Pneumonectomy for N2+ NSCLC

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Disclosures

- Ugalde- AstraZeneca, Medtronic, Johnson&Johnson, travel, speaker, ad board, honoraria
- Donington-AstraZeneca, travel, speaker, ad board, honoraria

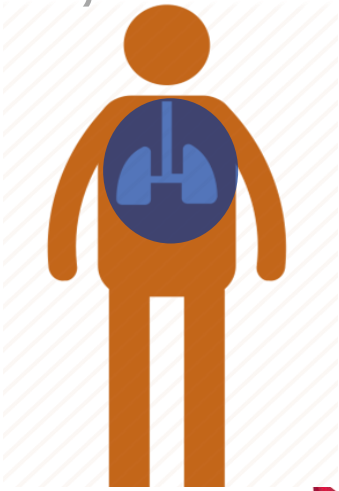
Stage III NSCLC

Therapeutically challenging subset

Pts are treated for cure, but cure is elusive, 10-30%

Chemotherapy → **High risk of systemic relapse**

Surgery
Radiotherapy
→ **Local-regional control**



Stage III TNM subsets

T and M	N0	N1	N2	N3
T1a/b/c	IA	IIA	IIIA	IIIB
T2a/b	IB/IIA	IIB	IIIA	IIIB
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC
M1a/b/c	IVA/B/C	IVA/B/C	IVA/B/C	IVA/B/C

While prognosis is similar, heterogeneous group w/ respect to treatment

Stage III TNM subsets

T and M	N0	N1	N2	N3
T1	IA	IIA	IIIA	IIIB
T2a/b	IB/IIA	IIB	IIIA	IIIB
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC
M1a	IV A/B/C	IV A/B/C	IV A/B/C	IV A/B/C

IIIA Non-N2
Resection + adjuvant tx similar to stage II

IIIA N2
Resection determined by bulk and extent of nodal disease

IIIB/C
Less evidence for curative benefit w/ resection

Surgery for N2 IIIA NSCLC

N2 disease

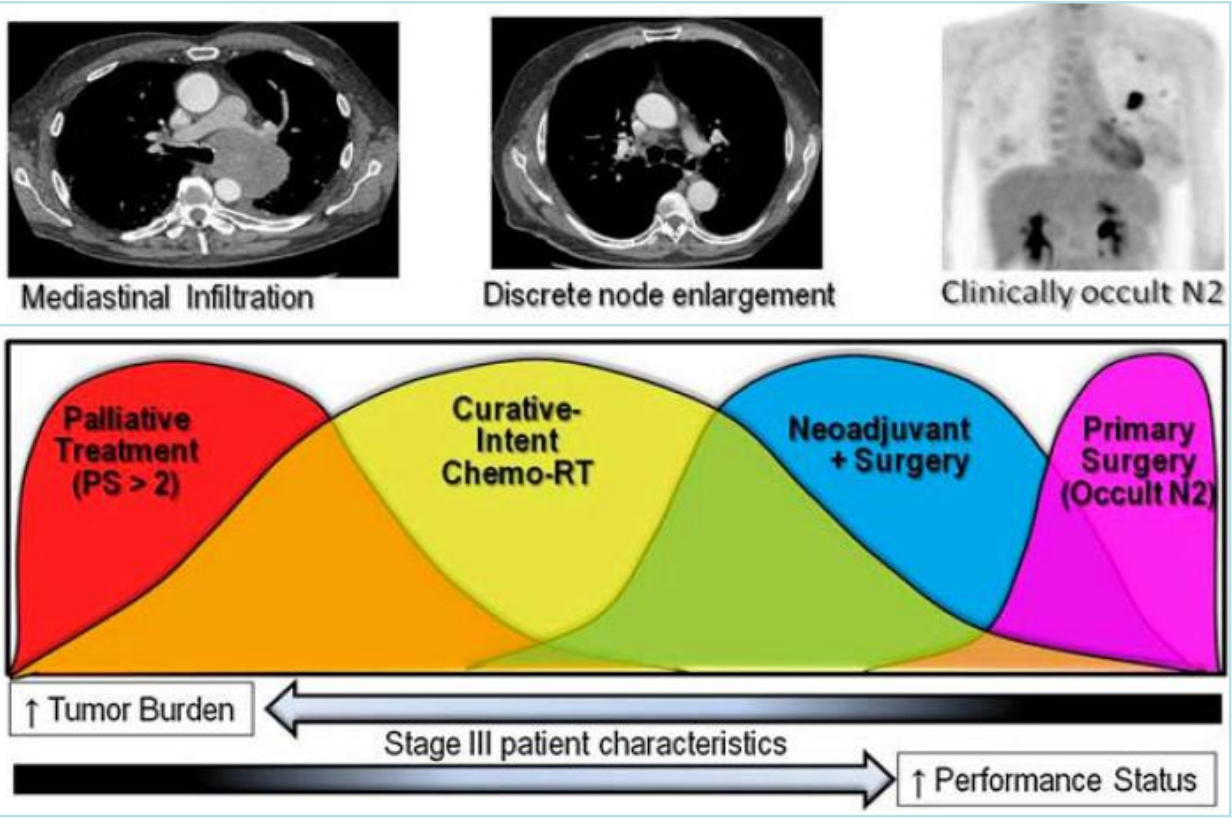
Occult: clinical N0/N1 disease with appropriate staging (CT & PET/ EBUS/mediastinoscopy), where N2 involvement is found during or after resection

Discrete/Potentially resectable: pathologically proven malignant ipsilateral nodes diagnosed during clinical staging

Infiltrative/Unresectable: bulky or fixed, cannot be discerned and measured, encasing vessels and airways

ΚΑΤΗΓΟΡΙΑ	ΥΠΟΚΑΤΗΓΟΡΙΑ	ΠΕΡΙΓΡΑΦΗ
Nx		Οι επιχώριοι λεμφαδένες δεν δύναται να εκτιμηθούν.
N0		ΔΕΝ υπάρχουν επιχώριοι λεμφαδένες .
N1	N1a	Διήθηση λεμφαδένων N1 ενός σταθμού.
	N1b	Διήθηση λεμφαδένων N1 περισσότερων από έναν σταθμών.
N2	N2a1	Διήθηση λεμφαδένων N2 χωρίς συμμετοχή των λεμφαδένων N1 (skip).
	N2a2	Διήθηση λεμφαδένων N2 ενός σταθμού με συμμετοχή των λεμφαδένων N1.
	N2b	Διήθηση λεμφαδένων N2 περισσότερων του ενός σταθμών με συμμετοχή των λεμφαδένων N1.
N3		Διήθηση λεμφαδένων N3.

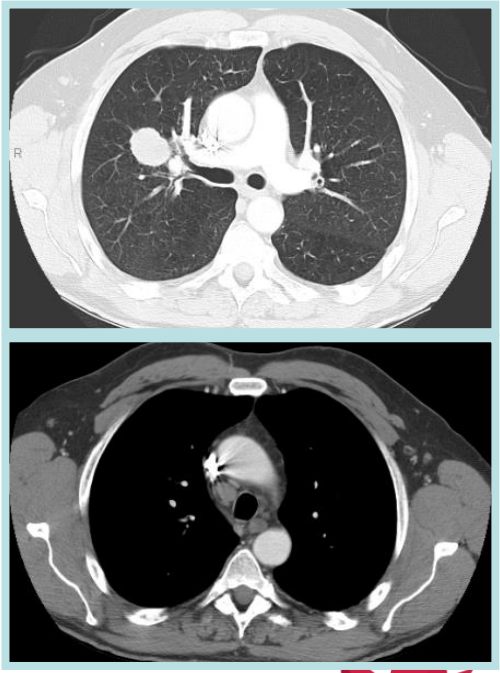
Πίνακας 6. Η δεύτερη άποψη της νέας ταξινόμησης των επιχώριων λεμφαδένων που απορρίφθηκε.



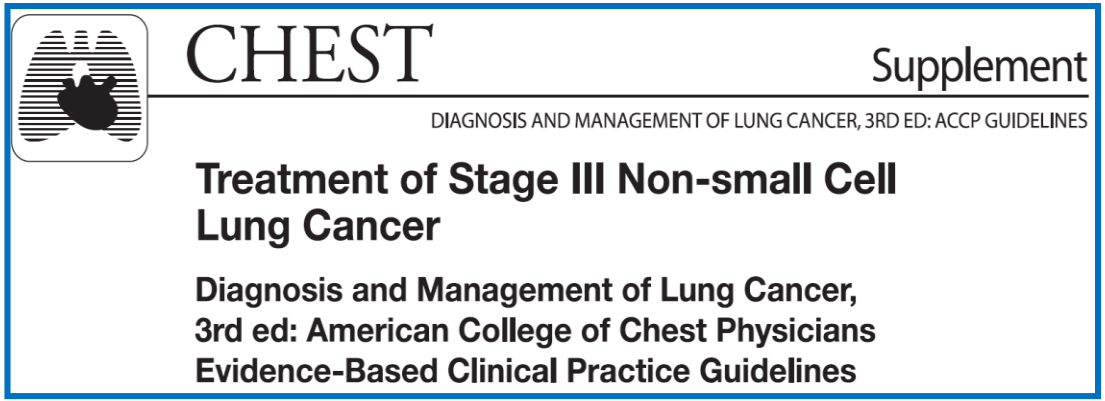
Ramnath, M. Chest, 2013.

Potentially Resectable N2

- Cure 30-35%
- pathologically proven malignant ipsilateral nodes at time of baseline clinical staging
- no management consistently proven superior
- node size, # involved stations, and institutional/practitioner bias guide treatment decisions
- Balancing survival and quality of life



3.5.2. In patients with discrete N2 involvement by NSCLC identified preoperatively (IIIA), either definitive chemoradiation therapy or induction therapy followed by surgery is recommended over either surgery or radiation alone (Grade 1A)
Remark: As the data do not permit the selection of one option or the other as superior, patient values and preferences should factor significantly in the decision.
Remark: All multimodality therapy should be performed in centers with experienced multidisciplinary teams that track their relevant clinical outcomes and are capable of minimizing and managing the toxicity and complications involved.
Remark: Further identification of patients more likely to benefit from surgical resection after induction therapy is not possible based upon pretreatment characteristics. Decisions to pursue surgical resection after induction therapy should be made prior to initiation of any therapy.



Ramnath, M. Chest, 2013.

What is the role of pneumonectomy in N2+ IIIA NSCLC?

Many Pneumonectomy Questions

- Does pneumonectomy have a role at all?
- What type of induction therapy is safe: chemotherapy or chemoradiotherapy?
- Is any radiation safe prior to pneumonectomy?
- Should patients with residual N2 disease undergo pneumonectomy?
- Can we identify patients with the greatest potential to benefit from resection?
- Surgical strategies for pneumonectomy after induction tx?

Pneumonectomy N2+ IIIA?

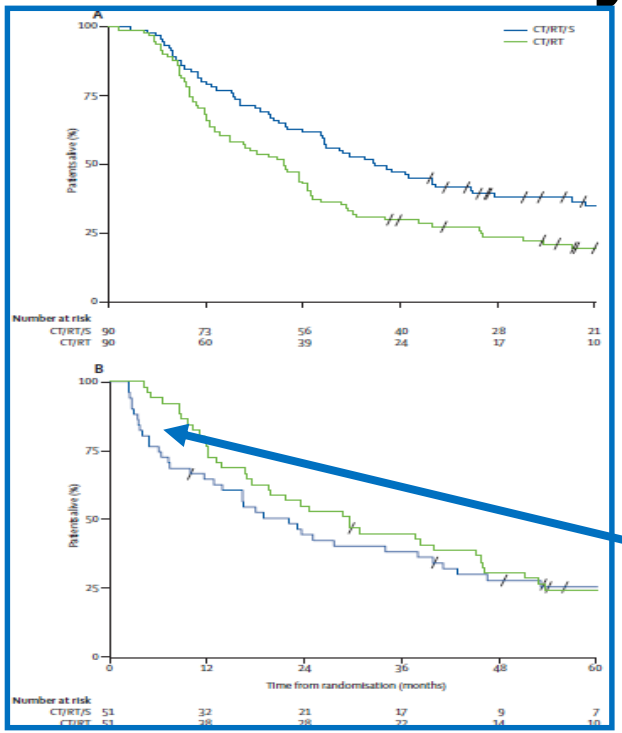
Pro-pneumonectomy

- Many single institution trials report acceptable mortality
- Increased mortality is artifact of surgical inexperience

No pneumonectomy

- Multi-institutional trials report mortality >10-27%

Pneumonectomy After Induction Tx



Intergroup trial 0139:

- Pneumonectomy associated w/ increased mortality
- 30% pts had pneumonectomy
- Trial included bulky N2 & majority of resections not by general thoracic surgeons
- Operative mortality
  - 1% lobectomy
  - 27% pneumonectomy

Albain, K. Lancet, 2009

Pneumonectomy After Induction Tx

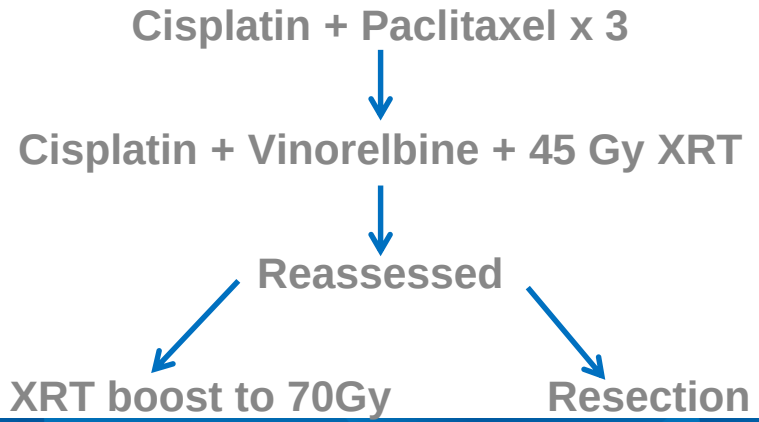
Donington, J. AATS, 2017.

RTOG 0229/0839:

- High dose concurrent CXRT
- All experienced general thoracic surgeons
- 93 resections
  - 77 lobectomy
  - 16 ext resections
- Operative mortality:
  - 1.3% lobectomy
  - 18.8% ext resection

Phase III Study of Surgery Versus Definitive Concurrent Chemoradiotherapy Boost in Patients With Resectable Stage IIIA(N2) and Selected IIIB Non–Small-Cell Lung Cancer After Induction Chemotherapy and Concurrent Chemoradiotherapy (ESPATUE)

Wilfried Ernst Erich Eberhardt, Christoph Pöttgen, Thomas Christoph Gauler, Godehard Friedel, Stefanie Veit, Vanessa Heinrich, Stefan Welter, Wilfried Budach, Werner Spengler, Martin Kimmich, Berthold Fischer, Heinz Schmidberger, Dirk De Ruysscher, Claus Belka, Sebastian Cordes, Rodrigo Hepp, Diana Lütke-Brintrup, Nils Lehmann, Martin Schuler, Karl-Heinz Jöckel, Georgios Stamatis, and Martin Stuschke



ESPATUE

- Prospective, randomized
- Closed early, poor response to initial tx, slow accrual
- No difference in OS or PFS
- 1/3 surgery pts underwent pneumonectomy, and additional 1/3 extended resection
- Operative mortality
  - 10% lobectomy
  - 0% pneumonectomy

Eberhardt W, JCO 2015.

Induction chemoradiation in stage IIIA/N2 non-small-cell lung cancer: a phase 3 randomised trial

Miklos Pless, Roger Stupp, Hans-Beat Ris, Rolf A Stahel, Walter Weder, Sandra Thierstein, Marie-Aline Gerard, Alexandros Xyrafas, Martin Früh, Richard Cathomas, Alfred Zippelius, Arnaud Roth, Milorad Bijelovic, Adrian Ochsenbein, Urs R Meier, Christoph Mamot, Daniel Rauch, Oliver Gautschi, Daniel C Betticher, René-Olivier Mirimanoff, Solange Peters, on behalf of the SAKK Lung Cancer Project Group

Swiss Trial:

- Prospective randomized, 232 pts
- Experienced surgical center in Europe
- Sequential chemo + XRT (44Gy) vs. chemo alone followed by surgery
- No improvement in survival w/ addition XRT
- Operative mortality
  - 0.8% lobectomy
  - 4.5% pneumonectomy

	Chemoradiotherapy group (n=99)	Chemotherapy group (n=94)
Types of surgery		
Lobectomy	58 (59%)	59 (63%)
Bilobectomy	13 (13%)	9 (10%)
Pneumonectomy	25 (25%)	19 (20%)
Resection score		
R0	90 (91%)	76 (81%)
R1	6 (6%)	11 (12%)
R2	3 (3%)	7 (8%)
Nodal downstaging (to N1 or N0)	63 (64%)	50 (53%)
Pathological complete remission	16 (16%)	11 (12%)

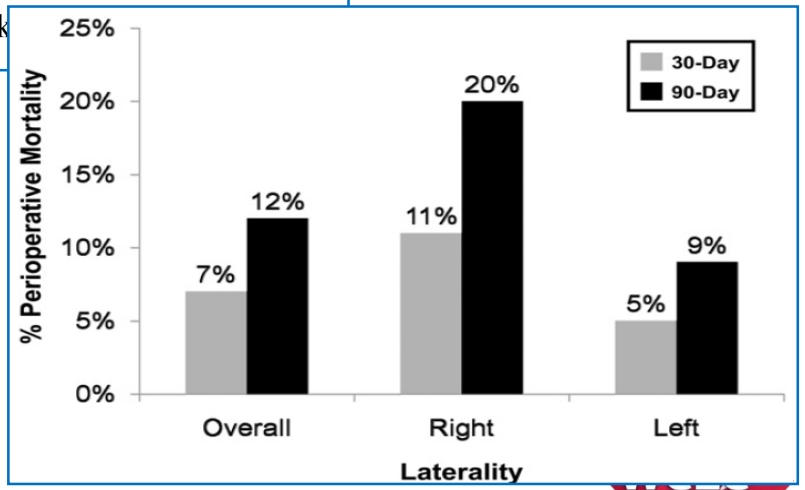
Pless M, Lancet, 2015.

Pneumonectomy After Induction Tx

An analysis, systematic review, and meta-analysis of the perioperative mortality after neoadjuvant therapy and pneumonectomy for non–small cell lung cancer

Anthony W. Kim, MD,[a] Daniel J. Boffa, MD,[a] Zuoheng Wang, PhD,[b] and Frank

- 27 trials, XRT in 13
- 7% 30-day mortality
- Mortality higher
  - Right > Left
  - 90-day > 30-day
  - low volume centers
- XRT not associated w/ increased mortality



Kim, A. JTCVS, 2012.

Pneumonectomy for IIIA NSCLC

- **Bulk and extent of mediastinal nodes dictates treatment** algorithms for N2 + stage IIIA
- Use of pneumonectomy remains controversial due to **elevated operative mortality in prospective trials**
- Further prognostic stratification may help to improve the management decisions
- **Important to balance resectability w/ overall survival and quality of life**