusions:

- The novel AJCC TNM classification is prognostic for recurrence-free survival in patients with surgically resected stage I-III tumors.
- Absolute recurrence risk is 10% for stage I and 27% for stage II tumors at 5-years.
- Longer term follow-up is needed since recurrences persist beyond 5 years.
- Stage IA patients are at exceptionally low risk of recurrence after surgery (0% at 5 years).

