



Roma, 8-11 novembre 2018



ITALIAN CHAPTER



NEN del Pancreas Inquadramento clinico

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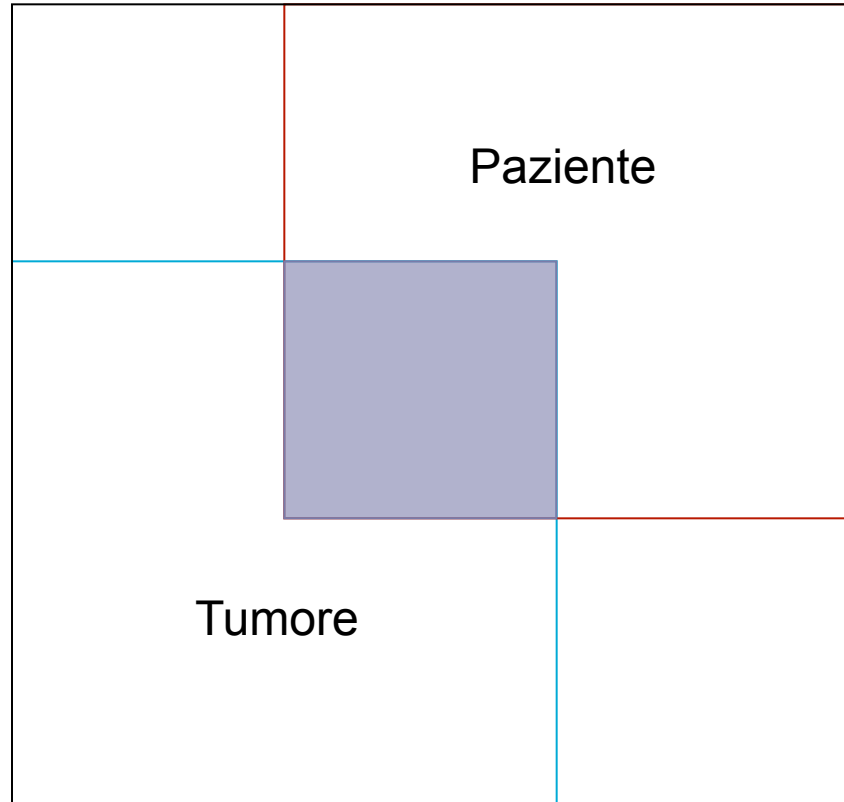
NEN pancreas: inquadramento clinico



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Inquadramento





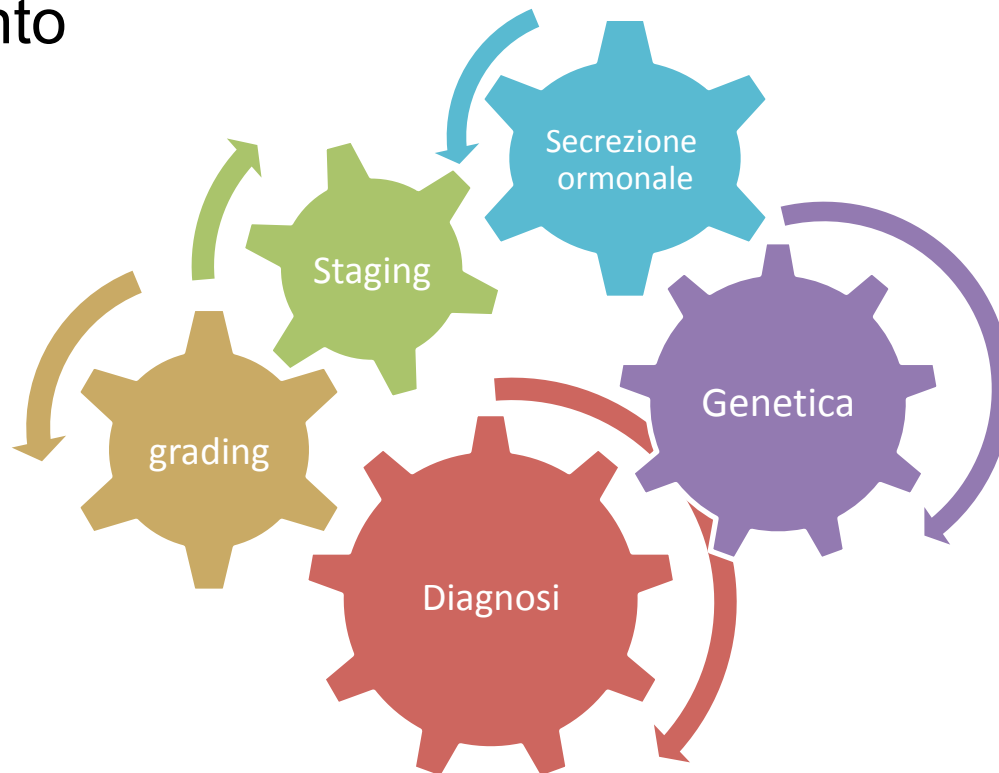
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Inquadramento





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NEN pancreas: diagnosi



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Diagnosi



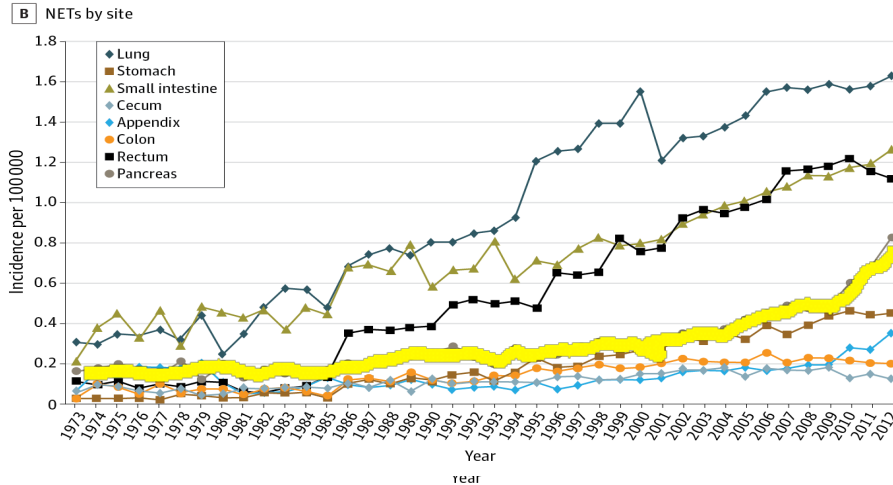


NEN pancreas: diagnosi

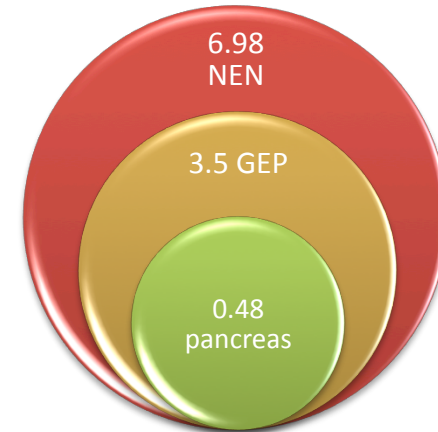


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- Incidenza
- dal 1973 al 2012 aumento di incidenza dei NET
- Aumento di incidenza si è verificato in tutti i siti, gli stadi e i gradi



/100.000 p/a





NEN pancreas: diagnosi

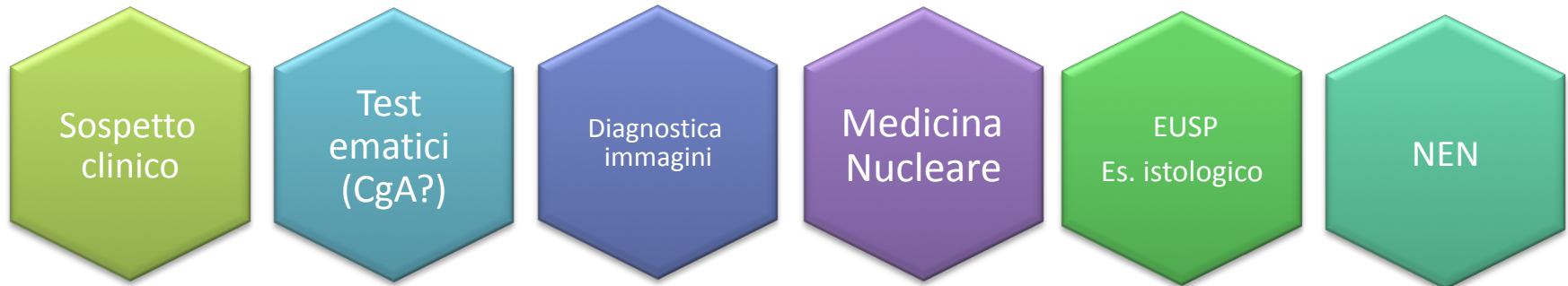
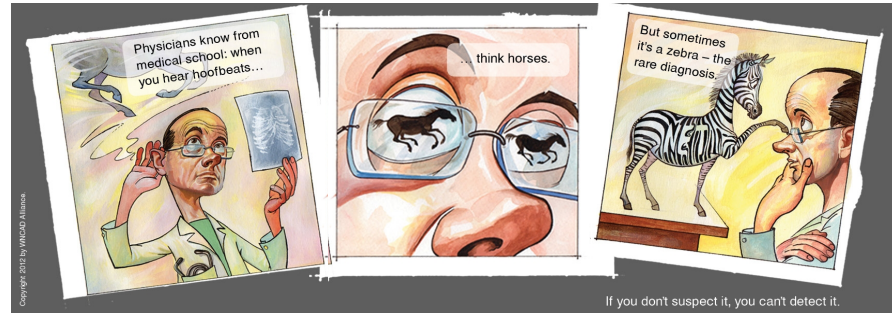


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- Diagnosi

NEN mai la prima ipotesi
Malattia non frequente =
malattia poco probabile





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NEN pancreas: diagnosi incidentale



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Stage	Incidental #pts	Symptomatic #pts	% of incidental
I	51	30	63%
IIa - IIb	33	39	46%
IIIa - IIIb	30	75	28%
IV	10	87	10%
Overall	124	231	35%



Crippa S, et al. Surgery 2014



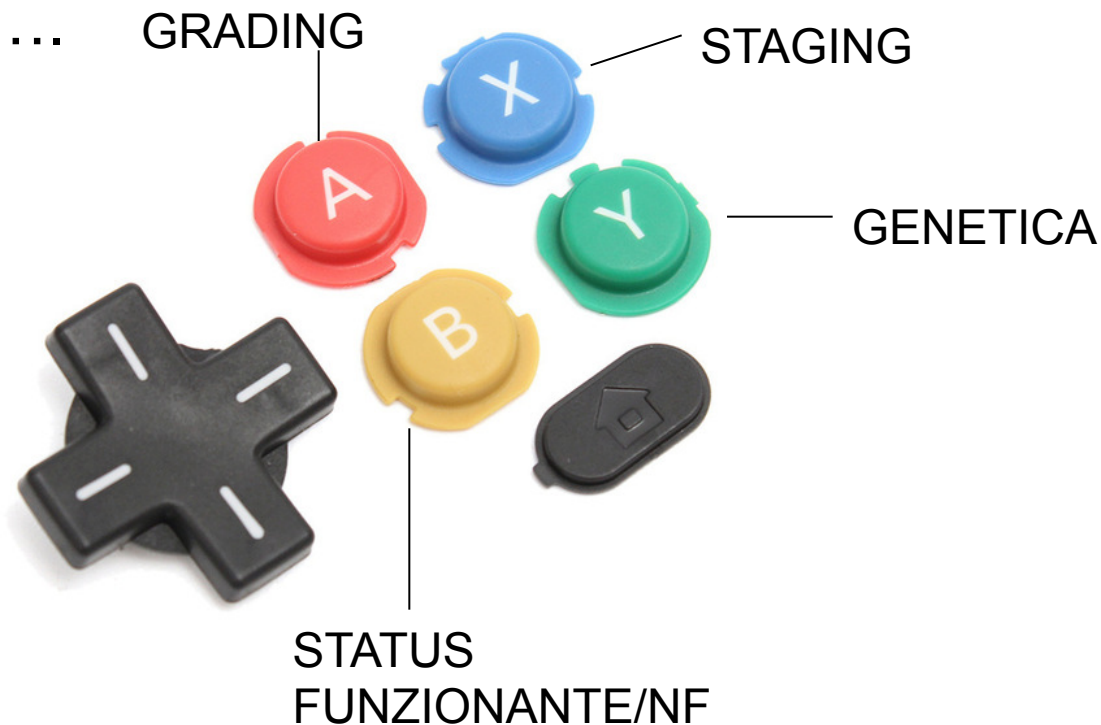
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Oltre alla Diagnosi....
Caratterizzazione





NEN pancreas: GRADING



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WHO 1980	WHO 2000/2004	WHO 2010	WHO 2017
Islet cell tumour (adenoma/carcinoma)	Well-differentiated endocrine tumour/carcinoma (WDET/WDEC)	G1/G2 NET	G1/G2/G3 NET (well-differentiated NEN)
Poorly differentiated endocrine carcinoma	Poorly differentiated endocrine carcinoma / small cell carcinoma (PDEC)	NEC (G3), large cell or small cell type	NEC (G3), large cell or small cell type (poorly differentiated NEN)
	Mixed exocrine–endocrine carcinoma (MEEC)	Mixed adenoneuroendocrine carcinoma	Mixed neuroendocrine–non-neuroendocrine neoplasm
Pseudotumour lesions	Tumour-like lesions (TLLs)	Hyperplastic and preneoplastic lesions	

NEC, neuroendocrine carcinoma; NET, neuroendocrine tumour.



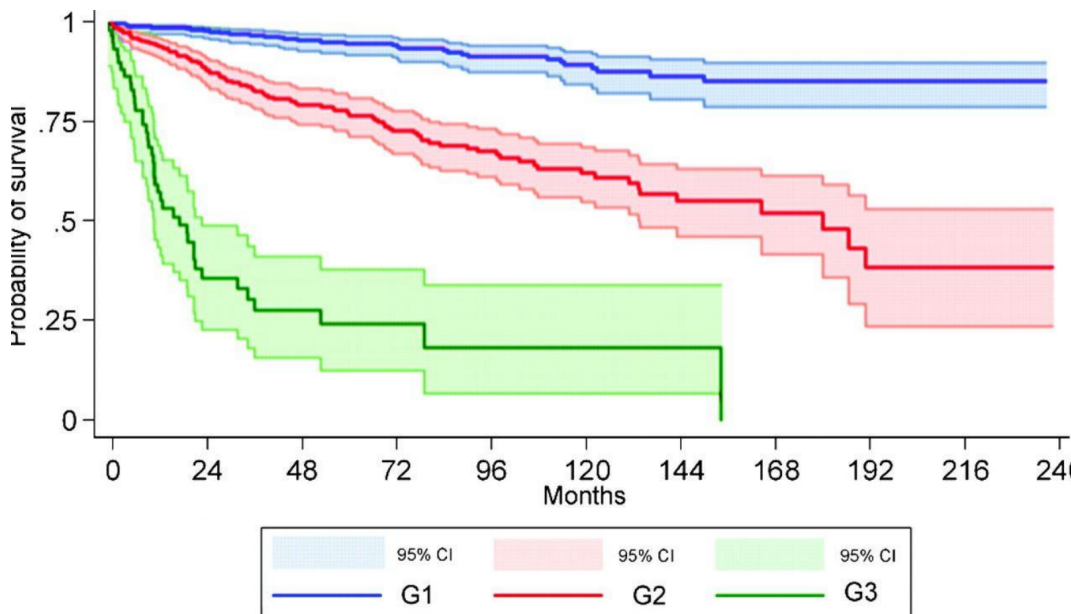
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WHO 2010



Rindi et al., J Natl Cancer Inst 2012; 104:746



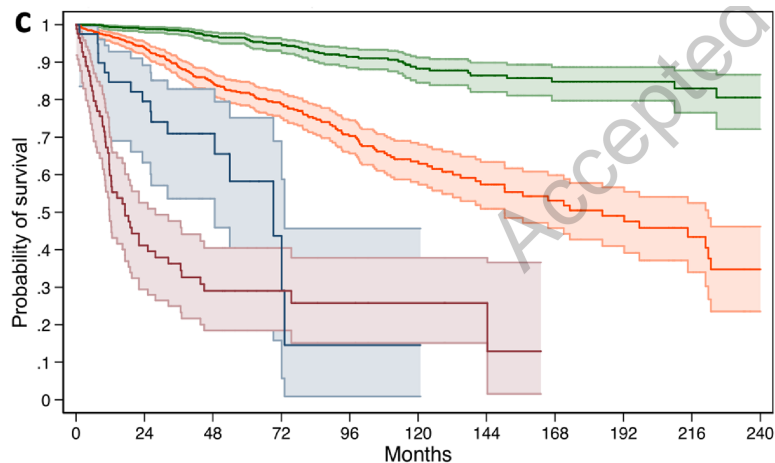
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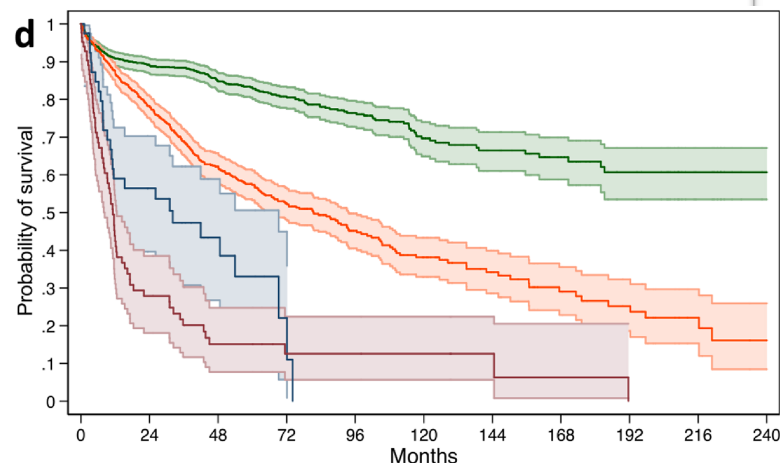
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WHO 2017



	0	24	48	72	96	120	144	168	192	216	240
Number at risk											
G1	1030	848	632	413	270	178	123	89	62	40	23
G2	809	632	423	282	172	103	63	45	32	18	8
G3	40	29	13	3	1	1	0	0	0	0	0
G3 PD	84	26	16	9	6	4	2	0	0	0	0

G1 95%CI █ G2 95%CI █ G3 95%CI █ G3 PD 95%CI █



	0	24	48	72	96	120	144	168	192	216	240
Number at risk											
G1	1030	756	548	338	216	132	86	59	40	25	16
G2	809	529	309	188	105	63	39	25	17	8	4
G3	40	20	9	2	0	0	0	0	0	0	0
G3 PD	84	19	9	5	5	4	2	1	0	0	0

G1 95%CI █ G2 95%CI █ G3 95%CI █ G3 PD 95%CI █



Rindi et al., Neuroendocrinology 2018; in press



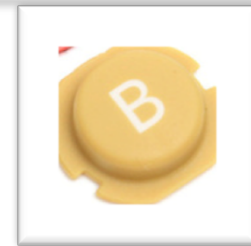
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Corretto staging è associato agli outcomes di sopravvivenza



C
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I

Definitions	ENETS TNM	UICC/AJCC/WHO 2010 TNM
T definition		
T1	Limited to the pancreas, <2 cm	Limited to the pancreas, <u>≤2</u> cm in greatest dimension
T2	Limited to the pancreas, 2–4 cm	Limited to the pancreas, >2 cm in greatest dimension
T3	Limited to the pancreas, >4 cm or invading <u>duodenum or bile duct</u>	<u>Beyond the pancreas</u> but without involvement of the superior mesenteric artery
T4	Tumor invading <u>adjacent organs</u> (stomach, spleen, colon, adrenal gland) or the wall of <u>large vessels</u> (celiac axis or the superior mesenteric artery)	Involvement of <u>celiac axis</u> or the <u>superior mesenteric artery</u> (unresectable tumor)

Classi

N	0/1
M	0/1

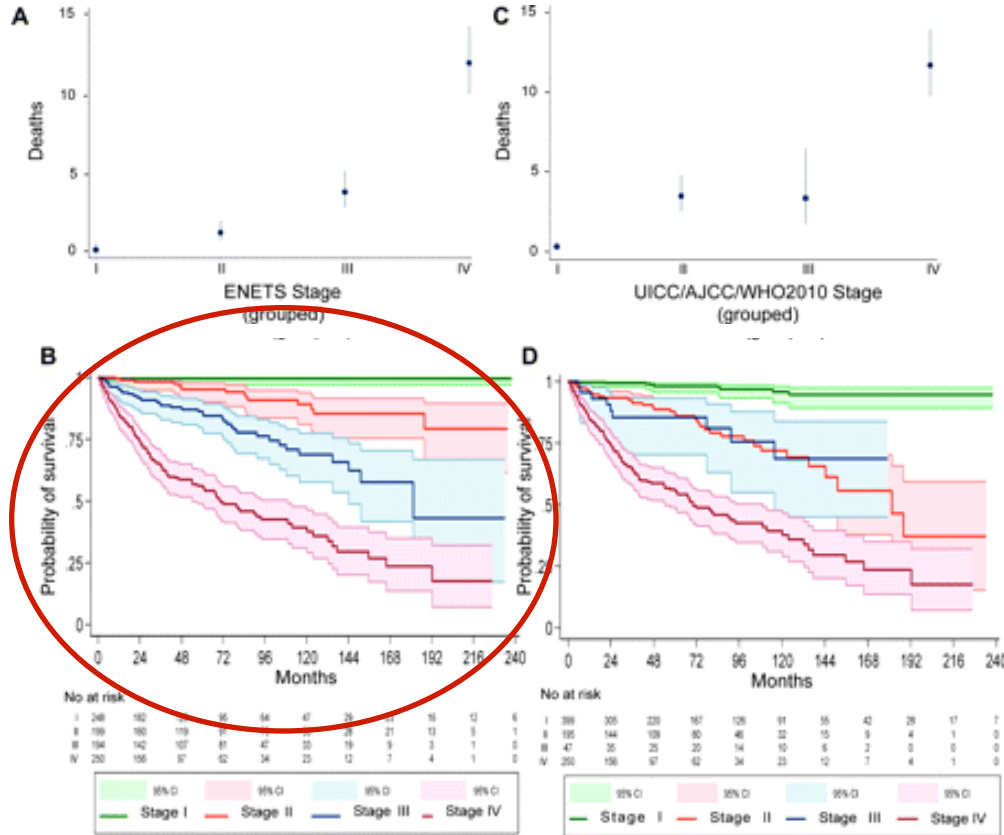


NEN pancreas: STAGING



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TNM ENETS rispetto al TNC UICC / AJCC / WHO 2010 è più accurato

Discrimina meglio gli stage II e III

Rindi et al., J Natl Cancer Inst 2012; 104:746



NEN pancreas: STAGING



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Modified Staging Classification for pNETs

Table 1. The AJCC Staging Definitions, the ENETS Staging Definitions, and the mENETS Staging Definitions for Pancreatic Neuroendocrine Tumors, With Cross-Tabulation of Stage Distributions

AJCC Staging Classification

T1	Tumor limited to the pancreas, ≤ 2 cm in greatest dimension
T2	Tumor limited to the pancreas, > 2 cm in greatest dimension but without involvement of the superior mesenteric artery or superior mesenteric vein
T3	Tumor limited to the pancreas, > 4 cm in greatest dimension and involving the duodenum or common bile duct
T4	Tumor invades adjacent structures
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
M0	No distant metastasis
M1	Distant metastasis

ENETS Staging Classification

T1	Tumor limited to the pancreas, ≤ 2 cm
T2	Tumor limited to the pancreas, 2-4 cm
T3	Tumor limited to the pancreas, > 4 cm, not involving the duodenum or common bile duct
T4	Tumor invades adjacent structures
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
M0	No distant metastasis
M1	Distant metastasis

Poca discriminazione fra stadio II e III e pochi Pz T4

AJCC			ENETS		
	N	M	Stage	T	M
IB	N0	M0	I	T1	N0
IIA	N0	M0	IIA	T2	N0
IIIB	N0	M0	IIIB	T3	N0
III	T1-3	N1	IIIA	T4	N1
IV	Any T	Any N	IIIB	Any T	Any N
	Any T	Any N	IV	Any T	Any M

- stadio I prognosi simile nei pazienti con stadio IIA
- stadio IIIA prognosi peggiore rispetto a stadio IIIB

mENETS*

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

ENETS

Systems	ENETS				AJCC			
	I	II	III	IV	I	II	III	IV
mENETS	700	602	0	0	1,294	8	0	0
	0	539	660	0	281	916	2	0
	0	0	358	0	2	278	78	0
	0	0	0	813	0	0	0	813

Abbreviations: AJCC, American Joint Cancer Committee; ENETS, European Neuroendocrine Tumor Society; mENETS, modified ENETS; M, distant metastasis; N, lymph nodes; T, primary tumor.

*The mENETS staging classification was proposed by maintaining the ENETS T, N, and M definitions and adopting the AJCC staging definitions.



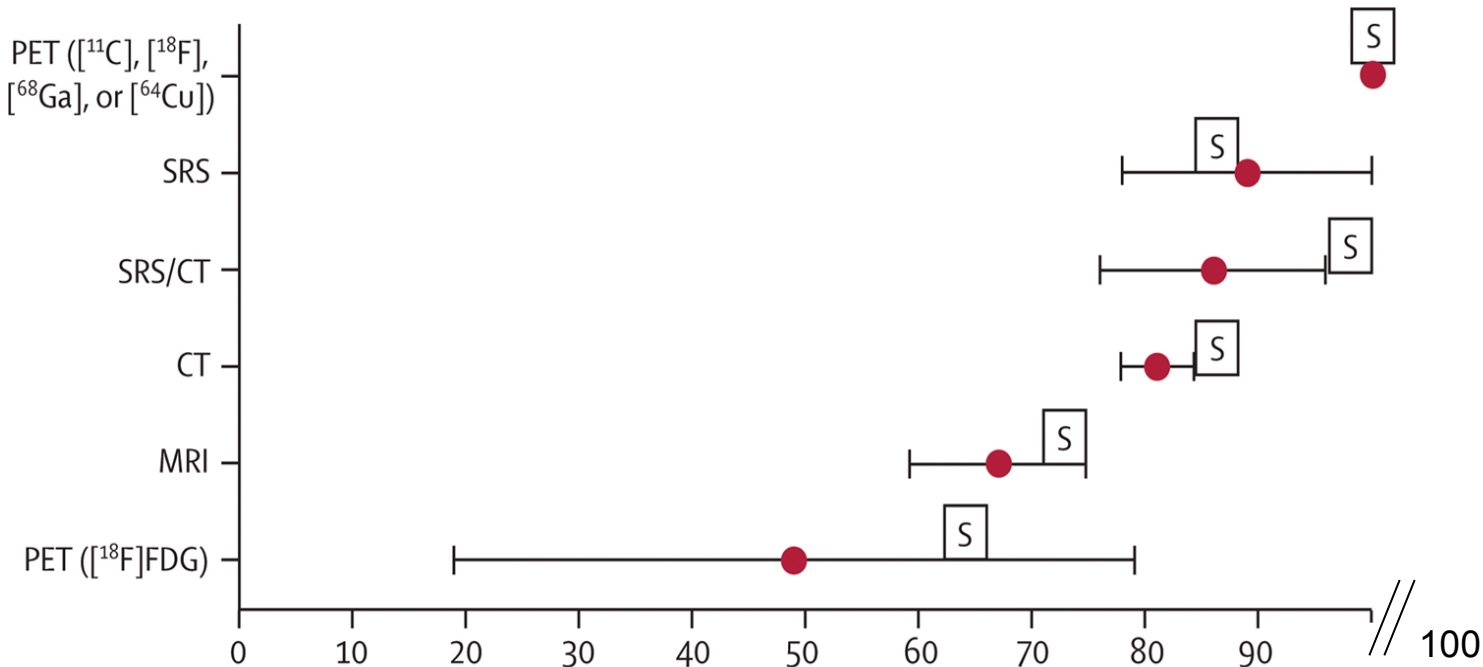
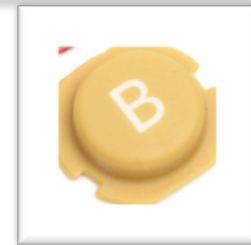
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Esami per stadiazione





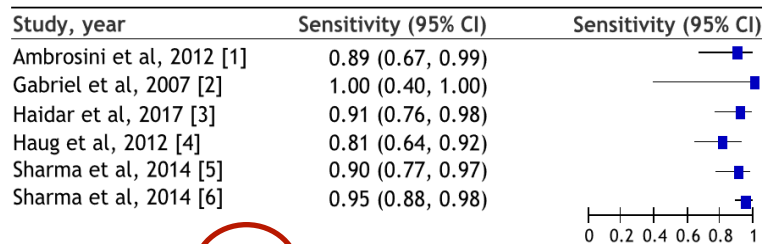
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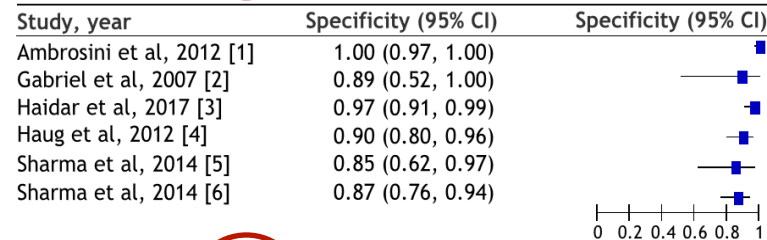
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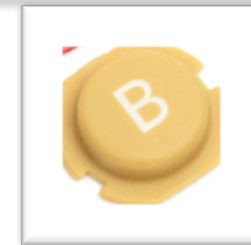
Ga-PET



Pooled Sensitivity = 0.91 (0.85, 0.94)



Pooled Specificity = 0.94 (0.86, 0.98)





NEN pancreas: STAGING



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Ga-PET- staging

Results: Twenty-two studies met the inclusion criteria. For the initial diagnosis of NETs, PET or PET/CT had a pooled sensitivity of 91% (95% confidence interval [CI], 85%–94%) and a pooled specificity of 94% (95% CI, 86%–98%). In the setting of staging and restaging, the sensitivity of PET or PET/CT for detecting primary and/or metastatic lesions ranged from 78.3% to 100%, whereas specificity ranged from 83% to 100%. Change in management occurred in 45% (95% CI, 36%–55%) of the cases, with majority of the changes involving surgical planning and patient selection for peptide receptor radionuclide therapy.

Conclusions: ⁶⁸Ga PET or PET/CT is recommended for initial diagnosis where conventional testing remained equivocal, for staging of patients with localized primary and/or limited metastasis where definitive surgery is planned, to determine somatostatin receptor status and suitability for peptide receptor radionuclide therapy, and for staging of patients where detection of occult disease will alter treatment options and decision making.

Key Words: ⁶⁸Ga, PET/CT, neuroendocrine tumors, clinical management, conventional imaging

(*Clin Nucl Med* 2018;43: 802–810)

14 studi
7 prospettici, 7 retrospettivi



	PET Ga	ceTC	MRI
Sens	78-100	47-100	72-97
Spec	83-100	33-98	90-100

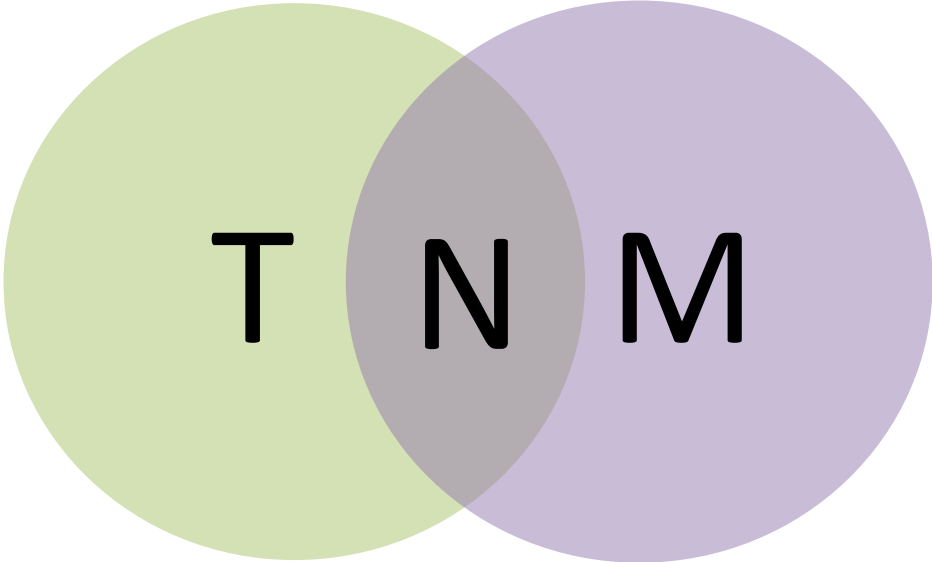


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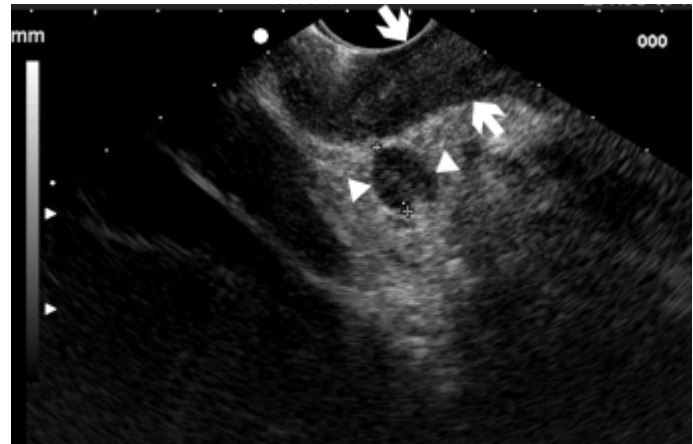


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EUSP?





NEN pancreas: STATUS



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Funzionante/ non funzionante NON secernente/non secernente



Tumore	Clinica
Insulinoma	TRIADE WHIPPLE Crisi ipoglicemica a digiuno; glicemia < 50 mg/dl e pronta risoluzione della crisi con somministrazione di glucosio
Gastrinoma	SINDROME ZOLLINGER-ELLISON Ulcere peptiche, diarrea, GERD
VIP-oma	SINDROME VERNER-MORRISON diarrea, ipokaliemia, ipocloridria
Glucagonoma	Sindrome 4D: Dermatite (Eritema necrolitico migrante), Diabete, Deep vein thrombosis (30%), Depressione
SmS-oma	Triade diarrea, diabete, colelitiasi

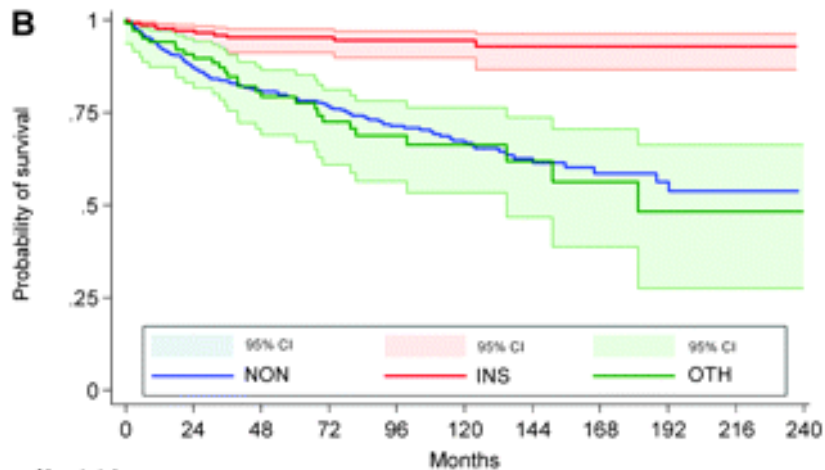


NEN pancreas: STATUS



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No at risk

NON	733	495	337	237	158	104	57	37	23	9	3
INS	222	174	136	112	86	65	41	28	18	11	4
OTH	109	79	56	42	29	24	12	8	3	1	0





NEN pancreas: GENETICA



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Possono manifestarsi nell'ambito di sindromi genetiche

MEN-1

- 80% delle MEN1 sviluppa NEN
- 50-55% NF-pNEN
- 47% sviluppa ZES (20-30% delle ZES ha MEN1)
- 5-15% ha insulinoma (4-6% degli insulinomi ha MEN1)

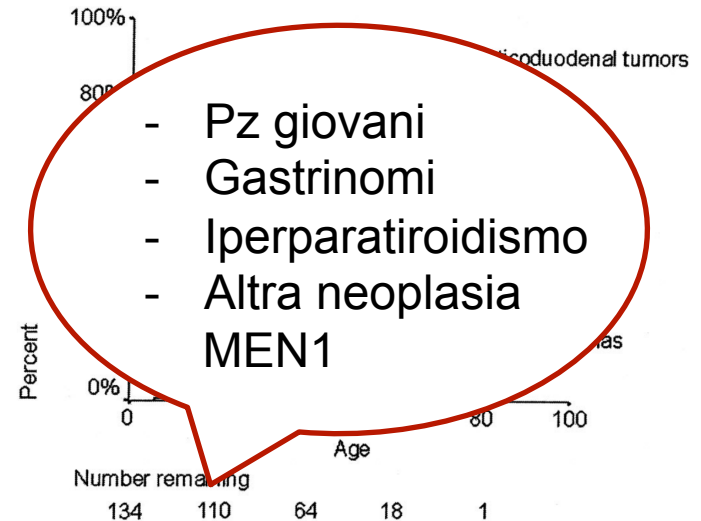
Ann Surg 2006;243: 265-272

VHL

- Nel 12-17% delle VHL è presente un NET

NF-1

- Si associa il somatostatinoma



Age (yr)	pNET	NF-pNET
20	9%	3%
50	53%	34%
80	84%	54%



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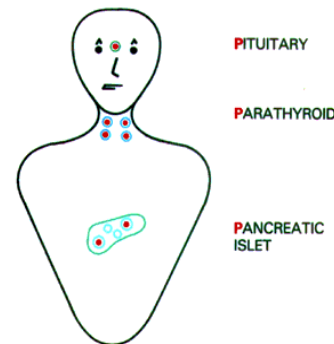


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Sex, No. (%)	1072	1072	503 (46.9)	569 (53.1)	NA
Genetic status, No. (%)	924				.29
Multiple endocrine neoplasia syndrome type 1		36 (3.9)	12 (2.8)	24 (4.79)	
Von Hippel-Lindau syndrome		14 (1.5)	6 (1.4)	8 (1.6)	
Sporadic		874 (94.6)	405 (95.7)	469 (93.6)	
Functioning tumor, No. (%)	1072	331 (30.9)	138 (27.4)	193 (33.9)	.02
Type of syndrome, No. (%)	331				.57

MULTIPLE ENDOCRINE NEOPLASIA TYPE I



Rindi et al., J Natl Cancer Inst 2012; 104:746

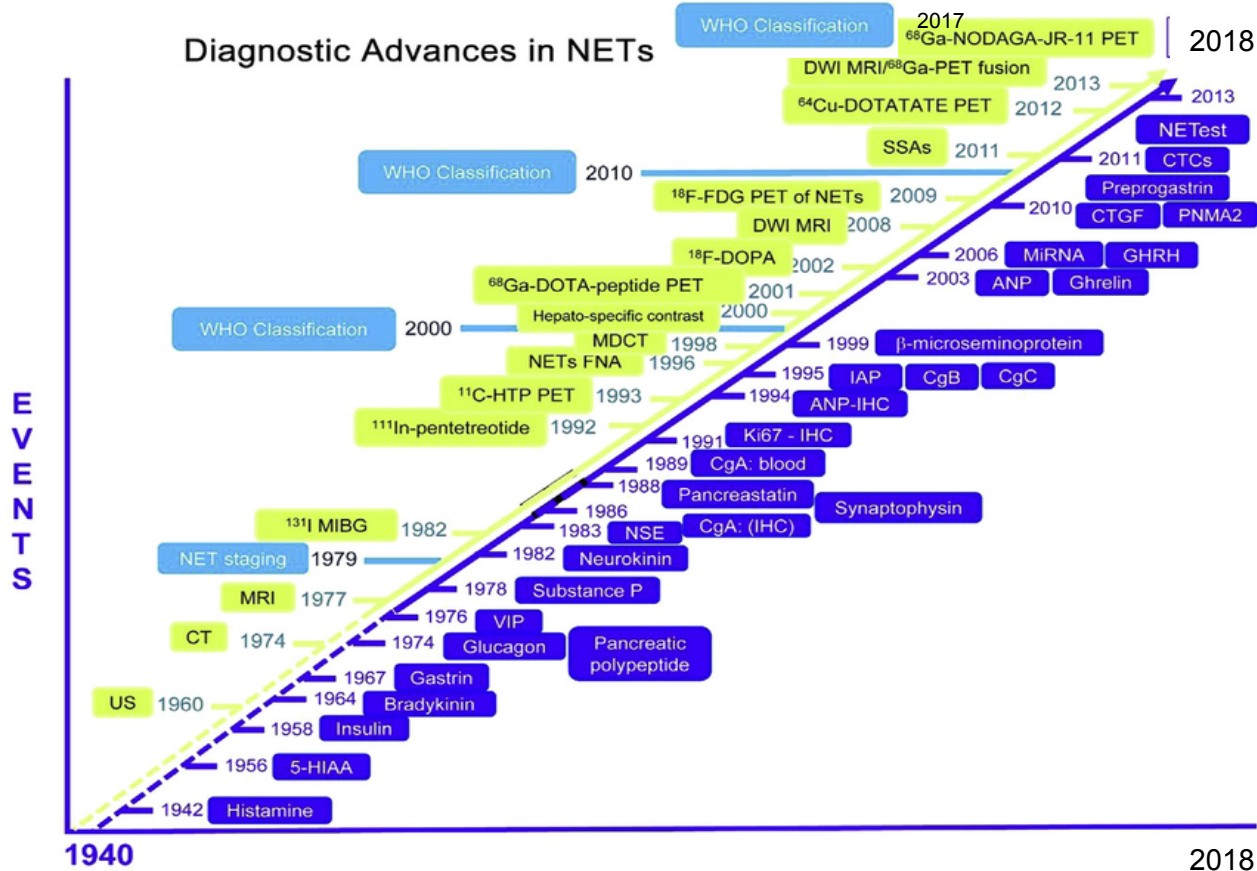


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