XVIII Semana Brasileira do Aparelho Digestivo

XVIII SBAD

23 a 26 novembro | 2019 | Centro de Eventos do Ceará | Fortaleza | CE

# TUMORES NEUROENDÓCRINOS DO PÂNCREAS: Quando operar, quando observar


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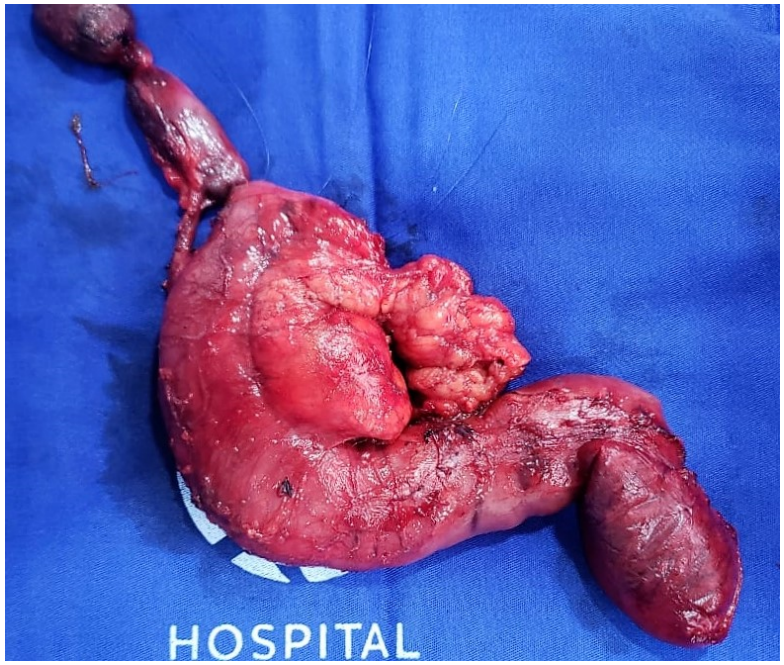
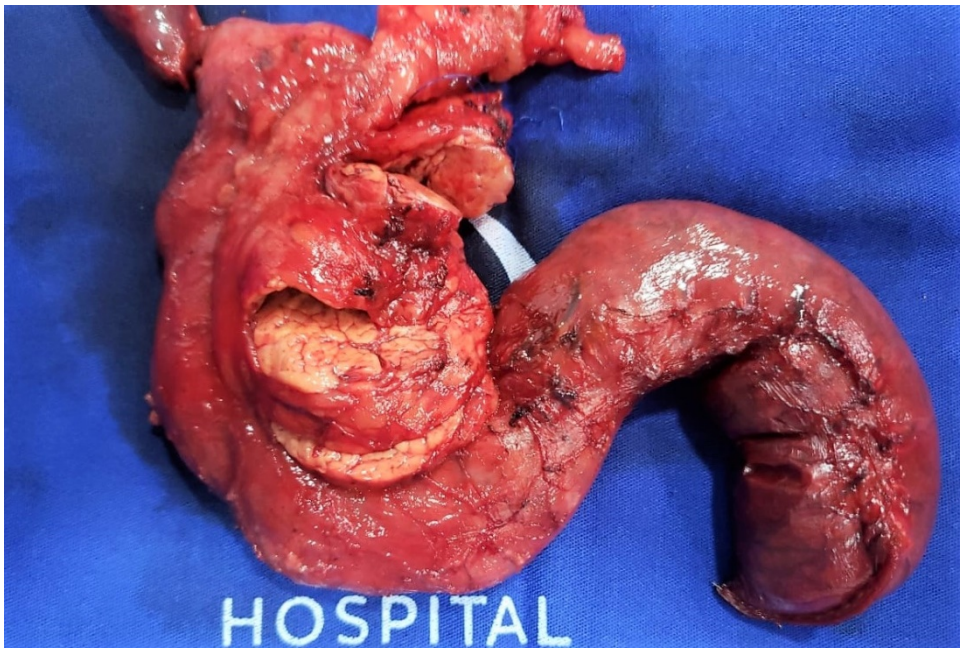
Unidade Hepatopancreatobiliar
Universidade Federal Maranhão - Brasil

# CASO CLÍNICO

W,masculino,53 anos
RNM – lesão hipervascular
1,6 cm
Cabeça do pâncreas
Compatível com TNE

# Duodenopancreatectomia
# Anatomopatológico – TNE
# Ki 67 2%

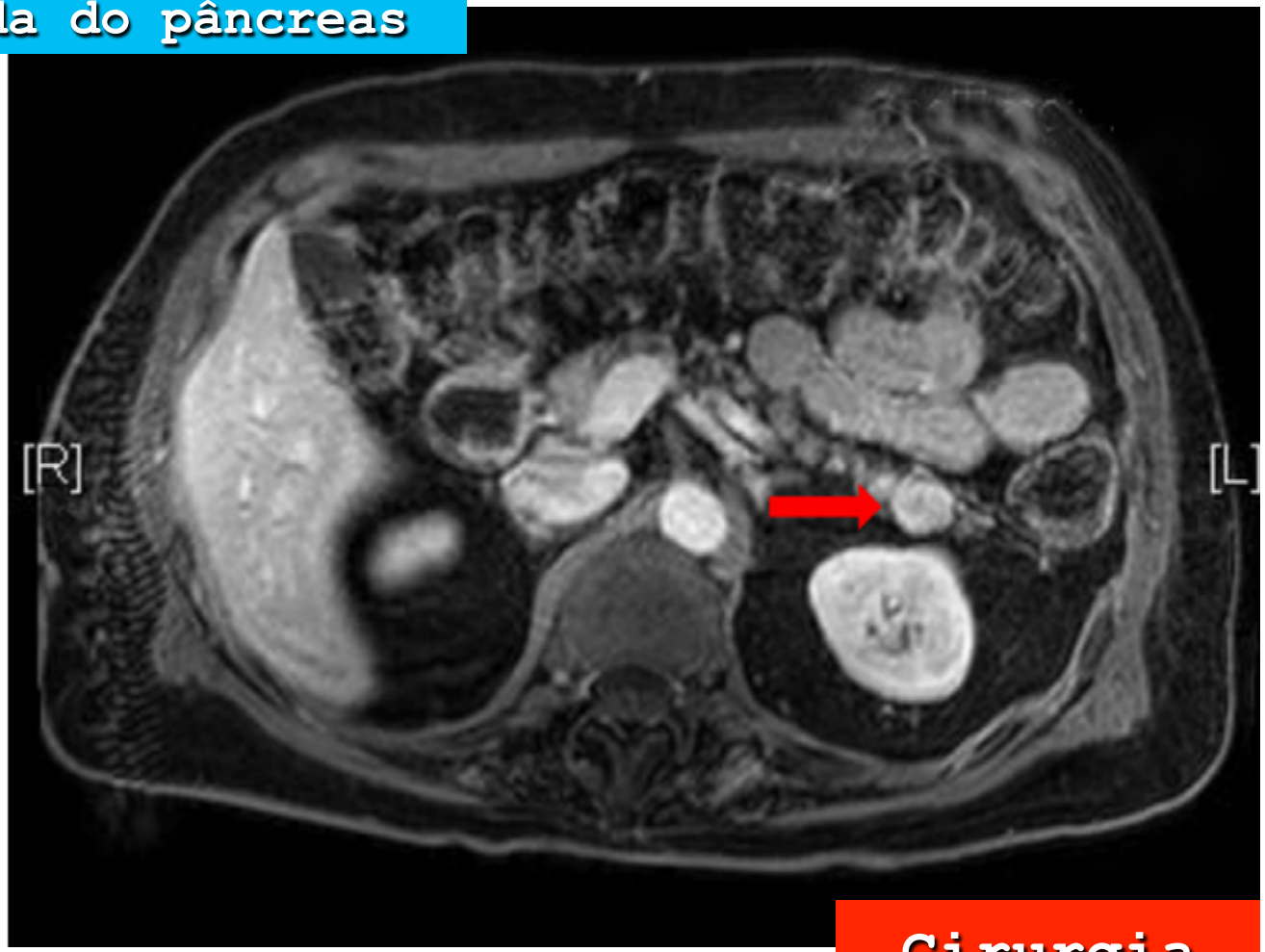


# TUMOR NEUROENDÓCRINO DO PÂNCREAS

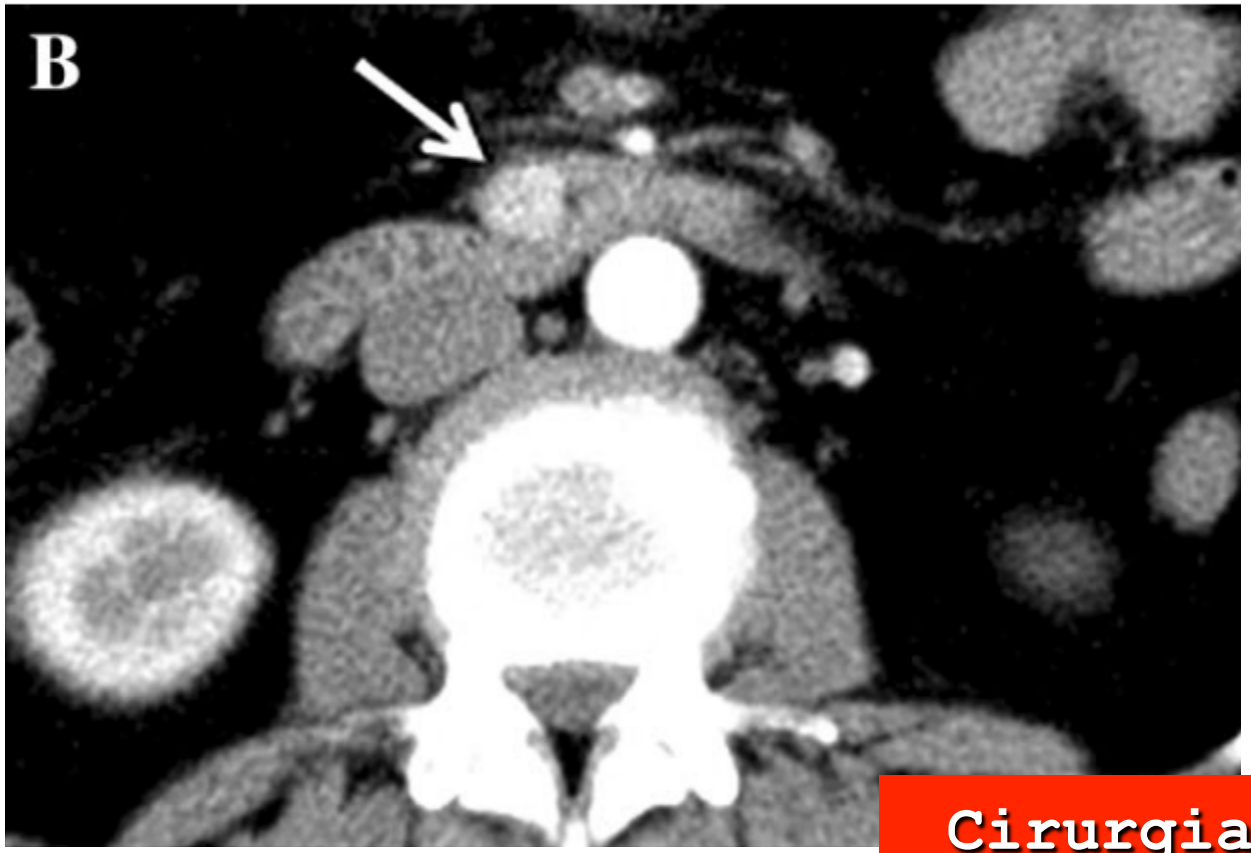
- 7% of neurendocrine tumors
- 1-3% pancreas tumors
- ↑ incidence in the past 3 decades
- Men = women
- Diagnostic betwen 60 and 80
- 5% familial syndromes
- 5-10 cases / 1 million (EUA)

- pNET – 2 cm
- Cauda do pâncreas

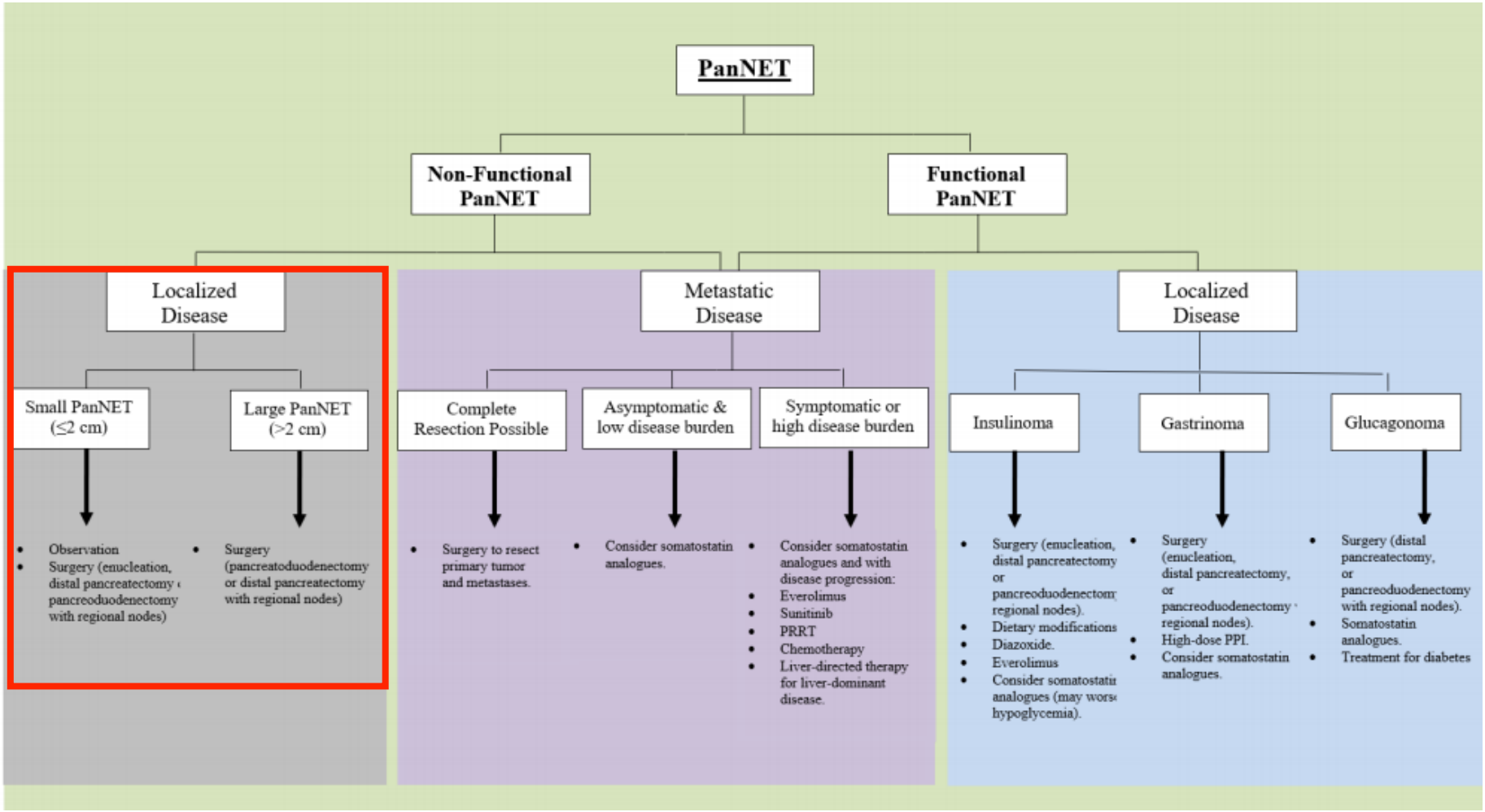



**Cirurgia**

- pNET – 1,8 cm
- Cabeça do pâncreas




Cirurgia




Akirov A , et al. Cancers 2019

**Table 1.** Functioning PNET syndromes

| Tumor | Symptom(s) |
|---|---|
| Insulinoma | Hypoglycemia |
| Gastrinoma | Severe peptic ulceration |
| Vipoma | Watery diarrhea, hypokalemia, achlorhydria (WDHA syndrome) |
| Glucagonoma | Glucose intolerance, necrolytic migratory, erythema, stomatitis/glossitis, hypoaminoacidemia |
| Somatostatinoma | Hyperglycemia, cholelithiasis, steatorrhea, achlorhydria |

**Table 2.** Neuroendocrine tumors grading

| Mitosis | Ki-67% | ENETS/WHO | Grade |
|---|---|---|---|
| < 2 | < 3 | NET | I |
| 2–20 | 3–20 | NET | II |
| > 20 | > 20 | NEC (small cell or large cells) | III |
| | | Mixed adenoendocrine carcinoma (MANEC) | |
| | | ENETS and AJCC TMN staging for PNET | |
| ENETS TNM | | AJCC/UICC TNM | |
| T1 Limited to pancreas, < 2 cm | | Limited to pancreas, < 2 cm | |
| T2 Limited to pancreas, 2–4 cm | | Limited to pancreas, > 2 cm | |
| T3 Limited to pancreas > 4 cm; or tumor invasion of duodenum or common bile duct | | Tumor invasion of peripancreatic tissue. Not involving major vascular invasion (truncus coeliacus, A. mesenterica superior) | |
| T4 Tumor invasion of any adjacent structure or involving major vascular invasion | | Involving major vascular invasion | |

# Consensus Guidelines for the Management and Treatment of Neuroendocrine Tumors

| **Pancreatic NET Pathology** | |
|---|---|
| **Mitotic rate or Ki67 should be obtained. When both mitotic rate and Ki67 are obtained, the higher grade is assigned. If specimen is inadequate, repeat biopsy is recommended.** | |
| Subtype | |
| Small cell, non–small cell (ie, large cell) | Recommend |
| Grading (proliferative rate) | Recommend |
| Mitotic rate | |
| G1 | <2 mitoses/10 HPF* |
| G2 | 2–20 mitoses/10 HPF |
| G3 | >20 mitoses/10 HPF |
| Ki 67 | |
| G1 | <3% |
| G2 | 3%–20% |
| G3 | >20% |

Kunz PL, et al. Pancreas 2013;42:557-77

# OMS 2017

**Table 1**

2017 WHO classification of PNETs

| WHO classification | Grade | Mitotic count (per 10 high-powered field) | Ki67 index |
|---|---|---|---|
| Well-differentiated neuroendocrine tumors (NETs) | Grade I (G1) | <2 | <3% |
| | Grade II (G2) | 2–20 | 3–20% |
| | Grade III (G3) | >20 | >20% |
| Poorly differentiated neuroendocrine carcinoma (NECs) | Grade III (G3) small cell or large cell | >20 | >20% |
| Mixed neuroendocrine & non-neuroendocrine subtype (MiNEN) | | | |

* adapted from (6).

# CLASSIFICAÇÃO DOS TNEs (OMS 2019)

| | G1 | G2 | G3 | NEC Large Cell | NEC Small Cell |
|---|---|---|---|---|---|
| Diferenciação | Bem | Bem | Bem | Pobre | Pobre |
| Índice Mitótico | < 2 | 2 - 20 | > 20 | > 20 | > 20 |
| Ki67 | < 3% | 3 – 20% | > 20% | > 20% | > 20% |

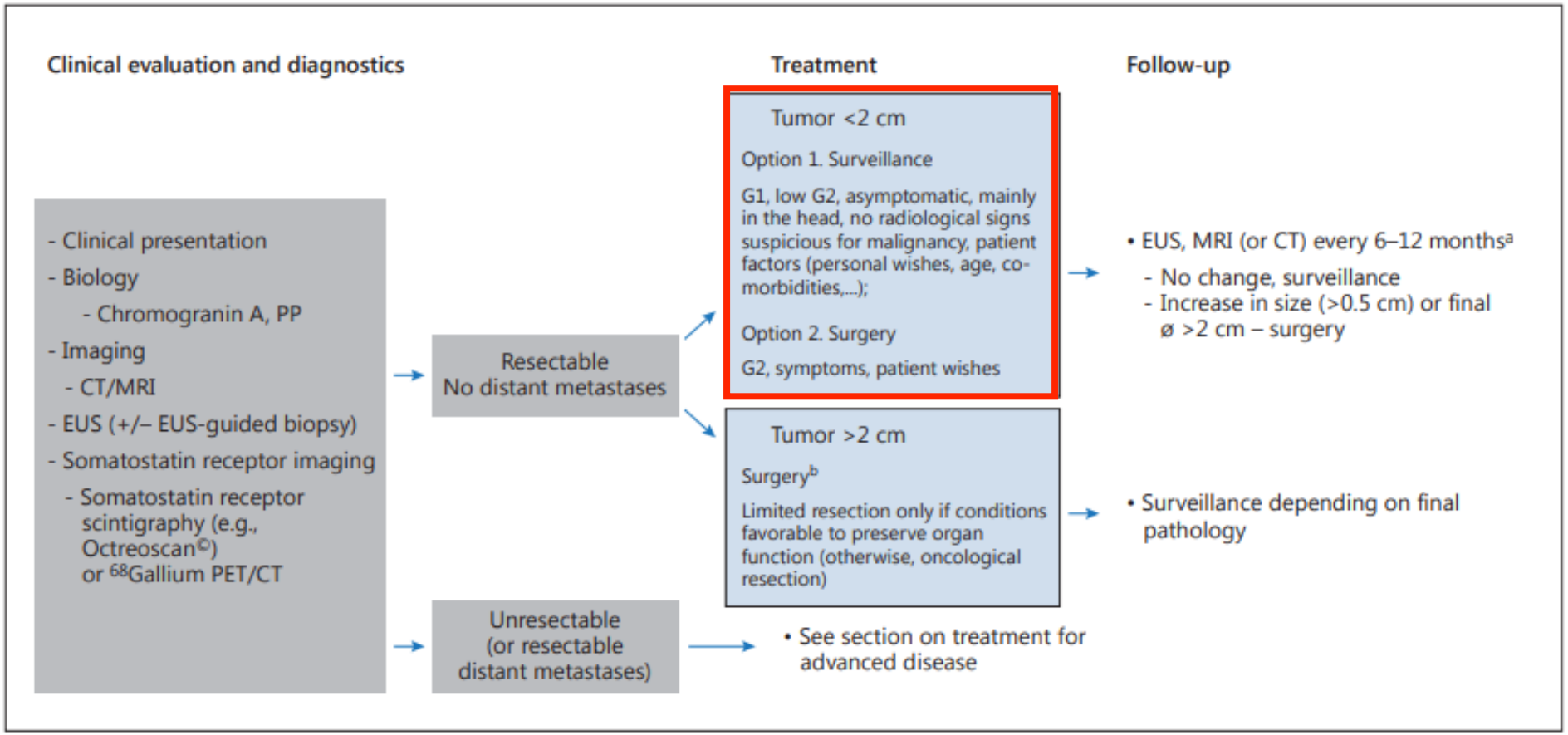
https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf

Neuro
-endocrinology

Neuroendocrinology 2016;103:153–171
DOI: 10.1159/000443171

Published online: January 5, 2016

# ENETS Consensus Guidelines Update for the Management of Patients with Functional Pancreatic Neuroendocrine Tumors and Non-Functional Pancreatic Neuroendocrine Tumors

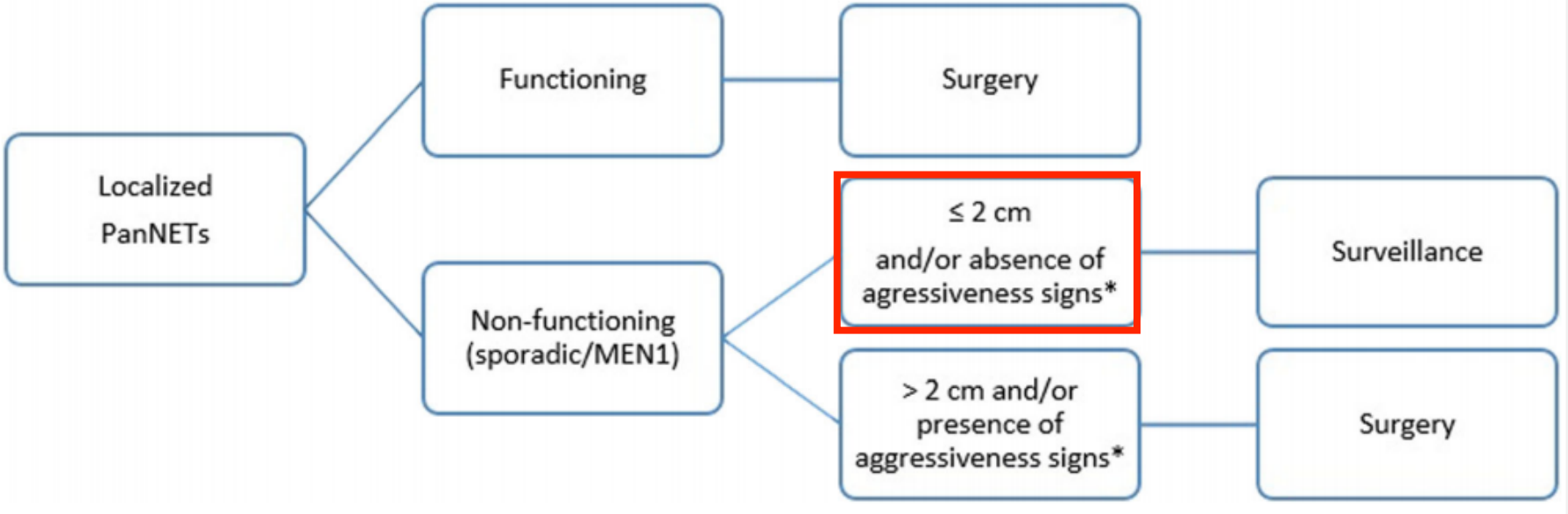



Falconi M , et al. Neuroendocrinology 2016;103:153–71

Reviews in Endocrine and Metabolic Disorders
https://doi.org/10.1007/s11154-018-9445-4

# How should incidental NEN of the pancreas and gastrointestinal tract be followed?

Riccardo Ariotti [1] · Stefano Partelli [1] · Francesca Muffatti [1] · Valentina Andreasi [1] · Francesca Della Sala [1] · Massimo Falconi [1]




Ariotti R, et al. Rev Endocr Metab Disord 2018

National Comprehensive Cancer Network®

# NCCN Guidelines Version 1.2019
# Neuroendocrine Tumors of the Pancreas

NCCN Guidelines Index
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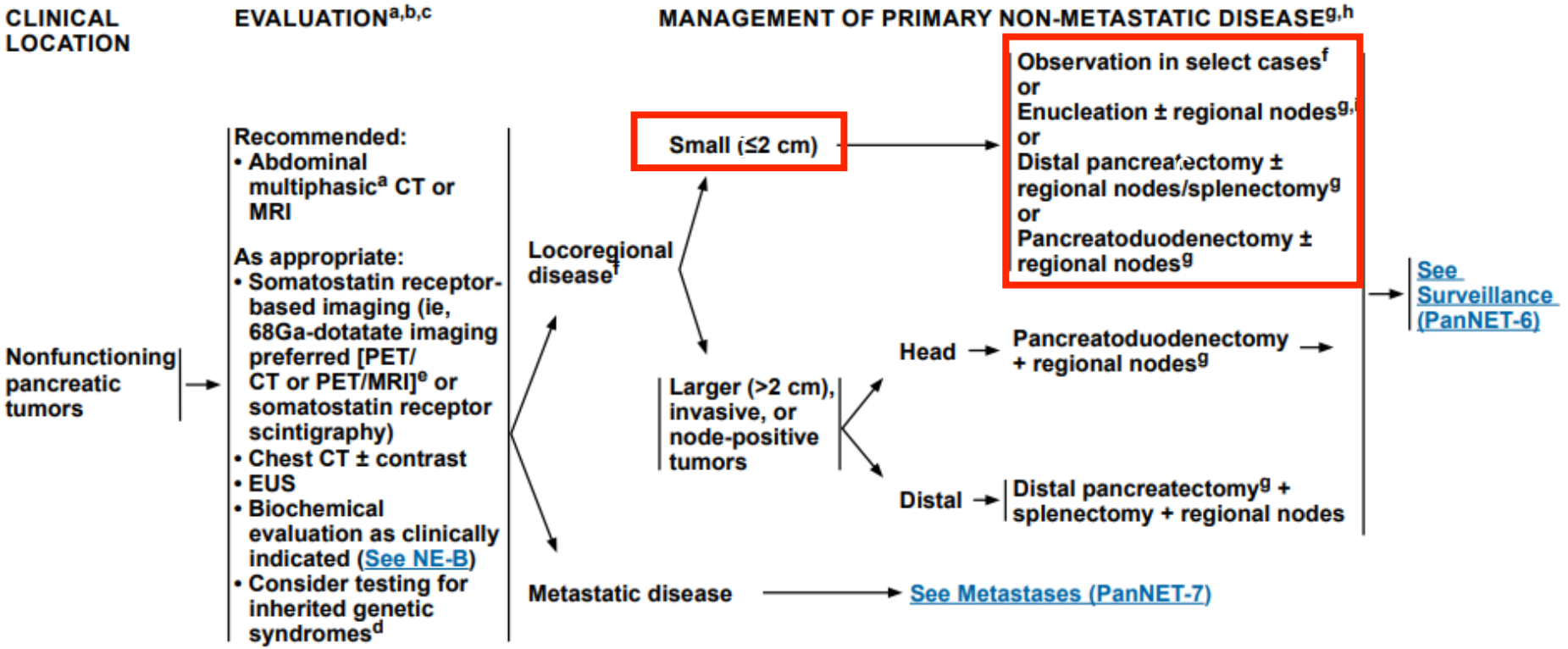
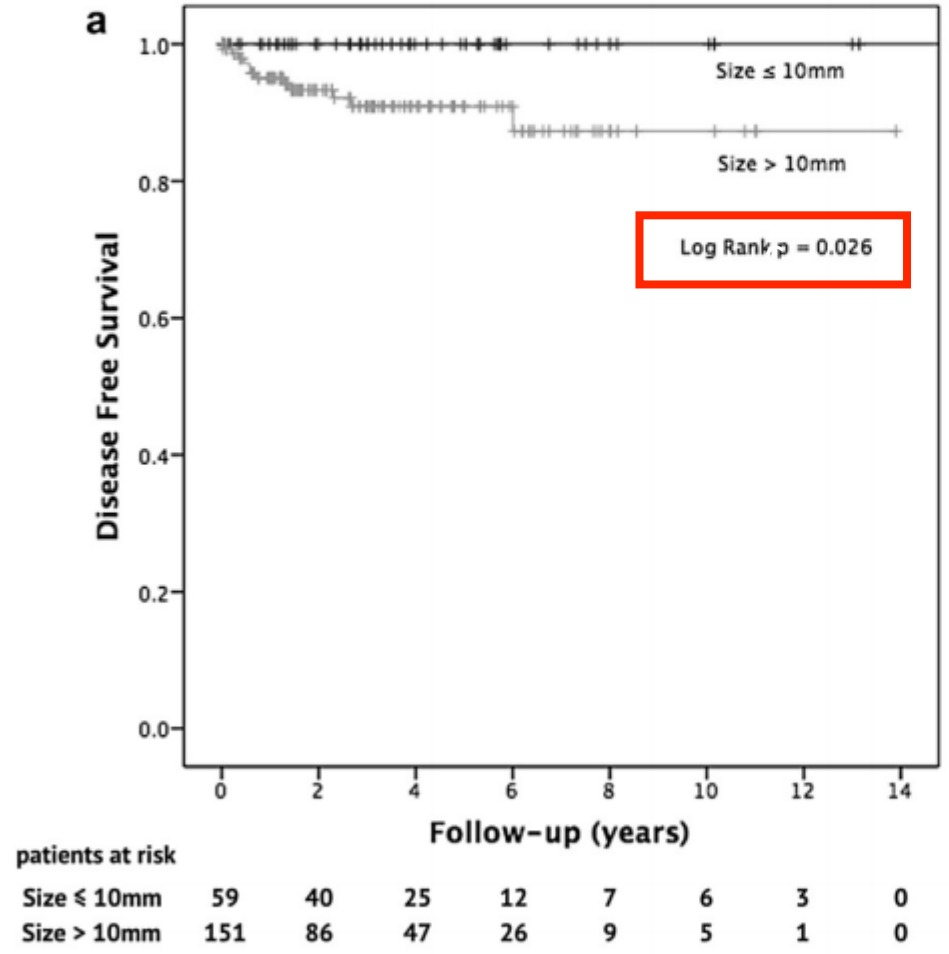
Discussion



ORIGINAL ARTICLE

# Prognosis of sporadic resected small (≤2 cm) nonfunctional pancreatic neuroendocrine tumors – a multi-institutional study




Sallinen VJ, et al. HPB 2018; 20:251-9

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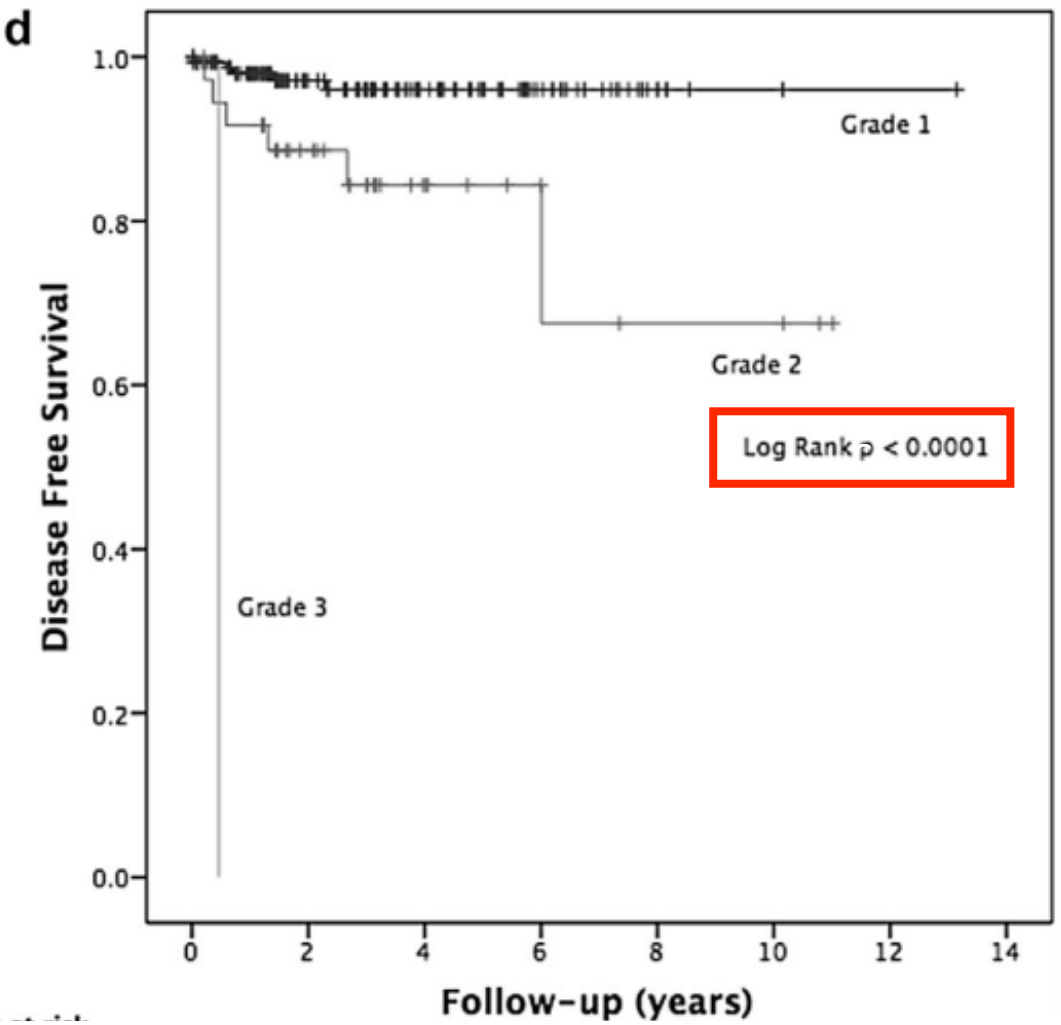
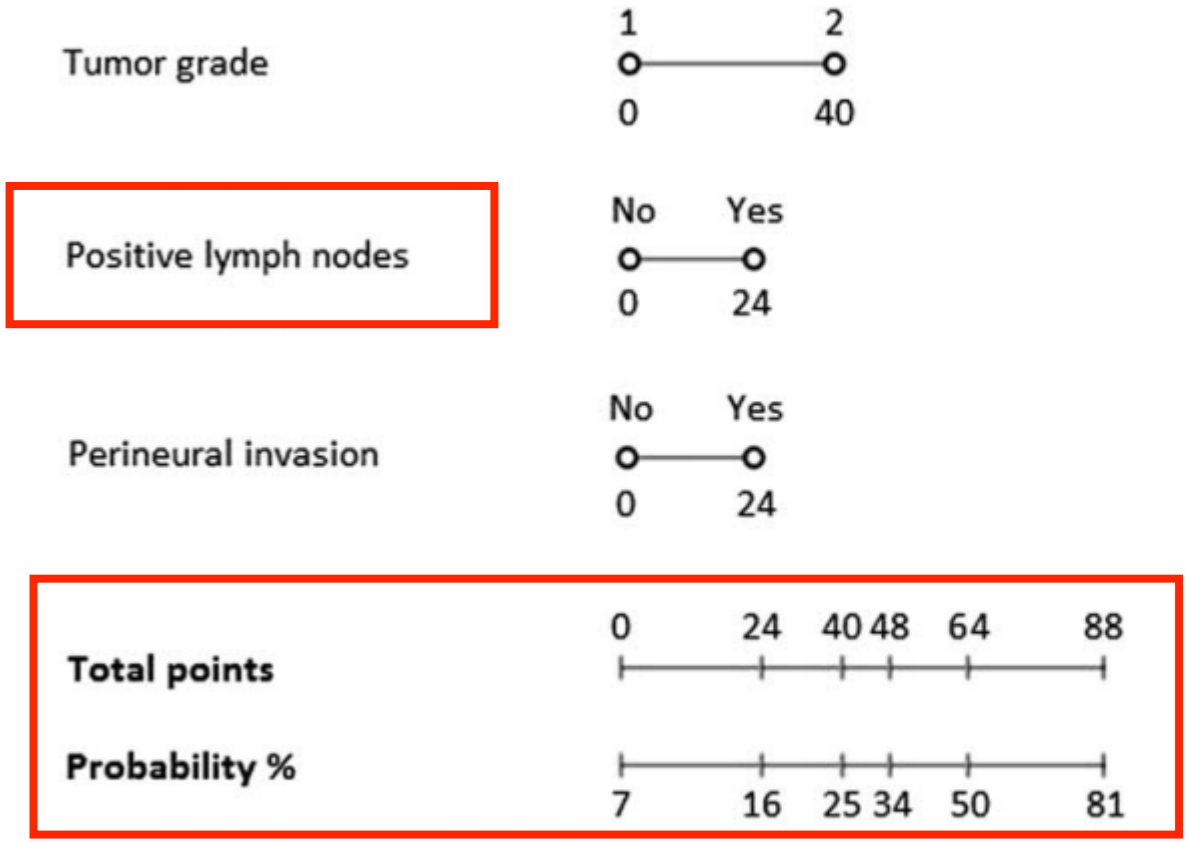


# A New Scoring System to Predict Recurrent Disease in Grade 1 and 2 Nonfunctional Pancreatic Neuroendocrine Tumors




Genç CG, et al. Ann Surg 2016

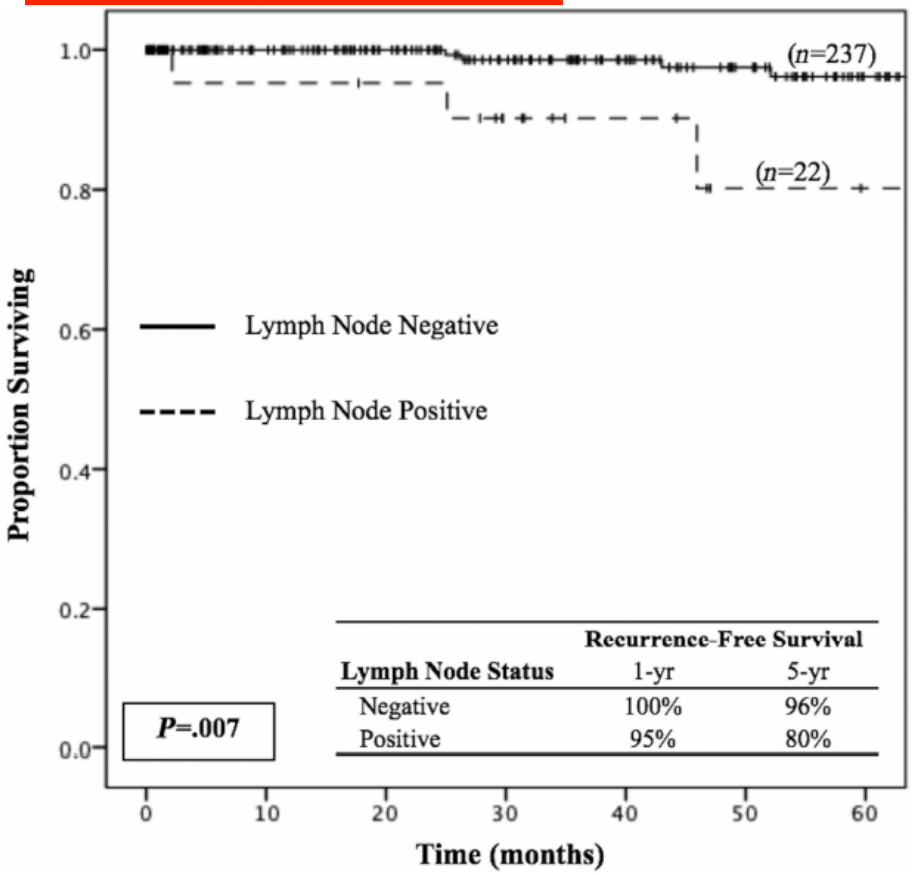
Surgery 166 (2019) 15–21

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

# The conundrum of < 2-cm pancreatic neuroendocrine tumors: A preoperative risk score to predict lymph node metastases and guide surgical management




Lopez-Aguiar AG, et al. Surgery 2019;166-15-21

**Table III**
Association of pathologic factors with risk for lymph node positivity in patients with < 2-cm low/intermediate grade, nonfunctional, PanNETS*

| Pathologic factors | Logistic regression | |
|---|---|---|
| | Lymph node positivity | |
| | OR (95% CI) | *P* value† |
| Tumor location in pancreas | | |
| Distal | **Ref** | — |
| proximal‡ | **4.0 (1.6–9.7)** | **.002** |
| Tumor size | | |
| <1 cm | Ref | — |
| 1–1.5 cm | 1.25 (0.4–4.2) | .716 |
| >1.5 cm | 1.7 (0.5–5.9) | .405 |
| Tumor differentiation | | |
| Well | Ref | — |
| Moderate | 1.5 (0.3–6.9) | .631 |
| Ki-67 index‡ | | |
| <3% | **Ref** | — |
| 3%–20% | **2.7 (1.0–7.2)** | **.054** |
| Final resection status | | |
| R0 | Ref | — |
| R1 | 3.3 (1.0–11.0) | .052 |
| Mitotic rate (per 10 HPF) | | |
| <2 | Ref | — |
| 2–20 | 3.9 (0.9–16.4) | .062 |
| Lymphovascular invasion | | |
| Negative | Ref | — |
| Positive | 17.2 (5.9–50.1) | <.001 |
| Perineural invasion | | |
| Negative | Ref | — |
| Positive | 4.9 (1.7–14.0) | .003 |
| Advanced T stage | | |
| T1/T2 | Ref | — |
| T3 | 8.6 (2.2–33.1) | .002 |

- Distal – 5,2%
- Proximal – 17,9% p<0,01

Lopez-Aguiar AG, et al. Surgery 2019;166-15-21

Ann Hepatobiliary Pancreat Surg 2018;22:66-74
https://doi.org/10.14701/ahbps.2018.22.1.66

Original Article

# Prognostic factors of non-functioning pancreatic neuroendocrine tumor revisited: The value of WHO 2010 classification

**Table 5.** Clinicopathologicfactors in association with WHO classification of NF-pNETs

| | | WHO classification | | | *p*-value |
|---|---|---|---|---|---|
| | | Grade 1 (%) | Grade 2 (%) | Grade 3 (%) | |
| Age | <50 | 27 (48.2) | 27 (48.2) | 2 (3.6) | |
| | ≥50 | 55 (50.0) | 45 (40.9) | 10 (9.1) | $p=0.389$ |
| Sex | Male | 39 (48.2) | 35 (43.2) | 7 (8.6) | |
| | Female | 43 (50.6) | 37 (43.5) | 5 (5.9) | $p=0.812$ |
| Symptom | Incidental | 64 (60.4) | 41 (38.7) | 1 (0.9) | |
| | Symptomatic | 18 (30.0) | 31 (51.7) | 11 (18.3) | $p<0.001$ |
| Tumor | Head | 28 (37.8) | 37 (50.0) | 9 (12.2) | |
| Location | Non head | 54 (58.7) | 35 (38.0) | 3 (3.3) | $p=0.008$ |
| T stage | T1 | 59 (85.5) | 9 (13.0) | 1 (1.5) | |
| | T2 | 18 (46.2) | 21 (53.8) | 0 (0.0) | |
| | T3 | 5 (8.6) | 42 (72.4) | 11 (19.0) | $p<0.001$ |
| N stage | Nx | 52 (81.2) | 11 (17.2) | 1 (1.6) | |
| | N0 | 31 (39.8) | 43 (55.1) | 4 (5.1) | |
| | N1 | 0 (0.0) | 17 (70.8) | 7 (29.2) | $p<0.001$ |
| M stage | M0 | 82 (50.6) | 68 (42.0) | 12 (7.4) | |
| | M1 | 0 (0.0) | 4 (100.0) | 0 (0.0) | $p=0.084$ |
| Pathologic tumor size | <1 cm | 14 (100.0) | 0 (0.0) | 0 (0.0) | |
| | ≥1 cm, <2 cm | 44 (77.2) | 13 (22.8) | 0 (0.0) | |
| | ≥2 cm | 24 (25.3) | 59 (62.1) | 12 (12.6) | $p<0.001$ |
| Imaging tumor size | <1 cm | 14 (100.0) | 0 (0.0) | 0 (0.0) | |
| | ≥1 cm, <2 cm | 38 (73.1) | 14 (26.9) | 0 (0.0) | |
| | ≥2 cm | 30 (30.0) | 58 (58.0) | 12 (12.0) | $p<0.001$ |

Ann Hepatobiliary Pancreat Surg 2018;22:66-74
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Original Article

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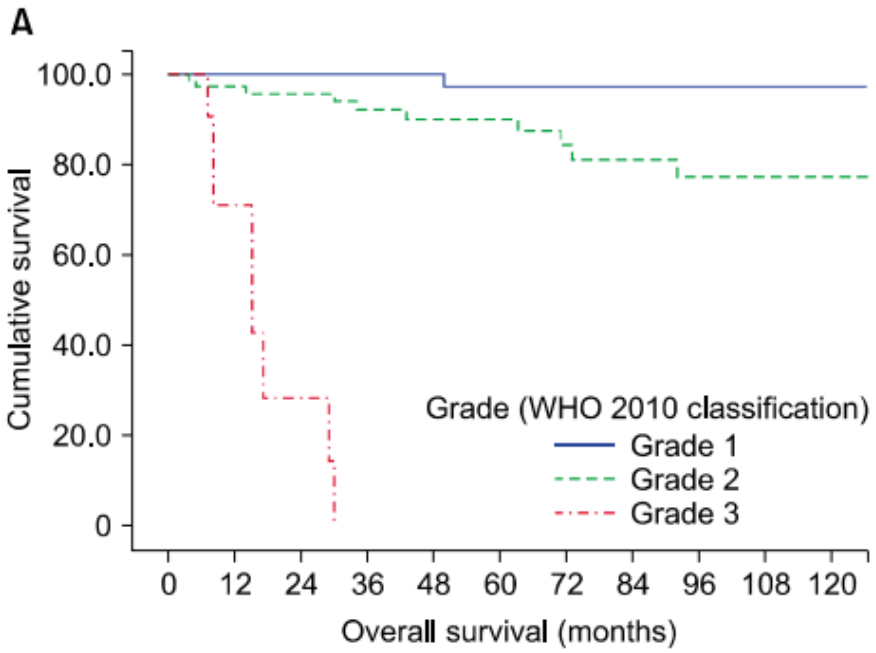


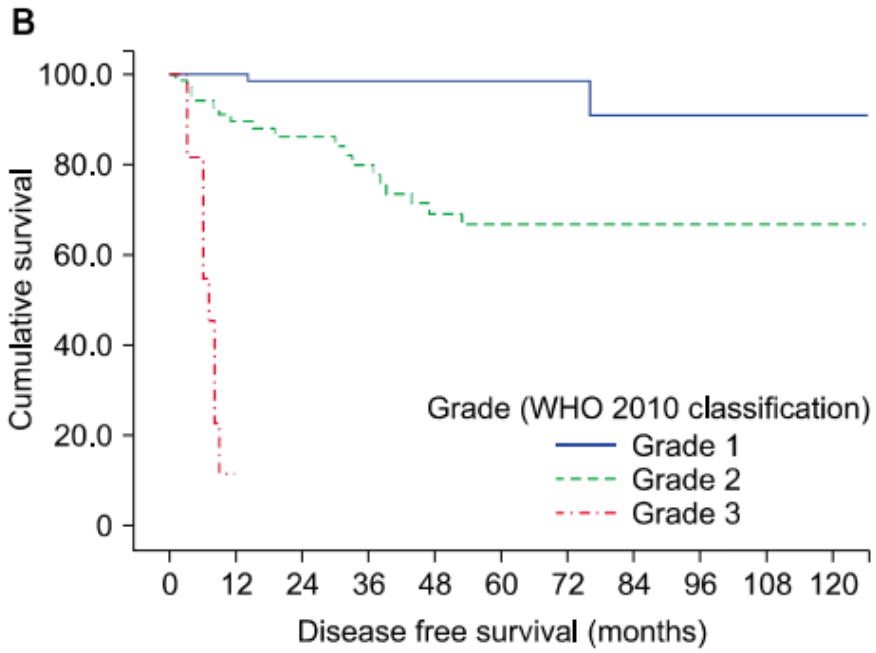

Ann Surg Oncol
DOI 10.1245/s10434-014-3769-4

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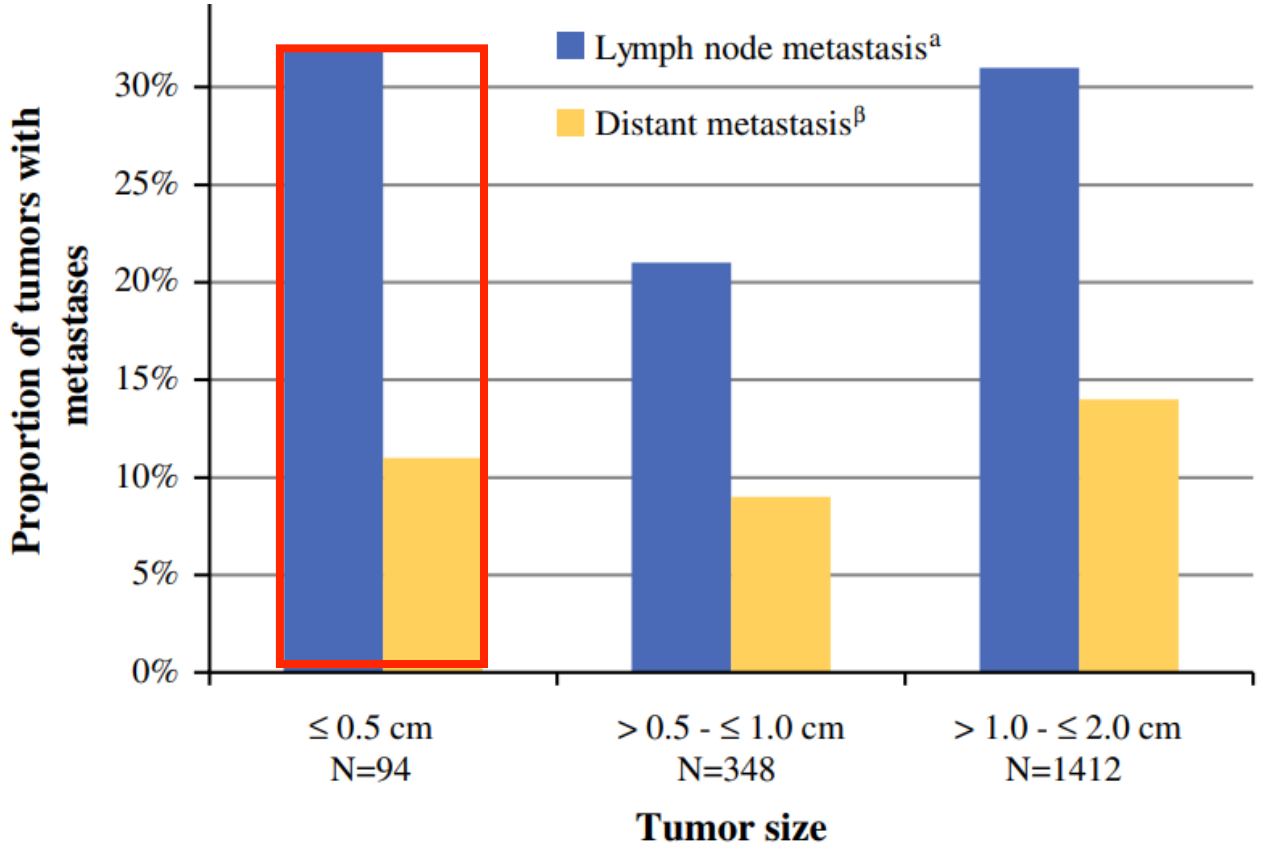
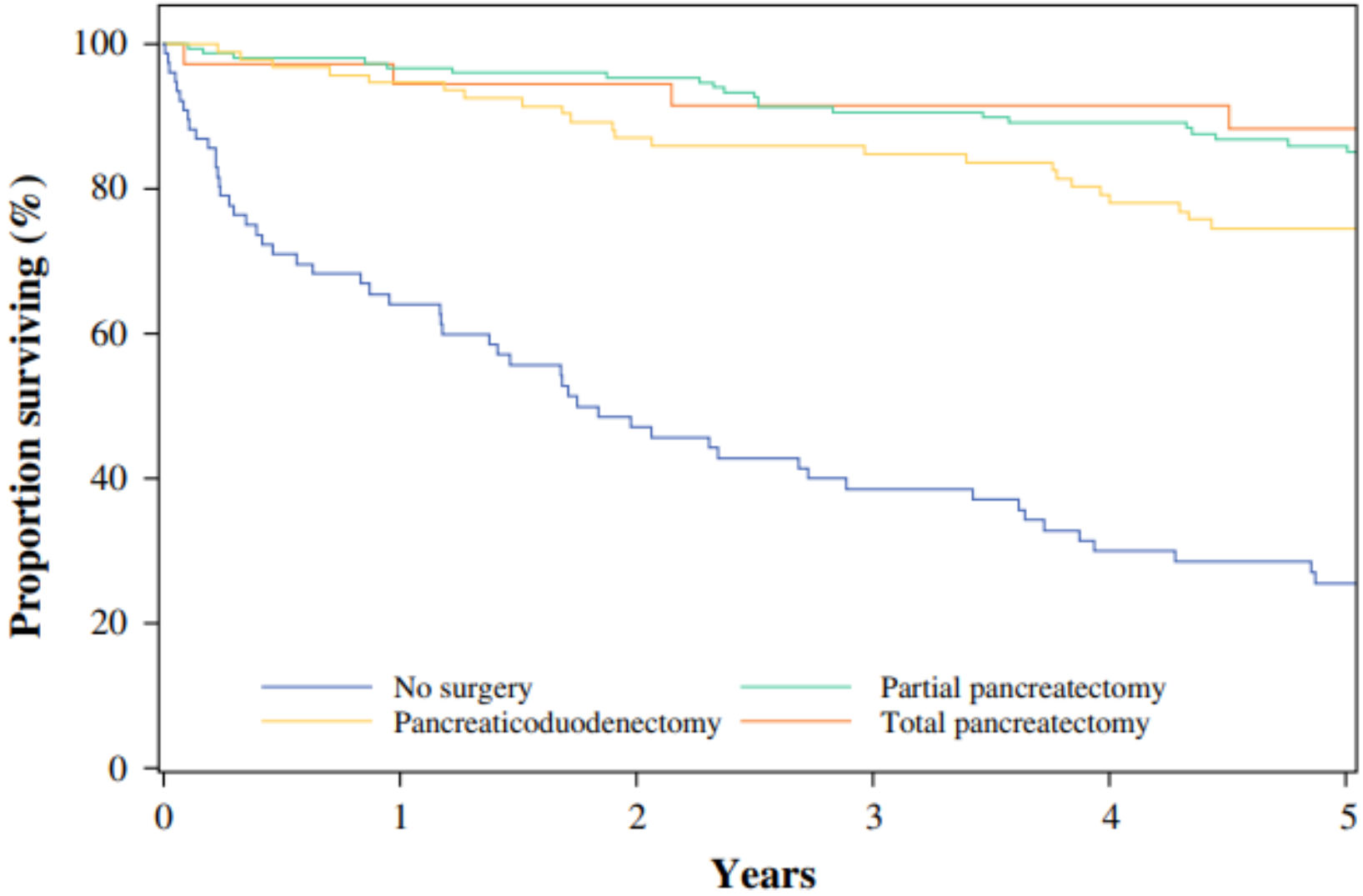
ORIGINAL ARTICLE – ENDOCRINE TUMORS

# Impact of Extent of Surgery on Survival in Patients with Small Nonfunctional Pancreatic Neuroendocrine Tumors in the United States




Gratian L, et al. Ann Surg Oncol 2014



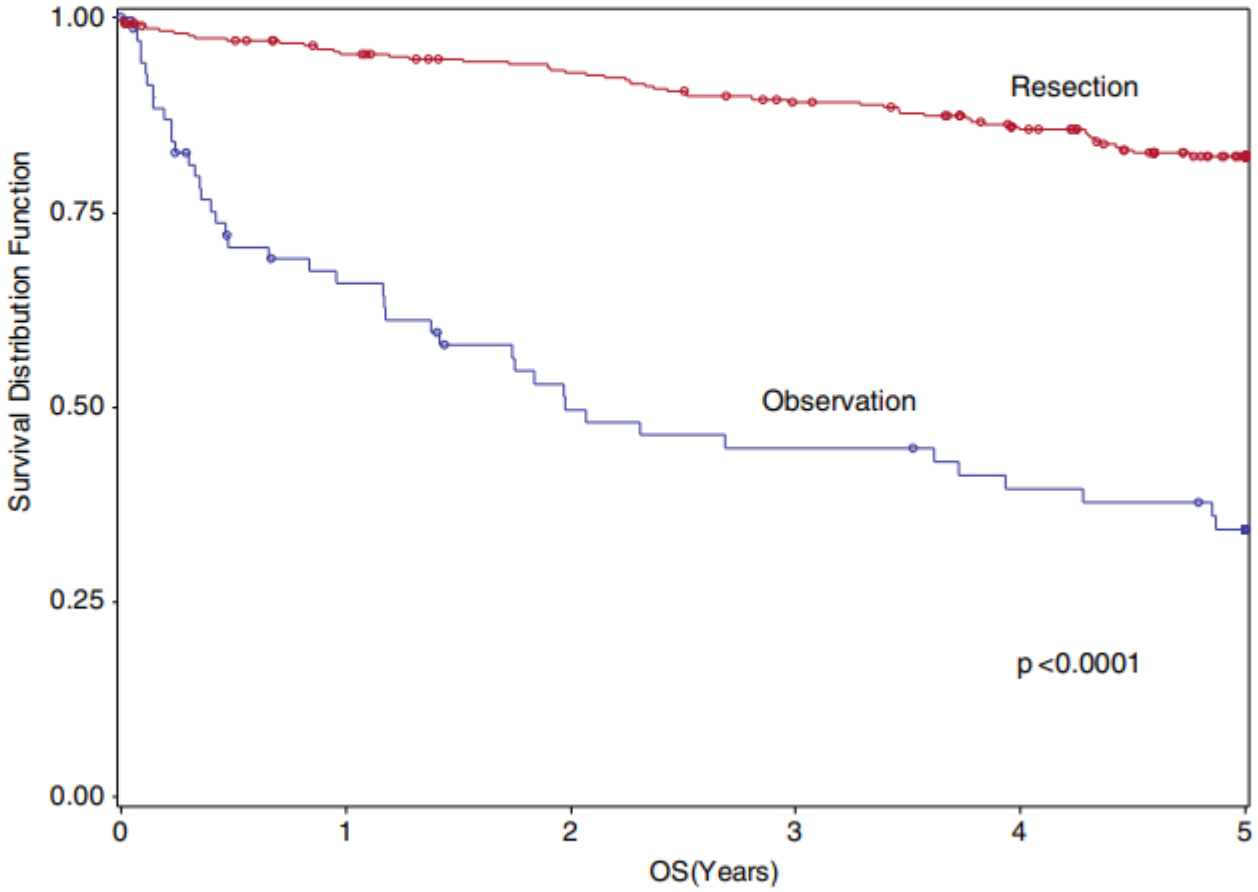

Gratian L, et al. Ann Surg Oncol 2014

J Gastrointest Surg
DOI 10.1007/s11605-014-2615-0

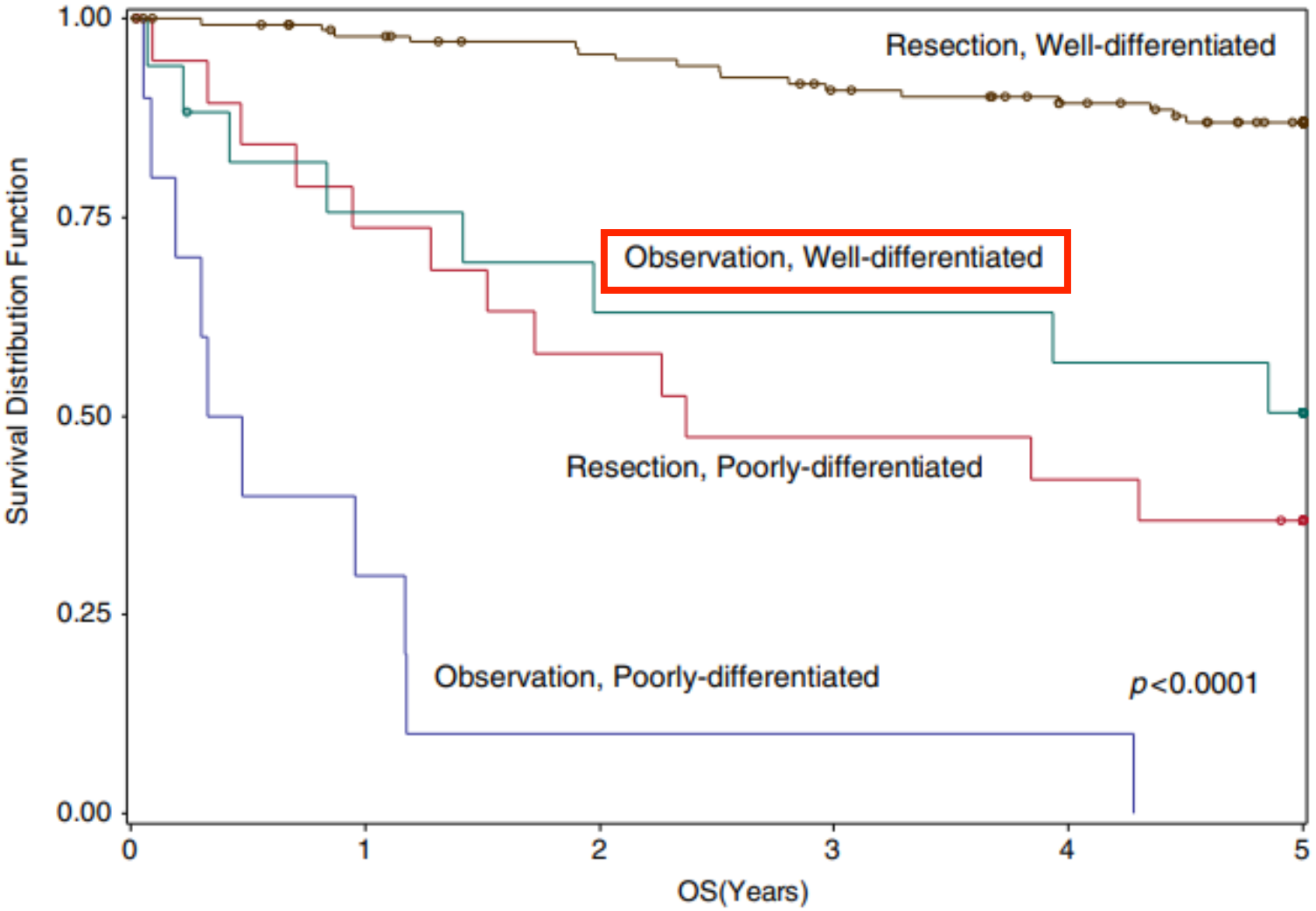
2014 SSAT PLENARY PRESENTATION

# Surgical Resection Provides an Overall Survival Benefit for Patients with Small Pancreatic Neuroendocrine Tumors

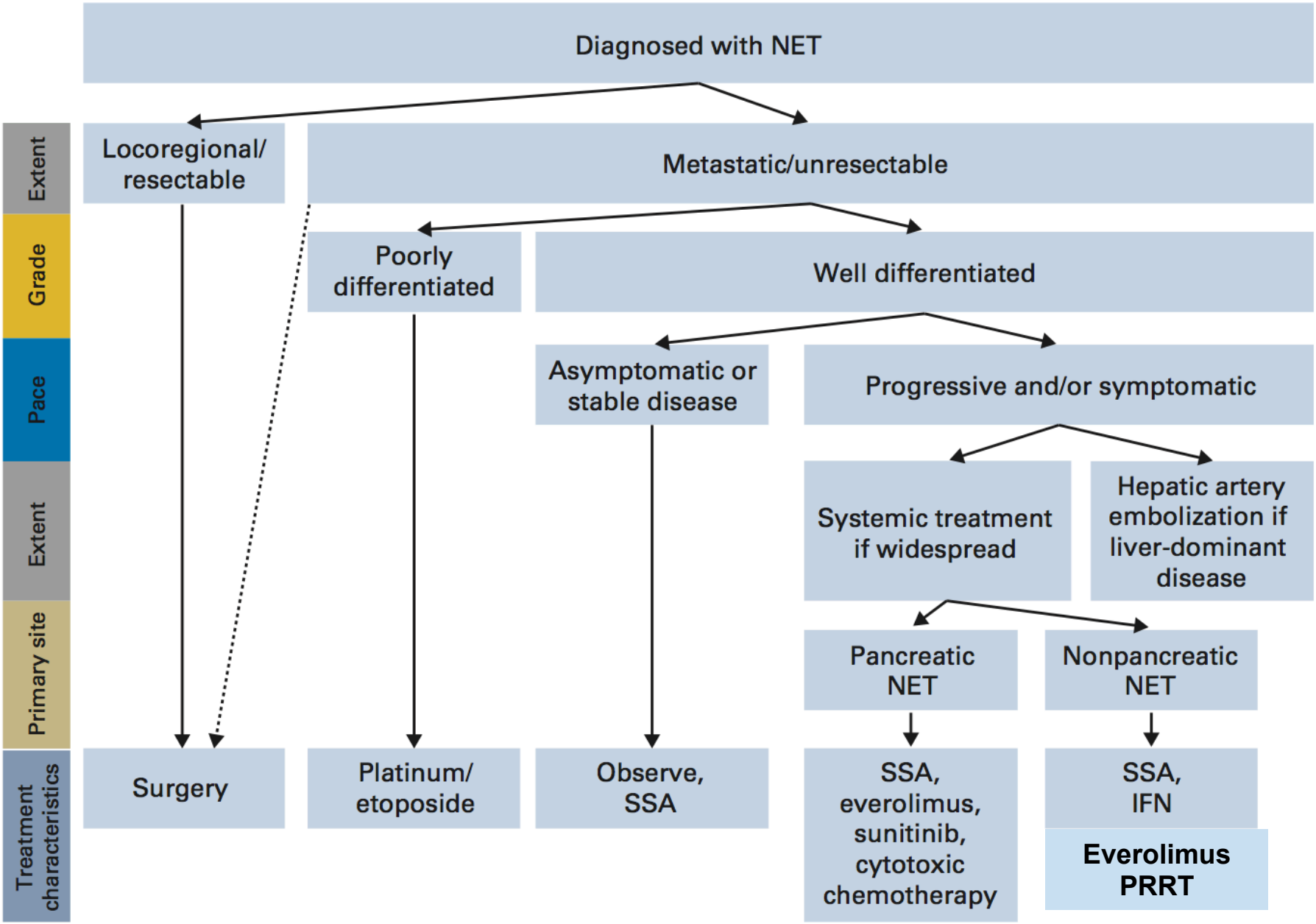
**Fig. 1** Kaplan-Meier survival estimates comparing patients with PNETs ≤2 cm who underwent surgical resection or observation




Sharpe SM, et al. J Gastrointest Surg 2014




Sharpe SM, et al. J Gastrointest Surg 2014




J Clin Oncol 33:1534, 2015

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# Operative resection in early stage pancreatic neuroendocrine tumors in the United States: Are we over- or undertreating patients?

**Table II**

Reasons for not undergoing operative resection of PanNETs <2 cm.

| | Tumor size | |
|---|---|---|
| | 0–1 cm | 1–2 cm |
| Resection not performed as first course of treatment | 209 (82.0%) | 345 (77.7%) |
| Resection not recommended due to patient risk factors | 13 (5.1%) | 37 (8.3%) |
| Patient deceased | 1 | 0 |
| Resection recommended but not done for unknown reasons | 3 (1.2%) | 9 (2.0%) |
| Resection recommended but patient refused | 7 (2.7%) | 29 (6.5%) |
| Resection recommended, unknown if performed | 11 (4.3%) | 18 (4.1%) |
| Unknown | 11 (4.3%) | 6 (1.4%) |

Chivukula SV, et al. Surgery 2019

**Table III**
Variables affecting likelihood to undergo operative resection of PanNETS <2 cm on multivariable analysis

| | OR | 95% Confidence interval | *P* value |
|---|---|---|---|
| Age | 0.95 | 0.95–0.96 | < .001 |
| Tumor size/lymph node status | | | |
| 2 cm or less with positive nodes | Ref | Ref | Ref |
| 0–1 cm and no positive lymph nodes | 0.28 | 0.17–0.44 | < .001 |
| 1–2 cm and no positive lymph nodes | 0.34 | 0.22–0.52 | < .001 |
| Location | | | |
| Location: Head | Ref | Ref | Ref |
| Location: Body/tail | 1.45 | 1.13–1.85 | .003 |
| Location: Missing | 0.99 | 0.74–1.33 | .97 |
| Grade | | | |
| Grade: Poorly or undifferentiated | Ref | Ref | Ref |
| Grade: Moderately differentiated | 2.30 | 1.09–4.86 | .03 |
| Grade: Well differentiated | 4.93 | 2.55–9.55 | < .001 |
| Grade: Missing | 0.48 | 0.25–0.94 | .03 |
| Hospital type | | | |
| Hospital type: Academic/research program | Ref | Ref | Ref |
| Hospital type: Community cancer program | 0.56 | 0.27–1.14 | .11 |
| Hospital type: Comprehensive community cancer | 0.68 | 0.53–0.86 | .001 |
| Hospital type: Integrated network cancer program | 1.42 | 0.97–2.07 | .07 |

Chivukula SV, et al. Surgery 2019

**Table IV**

Survival on univariate analysis of status of operative resection of the primary site in tumors of 0–1 cm and 1–2 cm, regardless of lymph node involvement

| | *n* | Survival rate at 5 y | Hazard ratio* (95% CI) | *P* value |
|---|---|---|---|---|
| Tumors 0–1.0 cm, regardless of lymph node involvement | | | | |
| No primary site resection | 312 | 77.1 | NA | .005 |
| Primary site resection | 1,452 | 83.3 | 0.28 (0.21–0.37) | |
| Tumors >1.0 and ≤2 cm, regardless of lymph node involvement | | | | |
| No primary site resection | 312 | 60.1 | NA | < .001 |
| Primary site resection | 1,452 | 89.1 | 0.28 (0.21–0.37) | |

*CI*, confidence interval.

* Reference group is no primary site resection.

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DOI: 10.1002/jso.25481

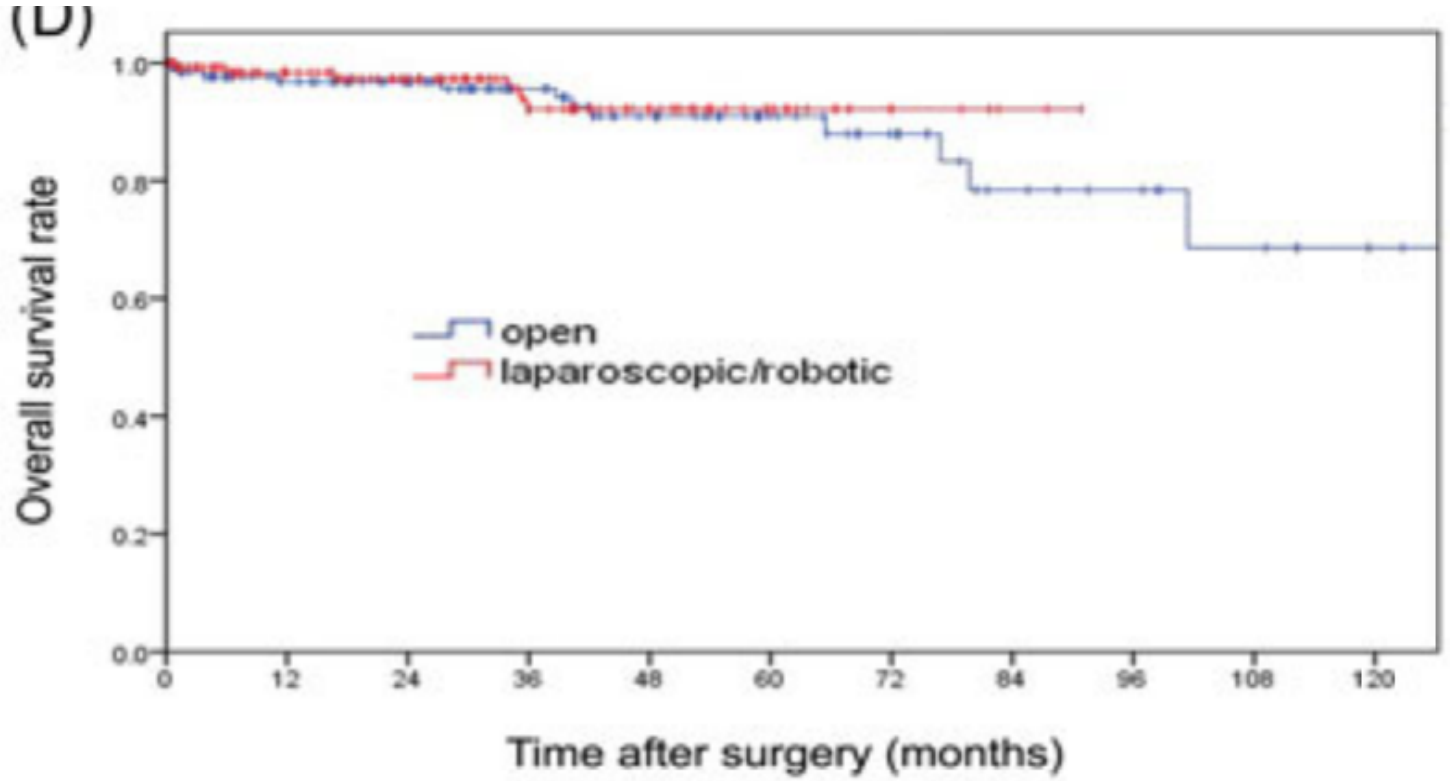
VIDEOLAPAROSCOPIA



WILEY Journal of SURGICAL ONCOLOGY

RESEARCH ARTICLE

# Minimally invasive versus open distal pancreatectomy for pancreatic neuroendocrine tumors: An analysis from the U.S. neuroendocrine tumor study group




Zhan XF, et al. J Surg Oncol 2019

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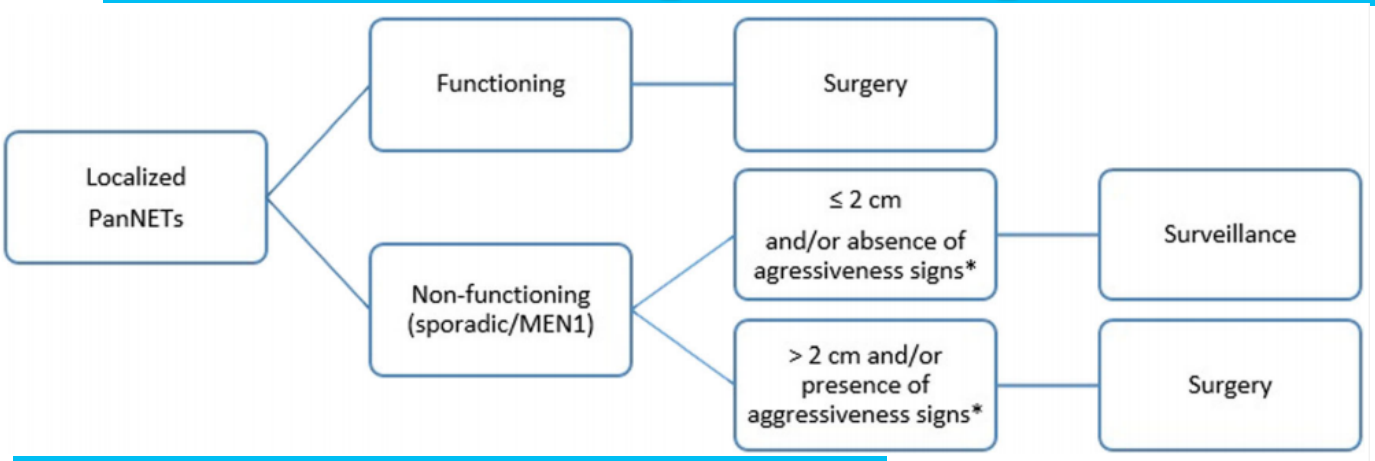


- ❑ > 10mm na cauda
- ❑ G2
- ❑ Sintomático
- ❑ Desejo do paciente
- ❑ Laparoscopia


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