

TNE no funcionantes de páncreas incidentales de pequeño tamaño: resultados de una serie con manejo no quirúrgico

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INTRODUCCIÓN

2% de los Tumores pancreáticos ¹

Incidencia 0,3 por 100.000 ¹

Pico de presentación 6-7^a décadas.

No diferencias en cuanto al sexo

No funcionantes: 70-90% ²

Esporádicos / Familiares: MEN1, Von Hippel Lindau, esclerosis tuberosa

1. Franko J. Non-functional neuroendocrine carcinoma of the pancreas: Incidence, tumor biology, and outcomes in 2,158 patients. J Gastrointest Surg. 2010

2. Halfdanarson Tr. Pancreatic Neuroendocrine tumors: incidence, prognosis and recent trend toward improved survival. Ann Oncol. 2008

INTRODUCCIÓN

Aumento de la incidencia de los tumores <2cm diagnosticados de forma incidental debido a la disponibilidad de nuevas técnicas diagnósticas.

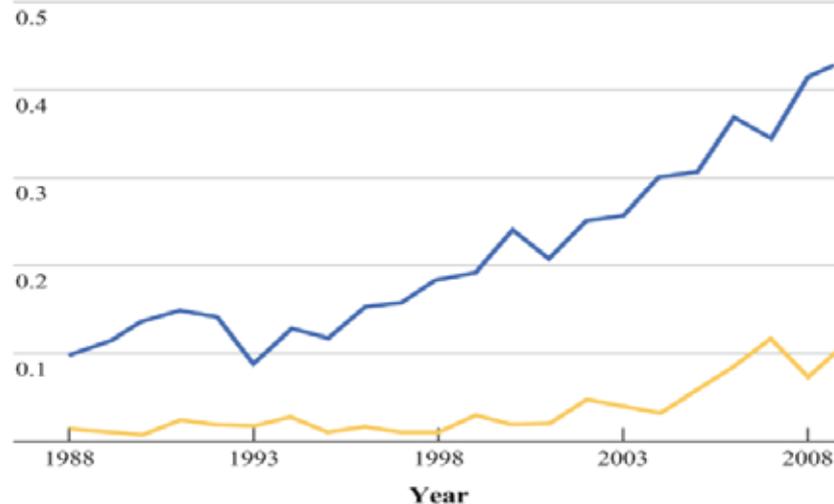
Ann Surg Oncol
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ORIGINAL ARTICLE

Population-Less
2 cm or Less

Eric J. Kuo, BS and 1

Incidence (per 100,000)
— PNETs > 2 cm, APC 7.5%, P < 0.0001
— PNETs ≤ 2 cm, APC 12.8%, P < 0.0001



ONCOLOGY
SOCIETY OF SURGICAL ONCOLOG

tumors

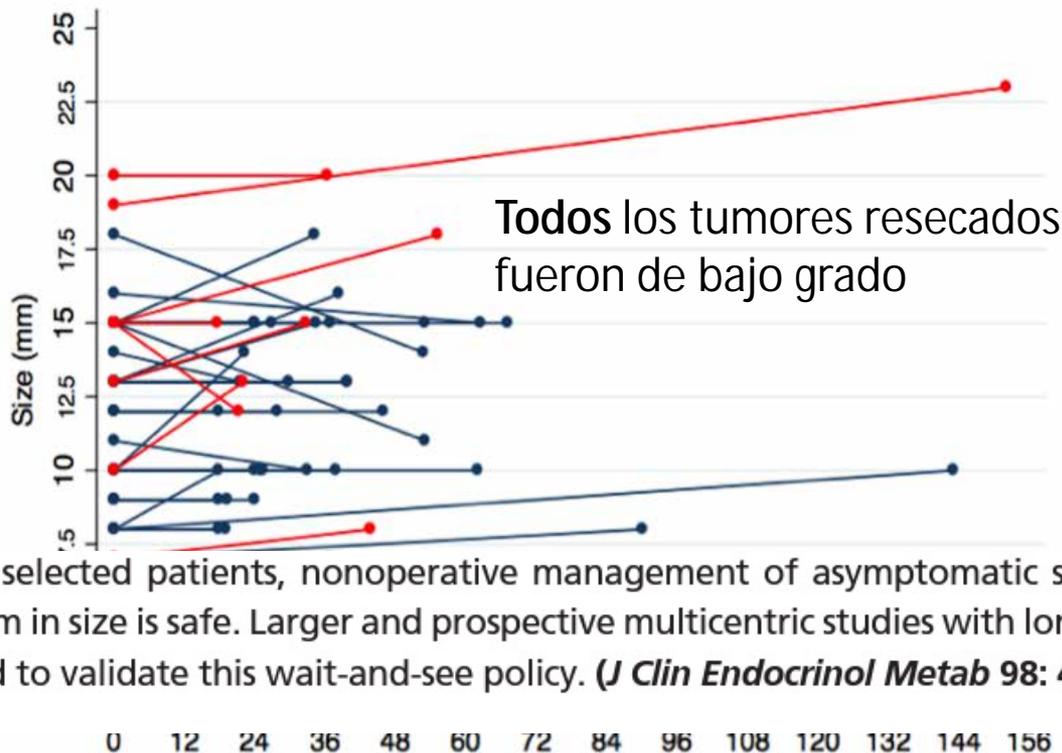
FIG. 2 Incidence of pancreatic neuroendocrine tumors ≤2 cm and >2 cm in size, SEER 1988–2009

INTRODUCCIÓN

La mayoría de los tumores <2cm, asintomáticos, incidentales y NF son de bajo grado de malignidad y crecimiento lento.

**Observa
Sporadi
Tumors**

Sébastien G.
Béatrice Larr
and Philippe



**Small
endocrine**

Infro,
imo Falconi,*

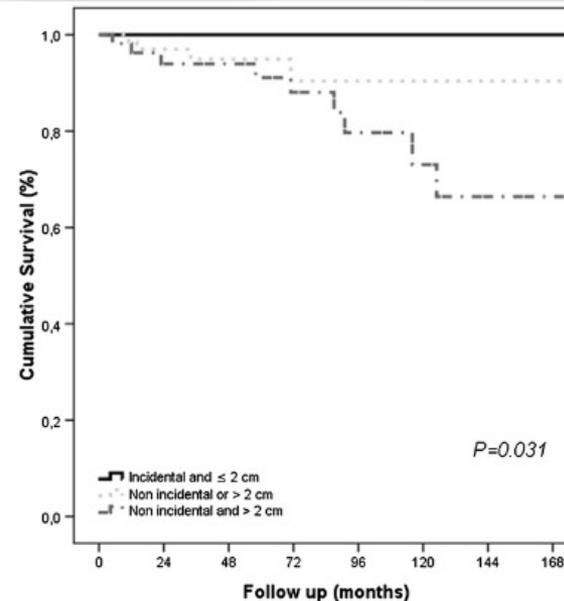
Conclusions: In selected patients, nonoperative management of asymptomatic sporadic NF-PNETs smaller than 2 cm in size is safe. Larger and prospective multicentric studies with long-term follow-up are now needed to validate this wait-and-see policy. (*J Clin Endocrinol Metab* 98: 4784–4789, 2013)

Tumor size correlates with malignancy in nonfunctioning pancreatic endocrine tumor

Rossella Bettini, MD,^a Stefano Partelli, MD,^b Letizia Boninsegna, MD,^{a,b} Paola Capelli, MD,^c Stefano Crippa, MD,^{a,b} Paolo Pederzoli, MD,^b Aldo Scarpa, MD,^c and Massimo Falconi, MD,^b Verona, Italy

Table II. Comparison of pathologic features among

Variable	Group 1 ≤2 cm (n = 90)	Group 2 <2 cm ≤4 cm (n = 46)
Histology (WHO)		
Benign	52 (57.8)	0 (0)
Uncertain behavior	22 (24.4)	31 (67.4)
WDEC	12 (13.3)	14 (30.4)
PDEC	4 (4.4)	1 (2.2)
Microvascular invasion		
Yes	13 (14.4)	18 (39.1)
No	77 (85.6)	28 (60.9)
Perineural infiltration		
Yes	21 (23.3)	11 (23.9)
No	69 (76.7)	35 (76.1)
Nodal metastases		
N1	13 (14.4)	10 (21.7)
N0-Nx	77 (85.6)	36 (78.3)
Liver metastases		
Yes	0 (0)	1 (2.2)
No	90 (100)	45 (97.8)
Ki67		
Median (IQR), %	1 (1-2)	2 (1-4)
Grading [REF]		
G1	77 (85.6)	30 (65.2)
G2	9 (10)	15 (32.6)
G3	4 (4.4)	1 (2.2)
Malignancy		
Yes	17 (18.9)	16 (34.8)
No	73 (81.1)	30 (65.2)



Pt. At Risk	51	24	19	11	6	4	1	1
Incidentally discovered and ≤ 2 cm	51	24	19	11	6	4	1	1
Non incidentally discovered or > 2 cm	71	52	33	20	13	9	5	4
Non incidentally discovered and > 2 cm	55	41	34	27	17	11	8	4

Fig 3. Disease-specific survival of patients after curative resection for NF-PET with tumors ≤2 that was incidentally discovered (n = 51) and the remaining patients (n = 119; P = .031).

Univariate analysis of clinical risk factors for malignancy in NF-PETs

Variable	Odds ratio	CI 95%	P value
Age	1	—	—
Sex	1.453	0.790 - 2.670	.229
Family history	1	—	—
Diabetes	0.923	0.500 - 1.706	.799
Chronic pancreatitis	1	—	—
Cholangitis	0.578	0.311 - 1.074	.083
Alcohol consumption	1	—	—
Smoking	3.668	1.910 - 7.045	<.0001
Family history	1	—	—
Diabetes	1.500	0.610 - 3.686	.377
Chronic pancreatitis	1	—	—
Cholangitis	6.083	3.086 - 11.992	<.0001

PDEC, Poorly differentiated endocrine carcinoma; WDEC, well-differentiated

Tumor size correlates with malignancy in nonfunctioning pancreatic endocrine tumor

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Verona, Italy

Conclusion. A strict correlation between tumor size and malignancy in nonfunctioning pancreatic endocrine tumors was demonstrated. A nonoperative management could be advocated for tumors ≤ 2 cm when discovered incidentally. (Surgery 2011;150:75-82.)

Small, nonfunctioning, asymptomatic pancreatic neuroendocrine tumors (PNETs): Role for nonoperative management

Louis C. Lee, MD,^a Clive S. Grant, MD,^a Diva R. Salomao, MD,^b Joel G. Fletcher, MD,^c Naoki Takahashi, MD,^c Jeff L. Fidler, MD,^c Michael J. Levy, MD,^d and Marianne Huebner, PhD,^e Rochester, MN

Table IV. Demographic and follow-up results for patients diagnosed with an incidental PNET

	Nonoperative group (n = 77)	Operative group (n = 56)
Median age, y (range)	67 (31–94)	60 (27–82)
Sex, n (%)		
Male	42 (55)	34 (61)
Female	35 (45)	22 (39)
Biopsy confirmation, n (%)	22 (29)*	32 (57)*
Median neoplasm start size (range), cm	<u>1.0 (0.3–3.2)</u>	1.8 (0.5–3.6)
Median neoplasm end size (range), cm	<u>1.0 (0.4–4.0)†</u>	—
Clinical follow-up, mean (range), months	45 (3–153)‡	52 (3–138)§

Conclusion. Small nonfunctioning PNETs usually exhibit minimal or no growth over many years. Nonoperative management may be advocated when serial imaging demonstrates minimal or no growth without suspicious features. (Surgery 2012;152:965-74.)

TRATAMIENTO QUIRÚRGICO vs OBSERVACIÓN

Controversias respecto al tratamiento óptimo de los TNE diagnosticados de forma incidental, no funcionantes, asintomáticos de pequeño tamaño.



TRATAMIENTO QUIRÚRGICO vs SEGUIMIENTO

Morbi-mortalidad asociada a la cirugía pancreática en pacientes previamente asintomáticos

- Mortalidad 1.7% - Complicaciones 29,6%
- Fístula pancreática grado B/C ²⁻³
 - 12-29%
- Insuficiencia pancreática: ³
 - 29-58%



1. Smith Jk et al. Complications after pancreatectomy for neuroendocrine tumors: a national study. J Surg Res. 2010
2. Falconi M. Parenchyma-preserving resections for small nonfunctioning pancreatic endocrine tumors. Ann Surg Oncol. 2010
3. Lee LC et al. Small, nonfunctioning, asymptomatic pancreatic neuroendocrine tumors (PNETs): Role for nonoperative management. Surgery 2012

TRATAMIENTO QUIRÚRGICO vs SEGUIMIENTO

¿Qué dicen las guías?

ENETS Consensus Guidelines for the Management of Patients with Digestive Neuroendocrine Neoplasms of the Digestive System: Well-Differentiated Pancreatic Non-Functioning Tumors

Neuroendocrinology 2012;95:120-134

DOI: [10.1159/000335587](https://doi.org/10.1159/000335587)

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all other Barcelona Consensus Conference participants¹

should be routinely resected [91]. Most of neoplasms ≤ 2 cm are likely benign or intermediate-risk lesions and only 6% of NF pancreatic NETs ≤ 2 cm are malignant when incidentally discovered [92]. In this setting, a non-operative approach could be advocated in selected cases for tumors ≤ 2 cm that are discovered incidentally. An intensive

TRATAMIENTO QUIRÚRGICO vs SEGUIMIENTO

¿Qué dicen las guías?

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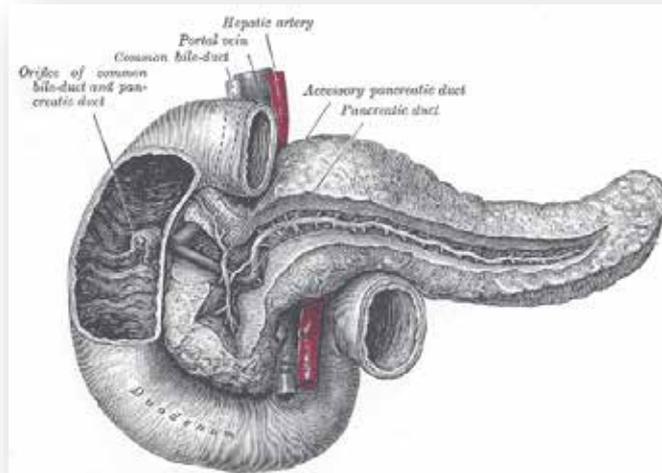
ORIGINAL ARTICLE – ENDOCRINE TUMORS

TABLE 1 Minimal consensus recommendations

Section	Minimal consensus recommendations (level of consensus)
Classification	Both the 2010 WHO and ENETS are acceptable classification systems (1) pNETs should be classified according to tumor grade based primarily on Ki67 index and mitotic count and staged according to the AJCC
Pathology	Every pathology report should include the entire CAP checklist plus Ki67 measured at the point of highest proliferation (1) Synaptophysin, chromogranin-A, and Ki67 immunohistochemistry are the minimal immunohistochemistry staining Diagnosis should be confirmed with core biopsy if possible (1) Multiple biopsies may be considered if results are discordant with clinical behavior and where additional information will influence clinical presentation and prognosis
Clinical presentation and prognosis	Prognostic factors to be considered when assessing pNET patients include tumor grade, tumor size, pace of clinical disease progression, and performance status
Imaging and laboratory testing	Appropriate cross-sectional imaging via triphasic CT and/or MRI is recommended for all patients EUS is a preferred route for a diagnostic biopsy of a pancreatic mass SRS is recommended at the time of diagnostic workup and/or preoperatively Measurement of CgA is recommended for all patients
Surgical management	Localized NF-pNETs Surveillance of pNETs is reasonable if the tumor is a small solitary lesion (≤ 2 cm) that has demonstrated stability over time (2B)

OBJETIVO

Analizar la evolución de los tumores neuroendocrinos de páncreas, diagnosticados de forma incidental, asintomáticos, de pequeño tamaño, sometidos a seguimiento clínico sin cirugía.

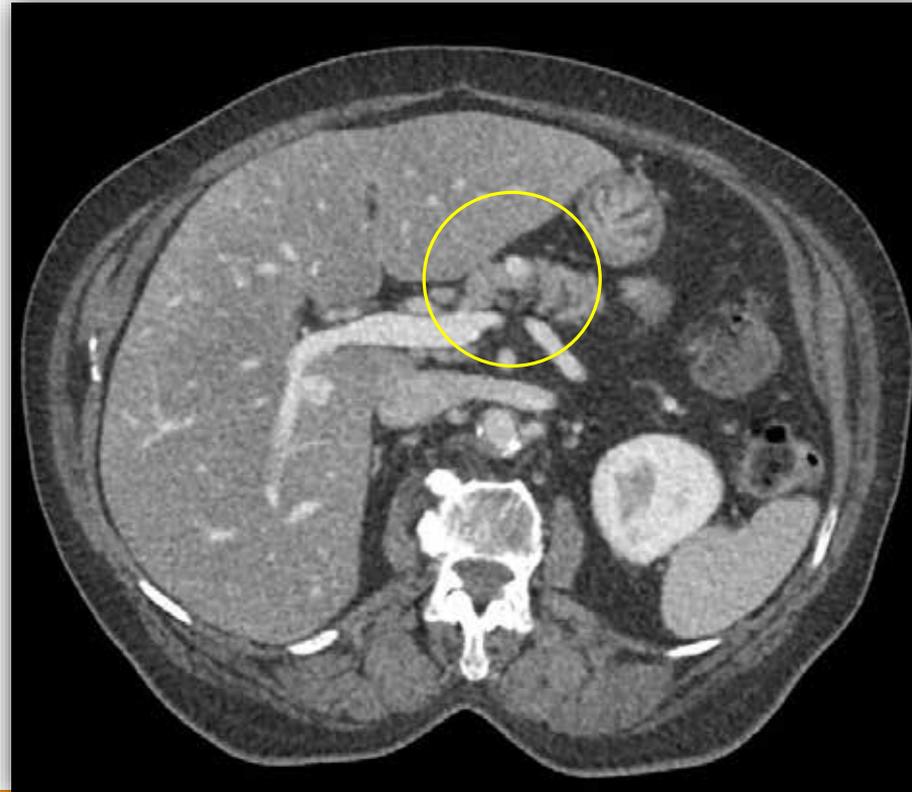


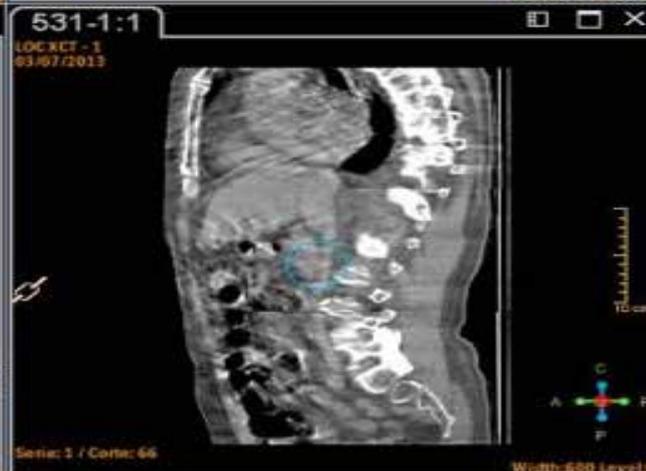
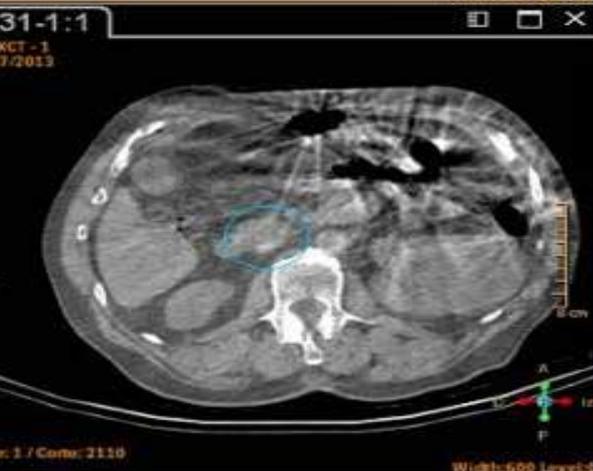
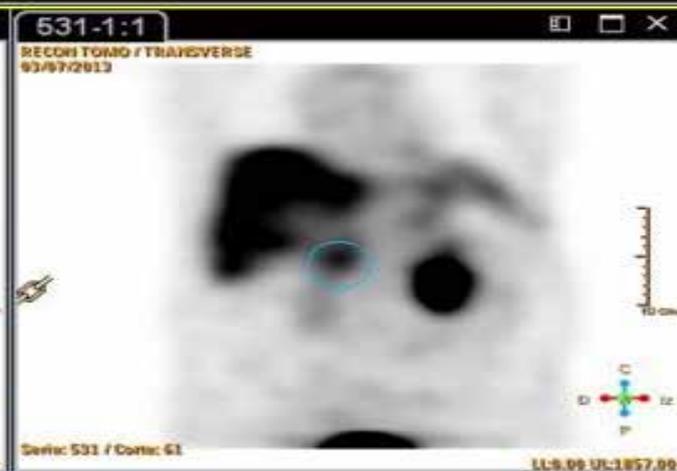
MATERIAL Y MÉTODOS

Seguimiento prospectivo de pacientes diagnosticados de TNE de páncreas desde Noviembre de 2007 a Junio de 2015.

Diagnóstico:

- TCH multidetector
- RMN
- Octreoscan
- Ecoendoscopia + punción en caso de dudas diagnósticas





MATERIAL Y MÉTODOS

CRITERIOS DE INCLUSIÓN

Diagnóstico incidental

Menores de 3cm

Asintomáticos

CRITERIOS DE EXCLUSIÓN.

*Signos de invasión local:
obstrucción ductal,
invasión vascular y
estructuras adyacentes,
Metástasis hepáticas.*

Mayores de 3cm

MATERIAL Y MÉTODOS

Seguimiento clínico en consultas externas:

- TCH/RNM cada 3 meses primer semestre.
- TCH/RNM cada 6 meses por dos años
- TCH/RMN cada año

RESULTADOS

N= 29p. (Nov 2007-Jun 2015)

Diagnóstico realizado de forma incidental.

TCMD: hipervascular en fase arterial-portal

RMN: hipointenso en T1/ iso-hiperintenso en T2

SPECT con Receptores de Somatostatina

Localización:

- Cabeza y cuello (61%)
- Cuerpo y Cola (39%)

Ecoendoscopia y PAAF en 2 casos en los que habían dudas diagnósticas

Bajo grado y Ki 67. < 2%.

RESULTADOS

<i>Edad Media (rango)</i>	<i>69 años (41-91)</i>
<i>Sexo, n (%)</i>	
<i>Hombres</i>	<i>13 (45%)</i>
<i>Mujeres</i>	<i>16 (55%)</i>
<i>Tamaño inicial (media; rango)</i>	<i>13mm (5-27mm)</i>
<i>Tiempo de seguimiento (media; rango)</i>	<i>39 meses (8-100)</i>
<i>Tamaño final (media; rango)</i>	<i>13 mm (5-34mm)</i>
<i>Aumento de tamaño, n (%)</i>	<i>8 (29%)</i>
<i>Media aumento (rango)</i>	<i>3mm (0-7mm)</i>
<i>Igual tamaño, n (%)</i>	<i>21 (71%)</i>
<i>Progresión locorregional, n</i>	<i>0</i>
<i>Metástasis a distancia</i>	<i>0</i>
<i>Resección</i>	<i>0</i>

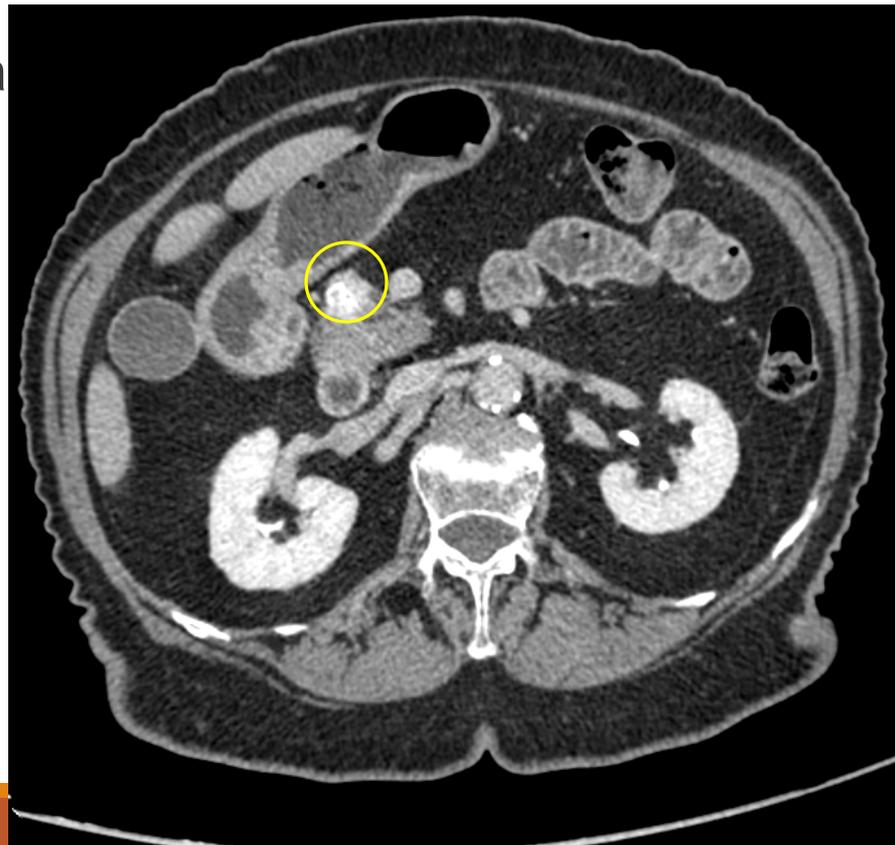
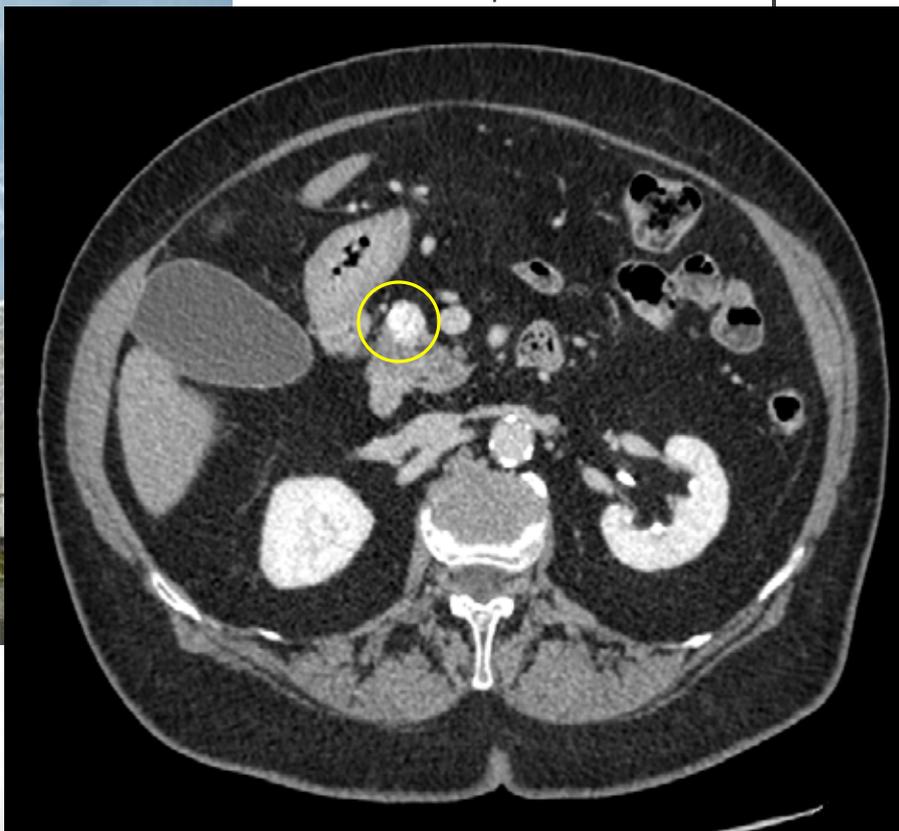
Incluimos 3 pacientes con tamaño tumoral >2 cm. Se decide observación por rechazo del paciente al tratamiento quirúrgico o comorbilidad asociada

RESULTADOS

M. 85 años.

AP: HTA, BAV. Marcapasos. Diverticulosis

Ca



CONCLUSIONES

En pacientes seleccionados, el manejo no quirúrgico de tumores neuroendocrinos pancreáticos <2cm, no funcionantes, asintomáticos e incidentales, plantea una opción válida.

Son necesarios estudios prospectivos, multicéntricos, con mayor número de pacientes y mayor tiempo de seguimiento para validar esta opción conservadora.



10^è
CONGRÉS
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15 y 16 de OCT 2015

GRACIAS

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