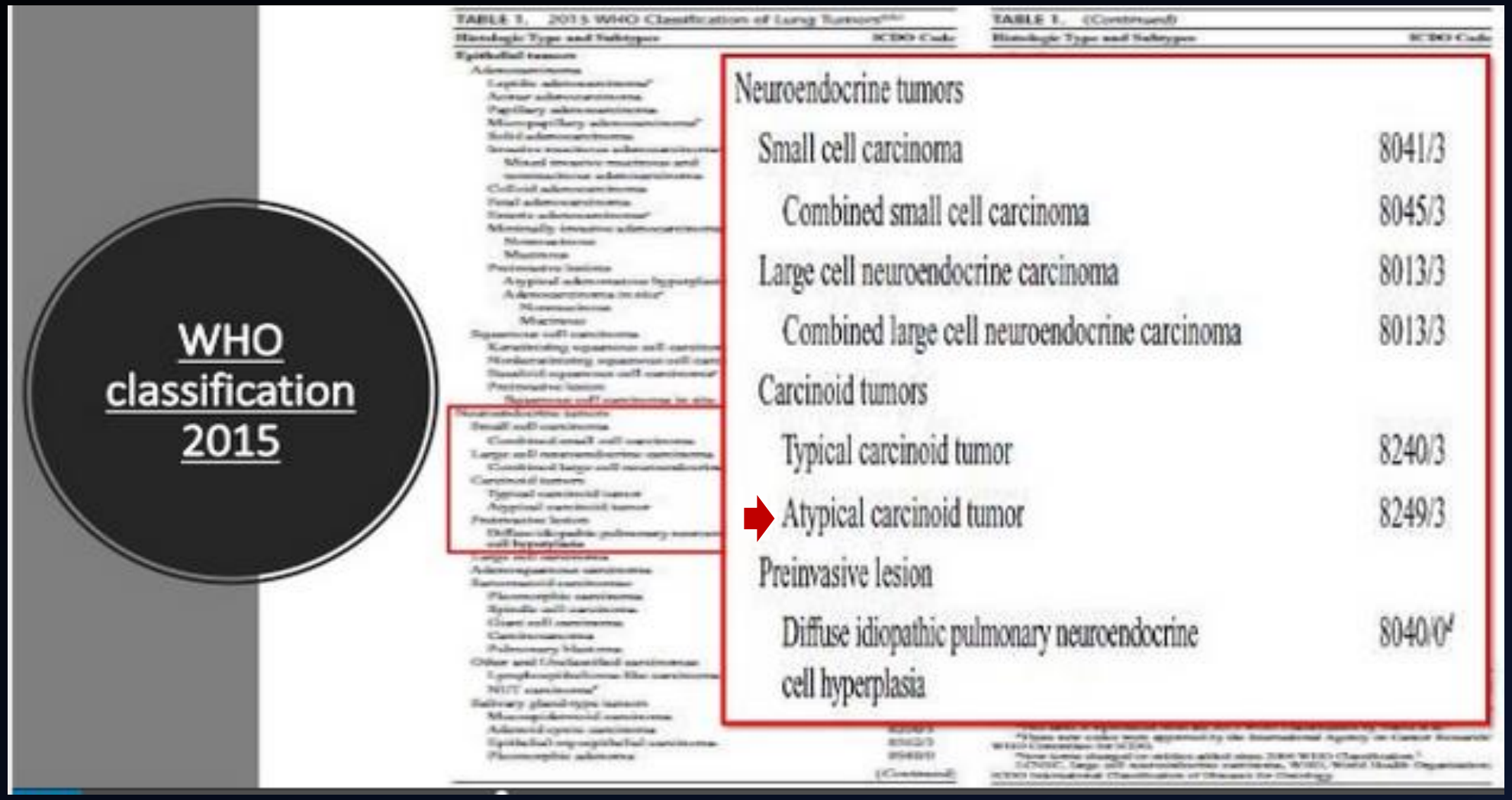
Άτυπο Καρκινοειδές

ΛΑΜΠΡΙΝΗ ΣΤΟΥΡΝΑΡΑ
ΠΝΕΥΜΟΝΟΛΟΓΟΣ
ΕΠΙΣΤΗΜΟΝΙΚΟΣ ΣΥΝΕΡΓΑΤΗΣ ΟΓΚΟΛΟΓΙΚΗΣ ΜΟΝΑΔΑΣ Γ’ΠΠ
ΝΟΣΟΚΟΜΕΙΟ ‘’ΣΩΤΗΡΙΑ’’

Δομή παρουσίασης

- Ταξινόμηση –ορισμός
- Επιδημιολογία
- Κλινική εικόνα -συμπτώματα
- Διάγνωση
- Θεραπεία???
- Συμπεράσματα

WHO classification 2015



Neuroendocrine tumors	
Small cell carcinoma	8041/3
Combined small cell carcinoma	8045/3
Large cell neuroendocrine carcinoma	8013/3
Combined large cell neuroendocrine carcinoma	8013/3
Carcinoid tumors	
Typical carcinoid tumor	8240/3
Atypical carcinoid tumor	8249/3
Preinvasive lesion	
Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia	8040/0[a]

Journal of Thoracic Oncology® • Volume10,Number9,September2015

Άτυπο Καρκινοειδές WHO classification

World Health Organization (WHO) classification of neuroendocrine tumours (NETs)

NET type	WHO grade	Histology	Mitosis (per 2 mm^2)	Presence of necrosis
Low-grade (well differentiated)	1	Typical carcinoid	<2	None
Intermediate-grade (well differentiated)	2	Atypical carcinoid	2–10	Present
High-grade (poorly differentiated)	3	Large-cell Small-cell	>10	Extensive High

Journal of Thoracic Oncology® • Volume10,Number9,September2015

Atypical Carcinoid Tumor of the Lung

A Surveillance, Epidemiology, and End Results Database Analysis

Conor E. Steuer, MD, Madhusmita Behera, PhD, Sungjin Kim, MS, Zhengjia Chen, PhD, Nabil F. Saba, MD, Rathi N. Pillai, MD, Taofeek K. Owonikoko, MD, PhD, Fadlo R. Khuri, MD, and Suresh S. Ramalingam, MD

- Μέση ηλικία 65 έτη (21-90)
- Γυναίκες : άνδρες 3:1
- Λευκή φυλή 87%
- Στάδιο νόσου

IA	IB	IIA	IIB	IIIA	IIIB	IV
39.3%	13.4%	4.5%	4.8%	11.8%	8.3%	17.8%

- Θεραπεία **77.5% χ/ο**

Τμηματεκτομή	3.88%
Σφηνοειδής	17.61%
Λοβεκτομή/Δι	73.73%
Πνευμονεκτομή	4.78%

Journal of Thoracic Oncology ® • Volume 10, Number 3, March 2015

Atypical Carcinoid Tumor of the Lung

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- Επιβίωση

Summary Stage	1 Year (*n*)	3 Years (*n*)
Overall population	86% (322/374)	67% (170/254)
Localized	92% (156/169)	85% (99/116)
Regional	94% (103/110)	69% (50/72)
Distant	61% (45/74)	26% (13/50)

Journal of Thoracic Oncology ® • Volume 10, Number 3, March 2015

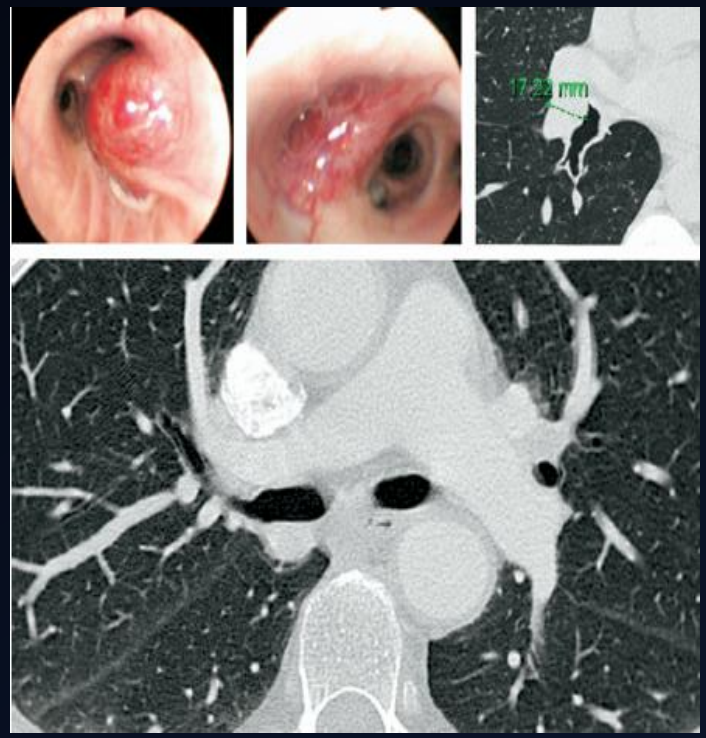
Συμπτώματα

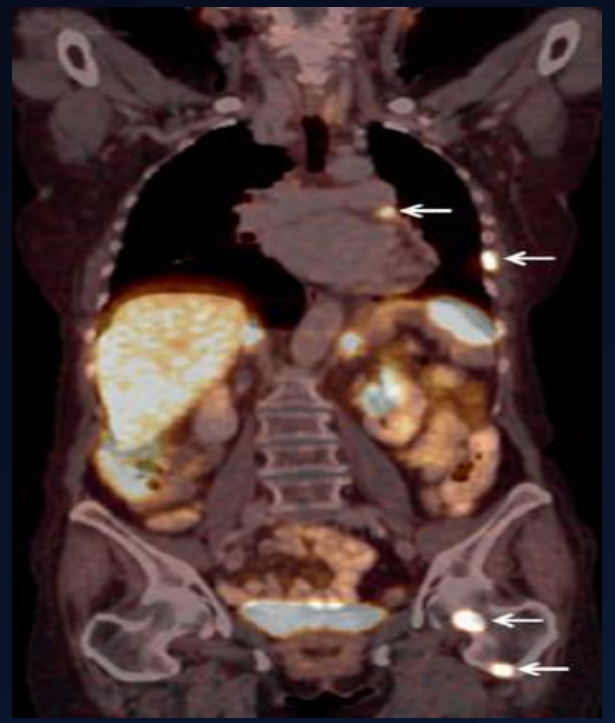
- Ασυμπτωματικοί
- Επίμονος βήχας
- Αιμόπτυση
- Υποτροπιάζουσες πνευμονίες
- Συριγμός
- Πόνος
- Δύσπνοια
- Σύνδρομο Cushing

Annals of Oncology 26: 1604–1620, 2015

Διάγνωση

- Ακτινογραφία θώρακος >40%
- CT Θώρακος ,κοιλίας
- **Βρογχοσκόπηση**
- FDG-18 PET/ CT
- Octreoscan (SRS)
- Ga DOTATATE PET/CT





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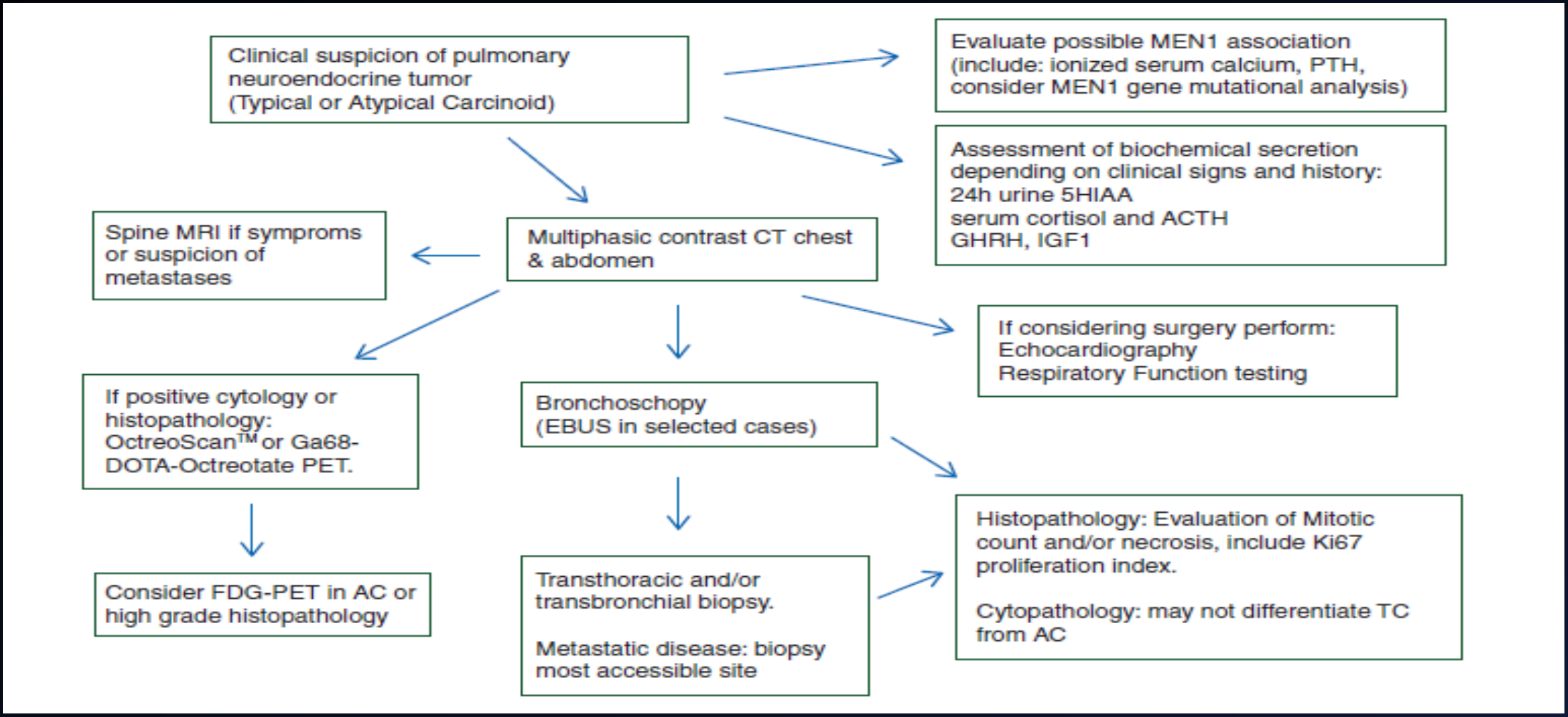
Διαγνωστικός αλγόριθμος



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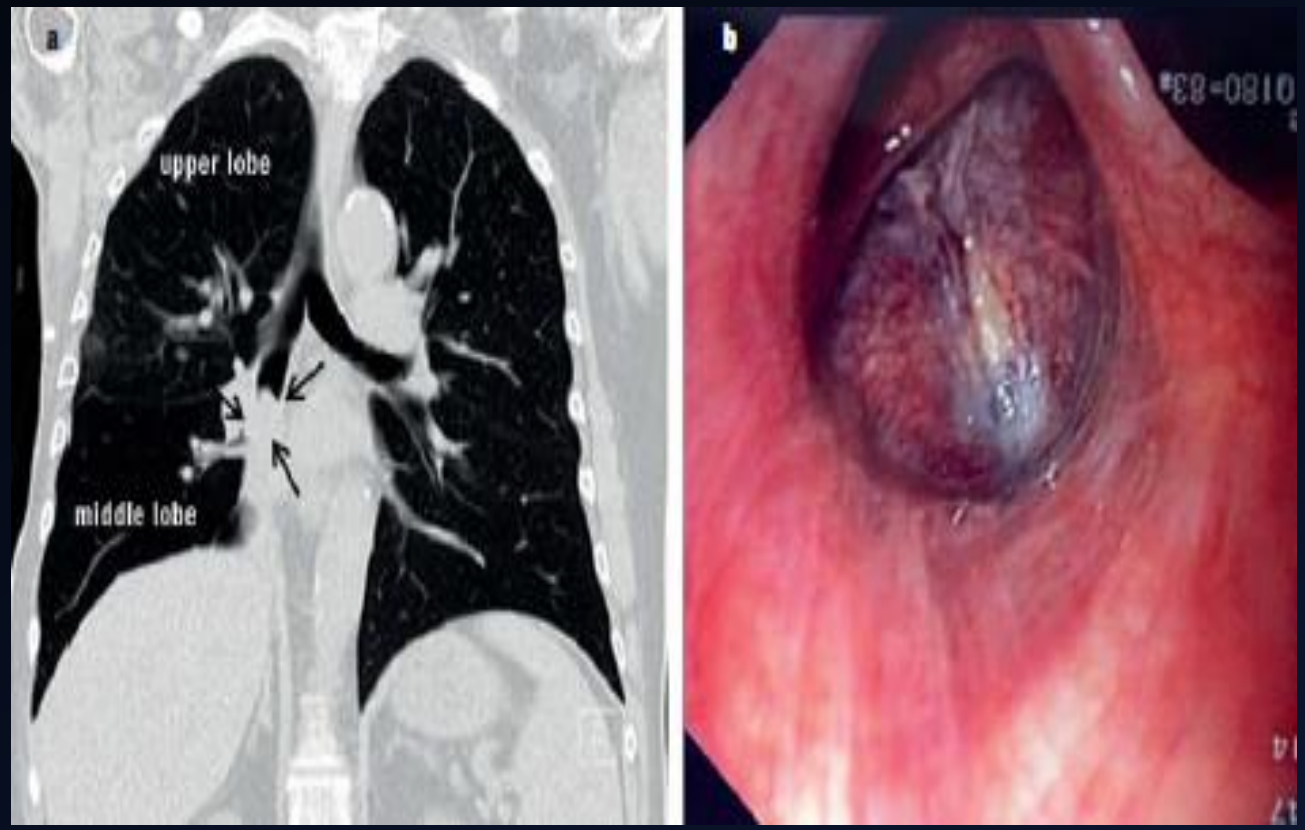
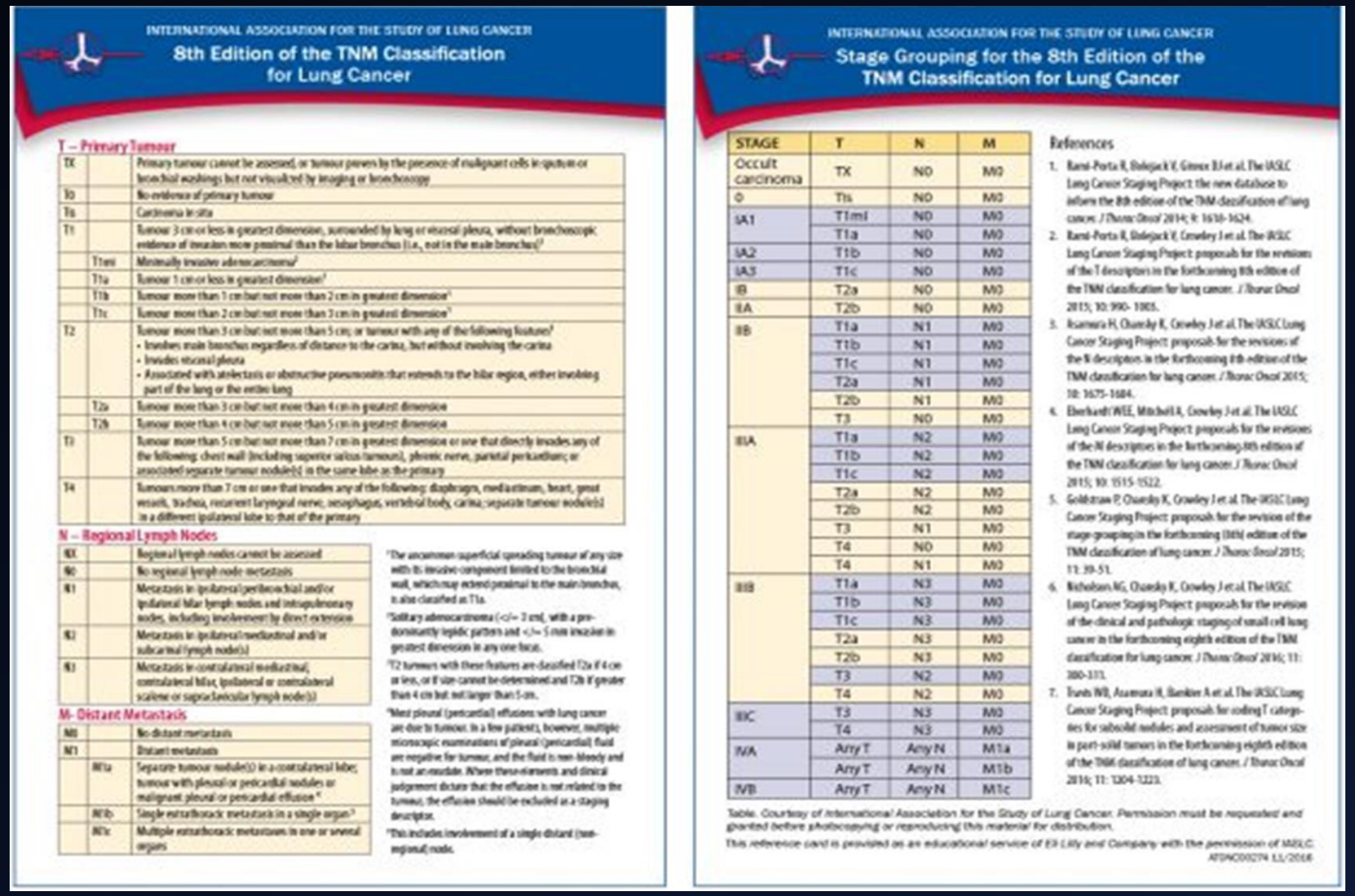
ΒΡΟΓΧΟΣΚΟΠΗΣΗ



Deutsches Ärzteblatt International | Dtsch Arztebl Int 2015; 112: 479–85

EBUS ΒΡΟΓΧΟΣΚΟΠΗΣΗ ΓΙΑ ΣΤΑΔΙΟΠΟΙΗΣΗ?

- ✓ Εάν η θεραπευτική απόφαση εξαρτάται από την ύπαρξη N2 νόσου ,τότε η σταδιοποίηση του μεσοθωρακίου μπορεί να γίνει με EBUS



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

8th Edition of the TNM Classification for Lung Cancer

T – Primary Tumour

TX		Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0		No evidence of primary tumour
Tis		Carcinoma in situ
T1		Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)[2]
	T1mi	Minimally invasive adenocarcinoma[3]
	T1a	Tumour 1 cm or less in greatest dimension[4]
	T1b	Tumour more than 1 cm but not more than 2 cm in greatest dimension[4]
	T1c	Tumour more than 2 cm but not more than 3 cm in greatest dimension[4]
T2		Tumour more than 3 cm but not more than 5 cm; or tumour with any of the following features[4] • Involves main bronchus regardless of distance to the carina, but without involving the carina • Invades visceral pleura • Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the entire lung
	T2a	Tumour more than 3 cm but not more than 4 cm in greatest dimension
	T2b	Tumour more than 4 cm but not more than 5 cm in greatest dimension
T3		Tumour more than 5 cm but not more than 7 cm in greatest dimension or one that directly invades any of the following: chest wall (including superior sulcus tumours), phrenic nerve, parietal pericardium; or associated separate tumour nodule(s) in the same lobe as the primary
T4		Tumours more than 7 cm or one that invades any of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina; separate tumour nodule(s) in a different ipsilateral lobe to that of the primary

N – Regional Lymph Nodes

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2		Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3		Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular lymph node(s)

M- Distant Metastasis

M0		No distant metastasis
M1		Distant metastasis
	M1a	Separate tumour nodule(s) in a contralateral lobe; tumour with pleural or pericardial nodules or malignant pleural or pericardial effusion[6]
	M1b	Single extrathoracic metastasis in a single organ[7]
	M1c	Multiple extrathoracic metastases in one or several organs

[2] The uncommon superficial spreading tumour of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.

[3] Solitary adenocarcinoma (<=/= 3 cm), with a predominantly lepidic pattern and <=/= 5 mm invasion in greatest dimension in any one focus.

[4] T2 tumours with these features are classified T2a if 4 cm or less, or if size cannot be determined and T2b if greater than 4 cm but not larger than 5 cm.

[6] Most pleural (pericardial) effusions with lung cancer are due to tumour. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumour, and the fluid is non-bloody and is not an exudate. Where these elements and clinical judgement dictate that the effusion is not related to the tumour, the effusion should be excluded as a staging descriptor.

[7] This includes involvement of a single distant (non-regional) node.

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Stage Grouping for the 8th Edition of the TNM Classification for Lung Cancer

STAGE	T	N	M
Occult carcinoma	TX	N0	M0
0	Tis	N0	M0
IA1	T1mi	N0	M0
	T1a	N0	M0
IA2	T1b	N0	M0
IA3	T1c	N0	M0
IB	T2a	N0	M0
IIA	T2b	N0	M0
IIB	T1a	N1	M0
	T1b	N1	M0
	T1c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
IIIA	T1a	N2	M0
	T1b	N2	M0
	T1c	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
IIIB	T1a	N3	M0
	T1b	N3	M0
	T1c	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N2	M0
	T4	N2	M0
IIIC	T3	N3	M0
	T4	N3	M0
IVA	Any T	Any N	M1a
	Any T	Any N	M1b
IVB	Any T	Any N	M1c

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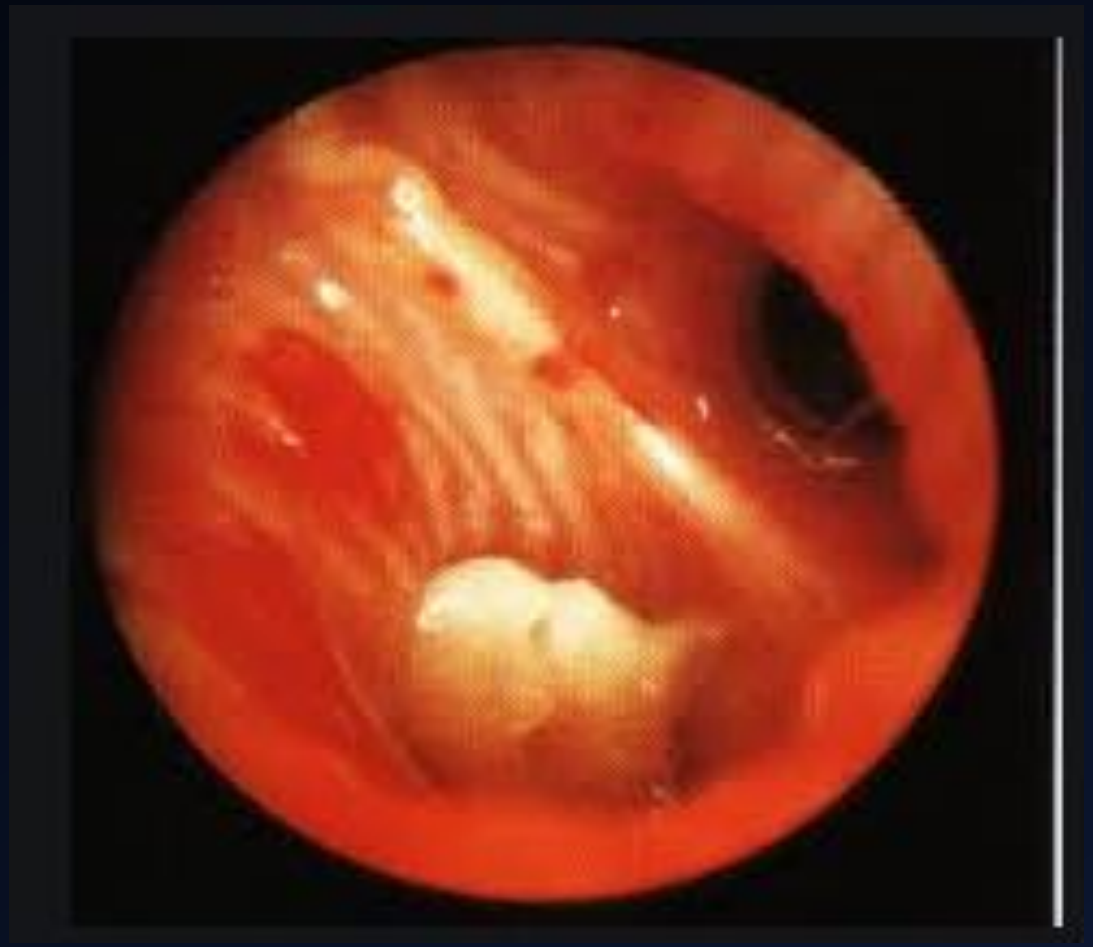
Annals of Oncology 26: 1604–1620, 2015

diagnosis: recommendations for the best practice

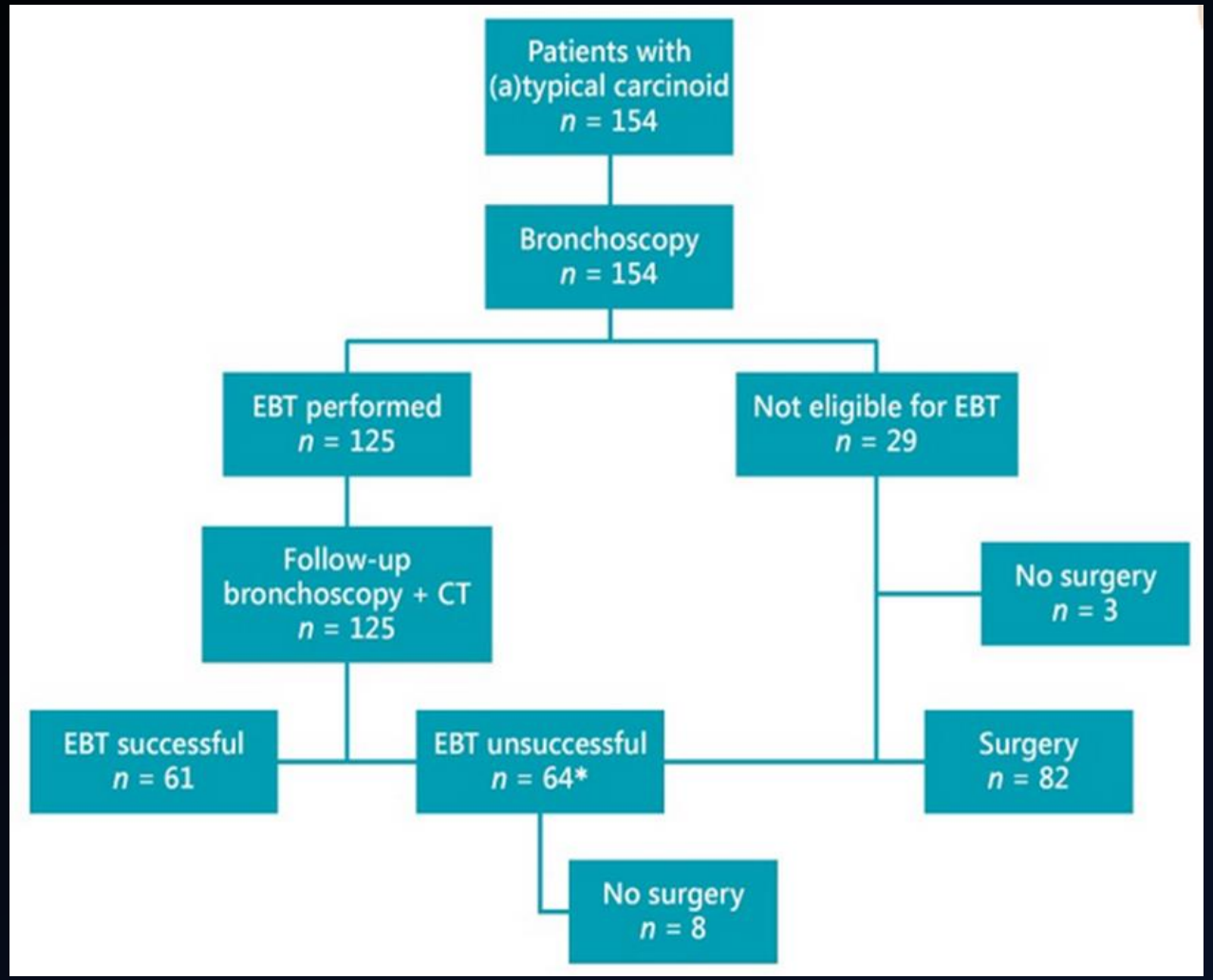
- Bronchoscopy may be required for the staging and assessment of central airway tumors preoperatively (Level of Evidence 4,Grade of recommendation A).
- Flexible bronchoscopy is preferable; however, in patients at high risk for bleeding, rigid bronchoscopy may be preferred for obtaining biopsy specimens (Level of Evidence 4, Grade of recommendation B).
- There is currently limited evidence regarding the added value of new bronchoscopic techniques to increase the sensitivity of detection of primary tumors or recurrence (Level of Evidence 4, Grade of recommendation D).

Annals of Oncology 26: 1604–1620, 2015

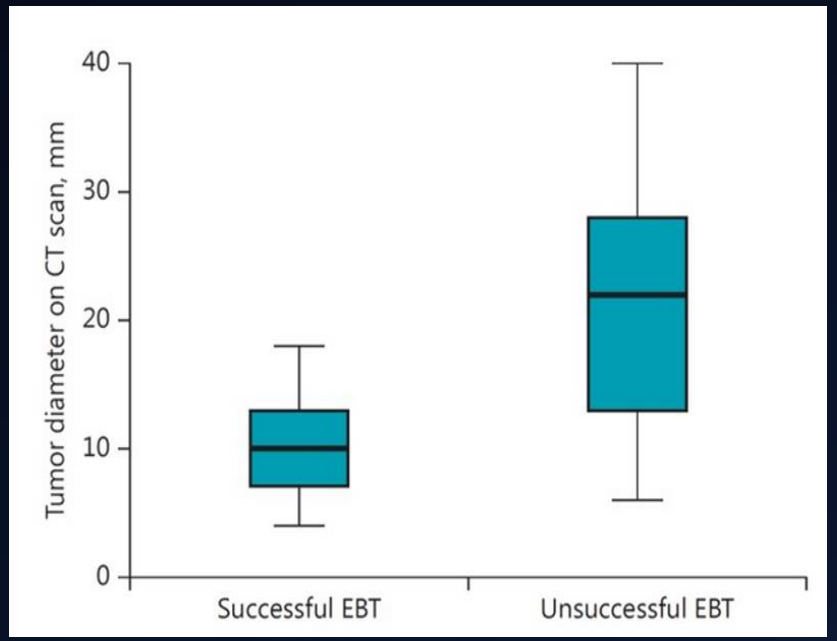
Βρογχοσκόπηση για τη θεραπεία άτυπου Καρκινοειδούς ???



Endobronchial Treatment for Bronchial Carcinoid: Patient Selection and Predictors of Outcome

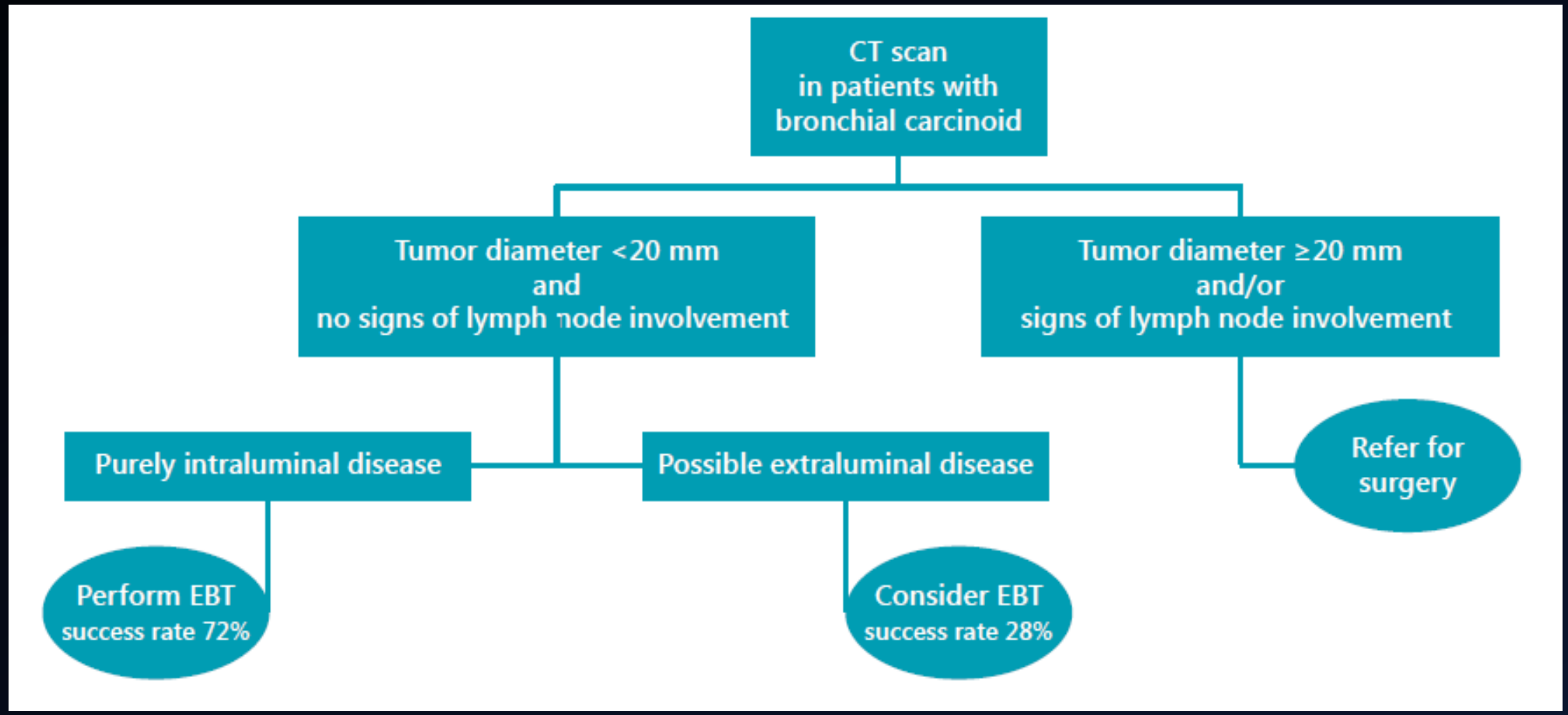


- Intraluminal disease
- Tumor diameter <20mm



Ellen Reuling et.al . Respiration. 2018 Apr; 95(4): 220–227.

Endobronchial Treatment for Bronchial Carcinoid: Patient Selection and Predictors of Outcome



Ellen Reuling et.al . Respiration. 2018 Apr; 95(4): 220–227

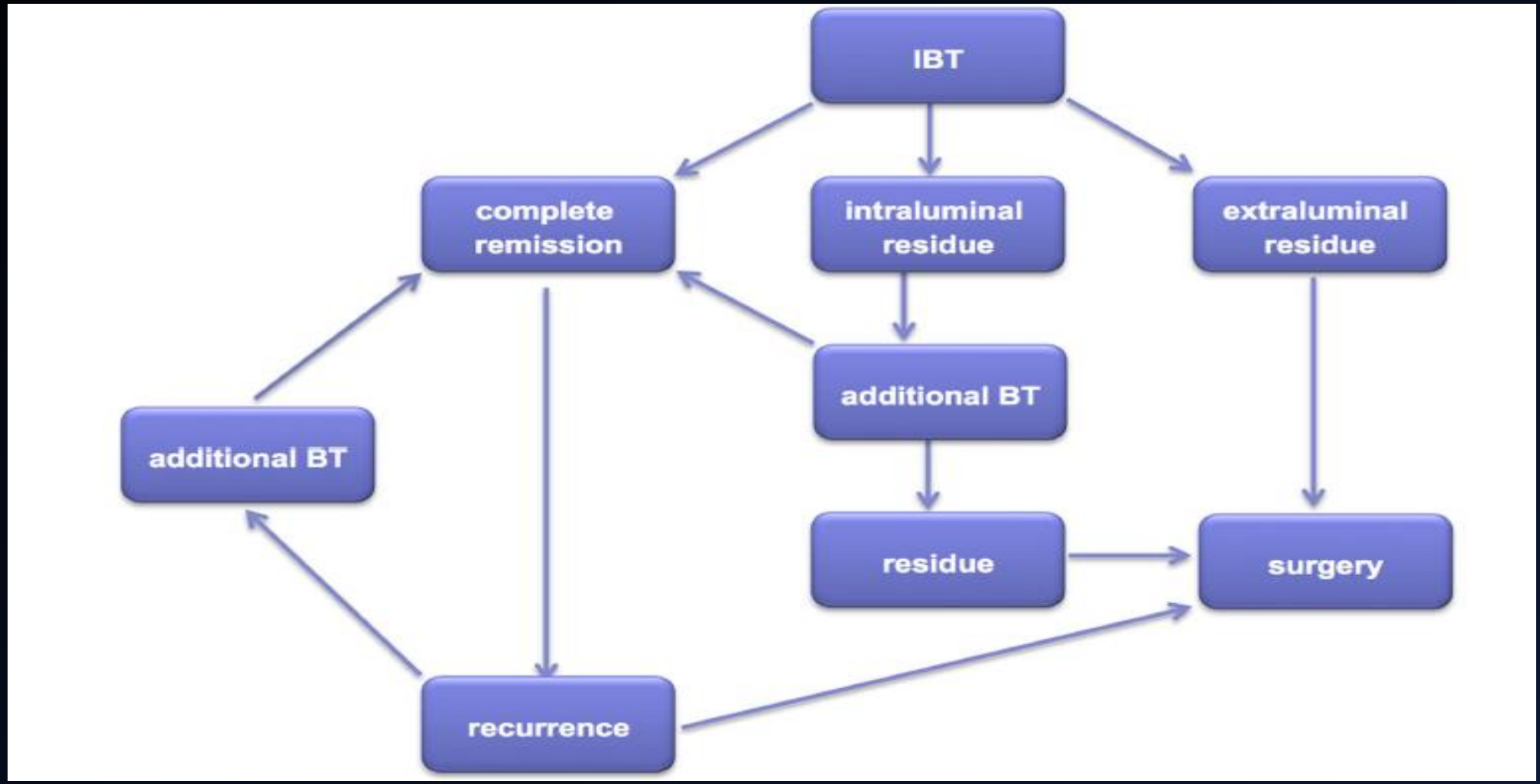
Endobronchial Treatment for Bronchial Carcinoid: Patient Selection and Predictors of Outcome

LIMITATIONS

- Selection bias: large tumors where referred for surgery
- Single centre study
- Additional imaging techniques FDG PET-CT , Ga DOTATATE were not evaluated
- Large number of missing CT scans

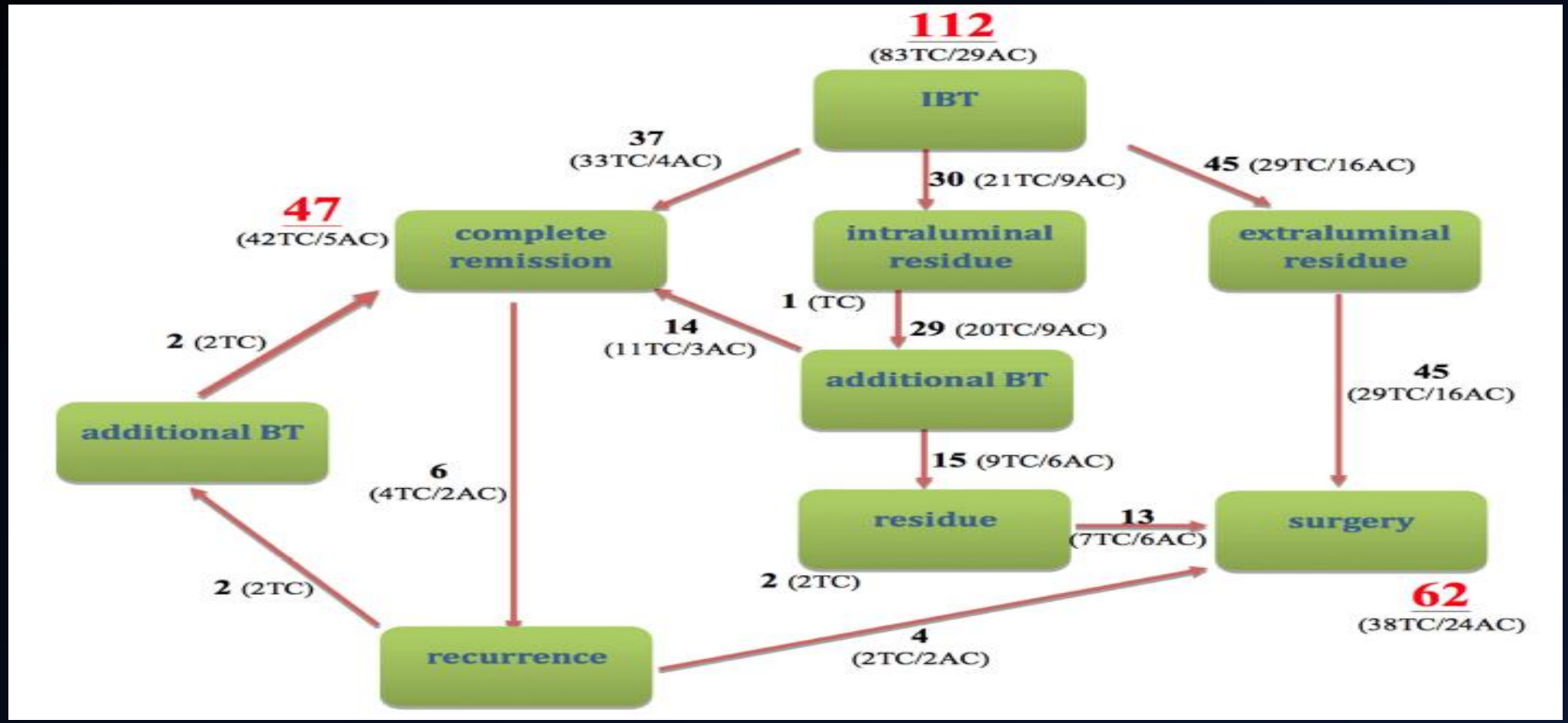
Ellen Reuling et.al . Respiration. 2018 Apr; 95(4): 220–227

Long-term follow-up after first-line bronchoscopic therapy in patients with bronchial carcinoids



Brokx HAP, et al. Thorax 2015;70:468–472. doi:10.1136/thoraxjnl-2014

Long-term follow-up after first-line bronchoscopic therapy in patients with bronchial carcinoids



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Long-term follow-up after first-line bronchoscopic therapy in patients with bronchial carcinoids

Table 2 Clinical outcome of patients with bronchial carcinoid after initial bronchoscopic treatment (IBT) with or without completion surgery

Histology	N	Treatment	Outcome	Alive	Dead	Remarks
Typical (83)	43	IBT	CR	36	7	All deaths unrelated
	3	IBT	Residual	3	0	1 unfit for surgery
						2 refused surgery
	37	Surgery	CR	36	1	1 unrelated death
Atypical (29)	5	IBT	CR	5	0	
	21	Surgery	CR	19	2	1 unrelated death
						1 treatment-related death
	3	Surgery	Metastatic	1	2	Hepatic and pulmonary metastases

No residual tumour detected macroscopically (videobronchoscopy, high resolution CT) and microscopically (biopsy and brush specimens).
CR, complete remission.

Brokx HAP, et al. Thorax 2015;70:468–472. doi:10.1136/thoraxjnl

Long-term follow-up after first-line bronchoscopic therapy in patients with bronchial carcinoids

Table 3 Follow-up (FU) of patients still alive in months from initial bronchoscopic treatment (IBT) until July 2014

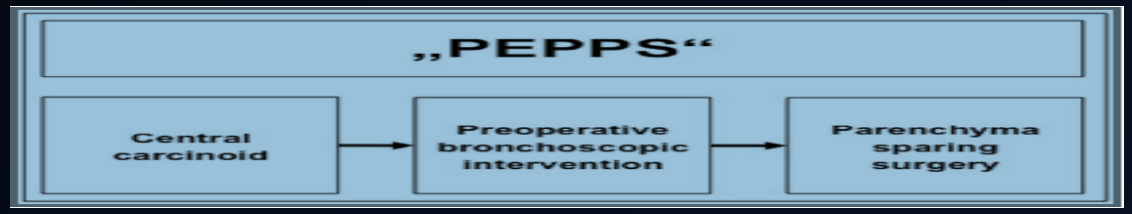
Carcinoid	Treatment (n)	Outcome (n)	Median FU (mo)	Range FU (mo)	Remarks
Typical (75)	IBT (38)	CR (33)	120	(73–241)	
		Residue (3)	168	(140–205)	1 unfit, 2 refused IBT—Recurrence BT—July 2014
		Recurrence (2)	10 and 63		
			98 and 29		
	Surgery (37)	CR (35)	129	(60–267)	
		Recurrence (2)	47 and 104		IBT—Recurrence Surgery—July 2014
			57 and 111		
Atypical (25)	IBT (5)	CR (5)	109	(83–170)	
	Surgery (20)	CR (18)	88.5	(60–159)	
		Recurrence (2)	116 and 198		IBT—Recurrence Surgery—July 2014
			113 and 79		

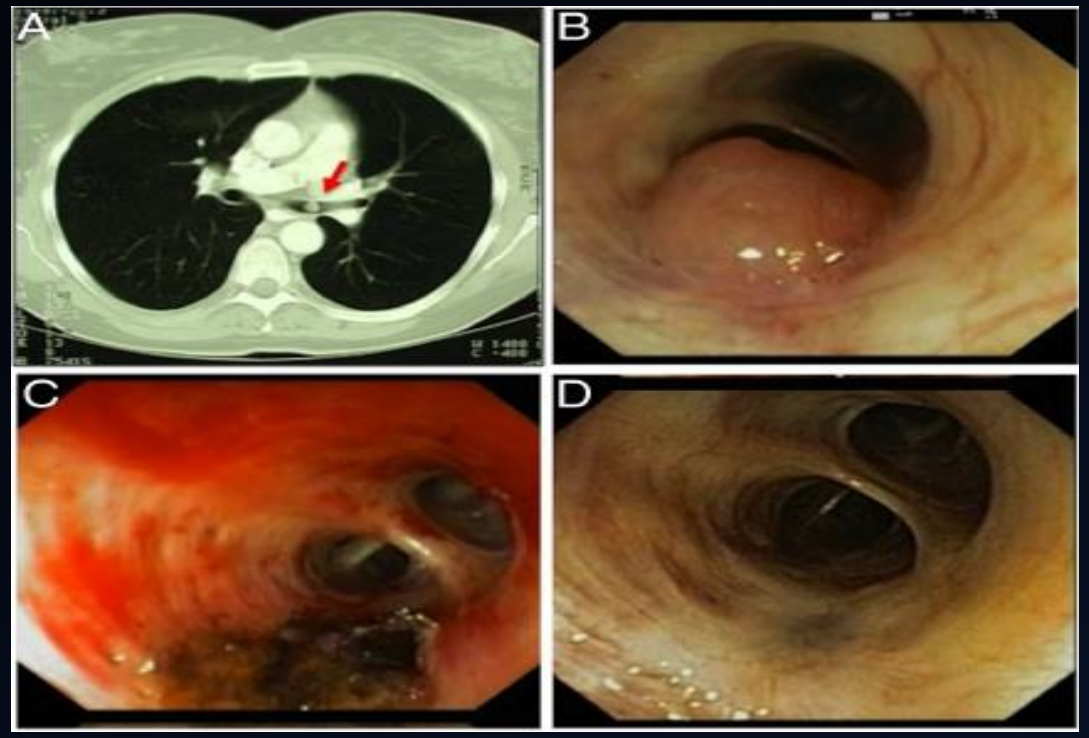
No residual tumour detected macroscopically (videobronchoscopy, high resolution CT) and microscopically (biopsy and brush specimens).
CR, complete remission; BT, bronchoscopic treatment.

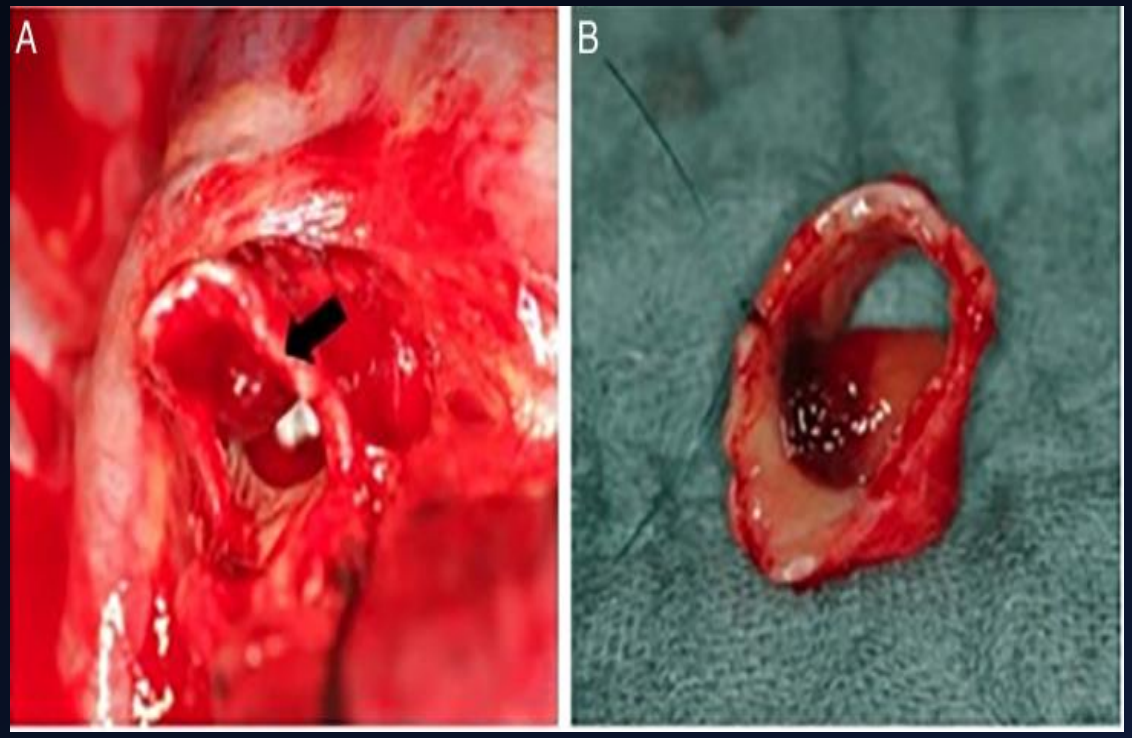
Brokx HAP, et al. Thorax 2015;70:468–472. doi:10.1136/thoraxjnl

Carcinoid tumours of the lung and the ‘PEPPS’ approach: evaluation of preoperative bronchoscopic tumour debulking as preparation for subsequent parenchyma-sparing surgery

PEEPS:PROCEDURE OF ENDOBRONCHIAL PREPARATION FOR PARENCHYMA-SPARING SURGERY

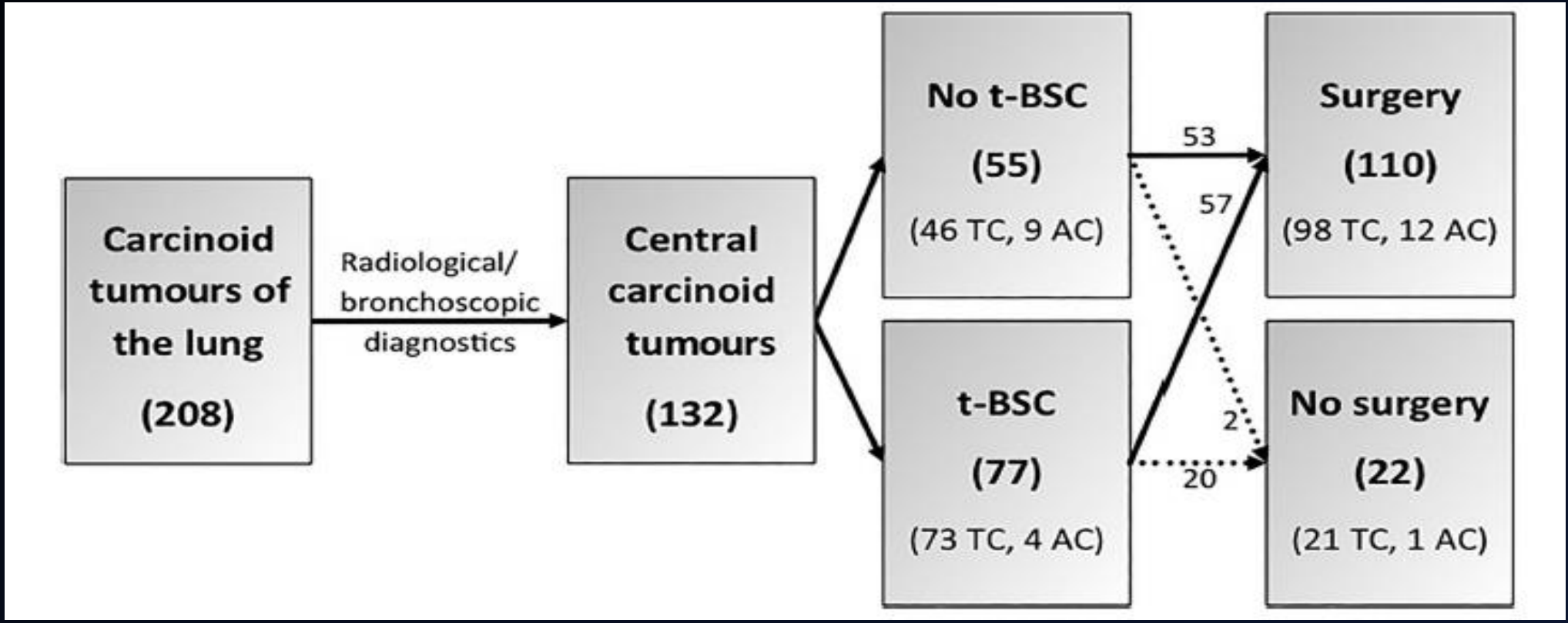






Neuberger M, Hapfelmeier A, Schmidt M, et al. BMJ Open Resp Res 2015;2:e000090.

Carcinoid tumours of the lung and the ‘PEPPS’ approach: evaluation of preoperative bronchoscopic tumour debulking as preparation for subsequent parenchyma-sparing surgery

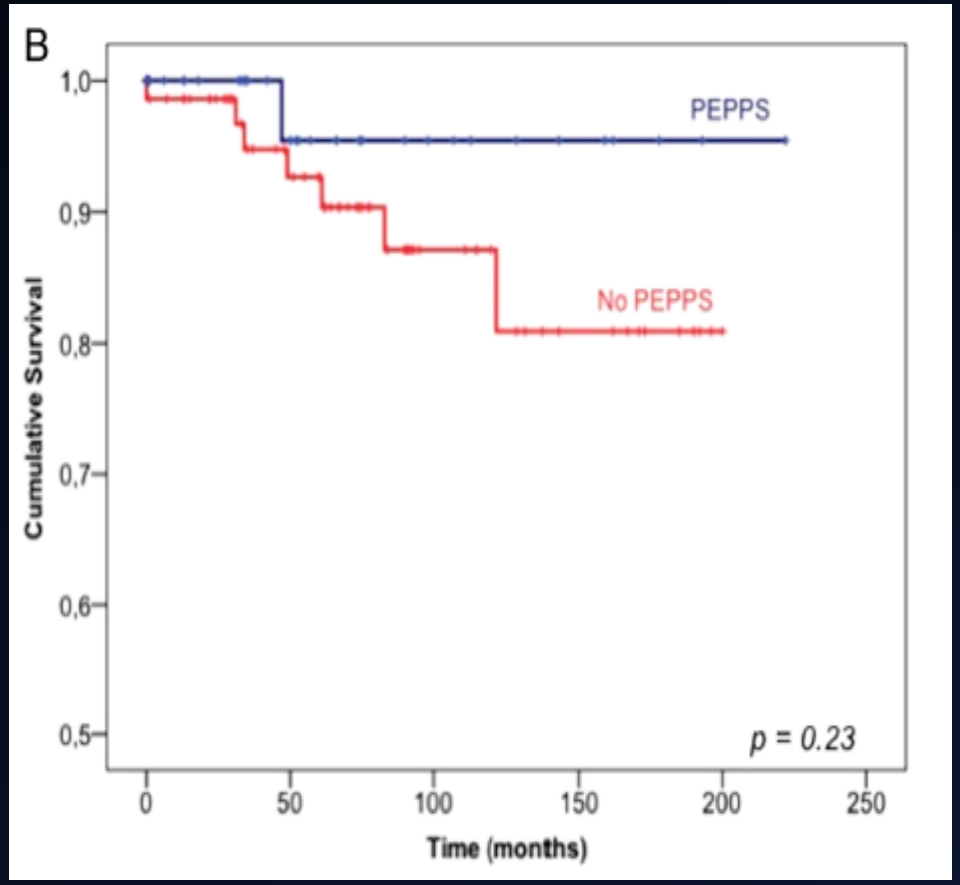


Neuberger M, Hapfelmeier A, Schmidt M, et al. BMJ Open Resp Res 2015;2:e000090.

Carcinoid tumours of the lung and the ‘PEPPS’ approach: evaluation of preoperative bronchoscopic tumour debulking as preparation for subsequent parenchyma-sparing surgery

- The use of parenchyma-sparing (class 2) surgery after preoperative bronchoscopic recanalisation in absolute and relative numbers
- Class 2 surgery: sleeve lobectomies, main bronchial sleeve resections segment resections

		Class 2 surgery	p Value
Preoperative therapeutic bronchoscopy	Yes (57) No (53)	67% (38) 43% (23)	0.021



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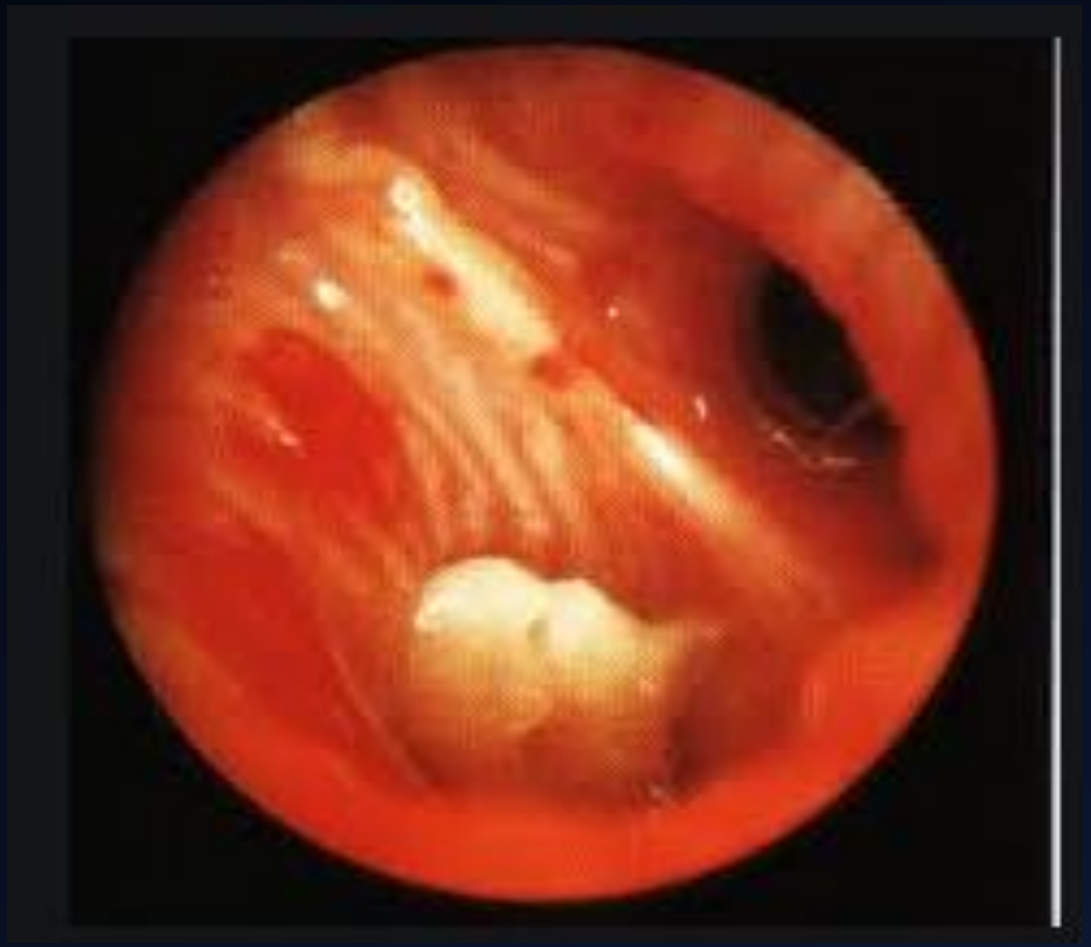
Carcinoid tumours of the lung and the ‘PEPPS’ approach: evaluation of preoperative bronchoscopic tumour debulking as preparation for subsequent parenchyma-sparing surgery

Table 4 Distant metastasis and local recurrence rates in dependence on interventional bronchoscopy, radicality, surgical procedure and Procedure of Endobronchial Preparation for Parenchyma-sparing Surgery (PEPPS) in relative and absolute numbers

	Distant metastasis		p Value	(Local) recurrence		p Value
Preoperative interventional bronchoscopy						
Yes	12%	(8)	>0.999	6%	(4)	>0.999
No	13%	(7)		4%	(2)	
Macroscopic tumour ablation by bronchosocpy						
Yes	25%	(2)	0.312	8%	(1)	>0.999
No	13%	(7)		7%	(4)	
Surgical class						
1	13%	(6)	0.324	9%	(4)	0.173
2	7%	(4)		2%	(1)	
PEPPS						
Yes	8%	(3)	0.534	3%	(1)	0.654
No	13%	(9)		6%	(4)	

Βρογχοσκόπηση για τη θεραπεία άτυπου καρκινοειδούς ???



recommendations for the best practice

- Local resection should be reserved for patients who are Considered unacceptably high risk for bronchopulmonary surgery (Level of Evidence 5, Grade of recommendation D).
- Endoluminal bronchoscopic therapy, more appropriately for TC, should be reserved for patients who are considered unacceptably high risk for bronchopulmonary surgery or occasionally as a possible bridge to surgery (Level of Evidence 5, Grade of recommendation D).

Annals of Oncology 26: 1604–1620, 2015

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2019
Neuroendocrine Tumors of the Gastrointestinal Tract, Lung, and Thymus (Carcinoid Tumors)

NCCN Guidelines Index
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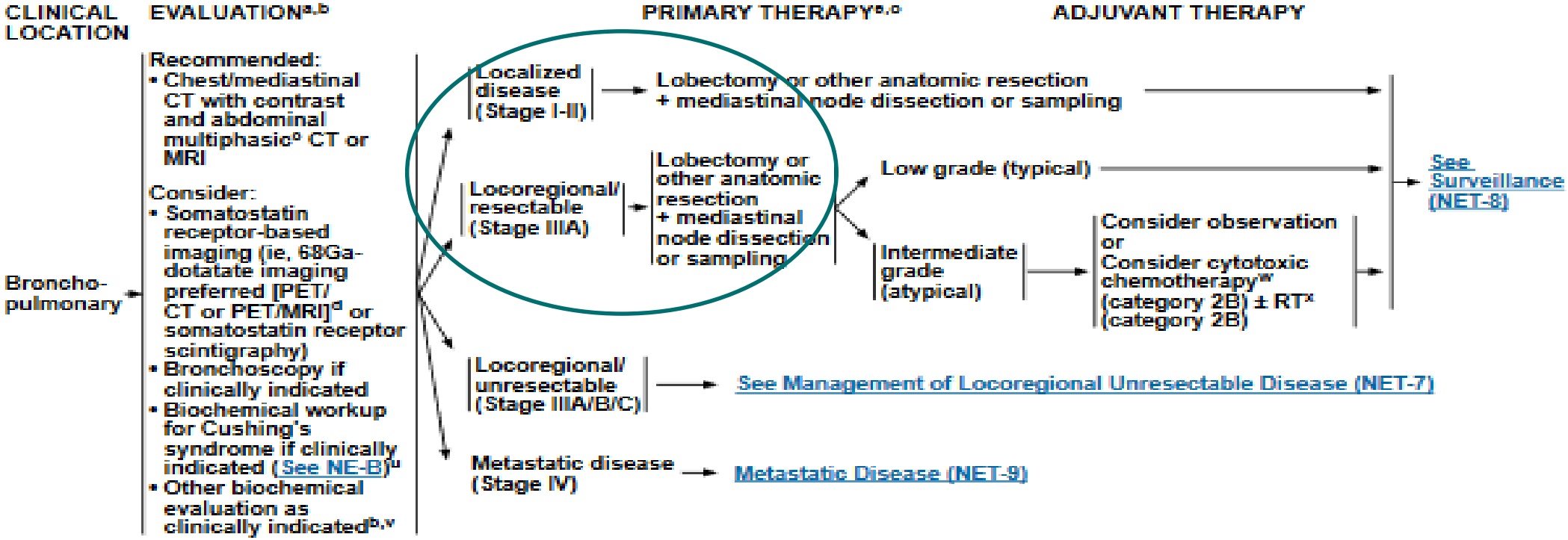
Discussion



[a] See Principles of Pathology for Diagnosis and Reporting of Neuroendocrine Tumors (NE-A).
[b] See Principles of Biochemical Testing (NE-B).
[c] Multiphasic imaging studies are performed with IV contrast.
[d] 68Ga-dotatate PET/CT or PET/MRI is more sensitive than somatostatin receptor with SPECT/CT for determining somatostatin receptor status. PET/CT or PET/MRI of skull base to mid-thigh; CT with IV contrast when possible. Data are limited on the optimal timing of scans following administration of somatostatin analogs.
[e] See Surgical Principles for Management of Neuroendocrine Tumors (NE-C).
[f] See Principles of Systemic Anti-Tumor Therapy (NE-D).
[u] If Cushing's syndrome suspected, assess for and treat ectopic sources of ACTH production.
[v] Bronchopulmonary neuroendocrine tumors are often associated with MEN1. See Multiple Endocrine Neoplasia, Type 1 (MEN1-1).
[w] Cytotoxic chemotherapy options include cisplatin/etoposide, carboplatin/etoposide, or temozolomide. Temozolomide is not recommended in combination with RT.
[x] Chemoradiation is thought to have most efficacy for tumors with atypical histology or tumors with higher mitotic and proliferative indices (eg, KI-67). There are limited data on the efficacy of chemoradiation for unresectable IIIA or IIIB low-grade lung neuroendocrine tumors; however, some panel members consider chemoradiation in this situation.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Συμπεράσματα

- Τα δεδομένα στη βιβλιογραφία είναι λίγα δεδομένου ότι πρόκειται για μια ομάδα νεοπλασμάτων αρκετά σπάνια
- Η ενδεδειγμένη θεραπεία για το άτυπο καρκινοειδές είναι η χειρουργική εξαίρεση
- Η βρογχοσκοπική θεραπεία στο άτυπο καρκινοειδές θα πρέπει υπό προϋποθέσεις να εφαρμόζεται σε ασθενείς υψηλού κινδύνου που δεν μπορούν να υποβληθούν σε χειρουργείο ή να αποτελεί ένα θεραπευτικό βήμα πριν το χειρουργείο
- Ακρογωνιαίος λίθος στη διάγνωση και θεραπεία είναι η συνεργασία της διεπιστημονικής ομάδας

Ευχαριστώ!