A Beneficência
Portuguesa
de São Paulo

Programa *Team Up* da Oncologia BP



Parceria: AstraZeneca

Classificação TNM do Câncer de Pulmão Não Pequenas Células

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BP – A Beneficência Portuguesa de São Paulo

Declaração de Conflitos de Interesse

Recebi honorários para palestras, consultoria e/ou pesquisa das seguintes empresas:

- Astra Zeneca
- Genentech / Roche
- Astellas
- Boehringer Ingelheim
- Merck
- Eli Lilly
- BMS
- MSD

Objetivos

1. Discutir os princípios da classificação TNM
2. Descrever as mudanças incorporadas na 8ª edição do *AJCC Cancer Staging Manual*

Pauta

1. Princípios do estadiamento
2. Descritor T
3. Descritor N
4. Descritor M
5. Agrupamento por estadio

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1. Princípios do estadiamento
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Sistema de Estadiamento

- Sistema de estadiamento foi desenvolvido e é mantido pela *American Joint Committee on Cancer* (AJCC) e *Union for International Cancer Control* (UICC)
- Revisões periódicas ocorrem a cada 5 a 7 anos – mais frequentes no futuro
- 8ª edição entrou em vigor em 01 de Janeiro de 2018
- Em câncer de pulmão, a *International Association for the Study of Lung Cancer* (IASLC) tem papel fundamental nas revisões
- Evolução para incorporação de características moleculares à anatomia (ainda não aplicada a câncer de pulmão)
- O termo **estadio** deve ser utilizado para descrever a categoria à qual o paciente pertence após o agrupamento com base nos descritores TNM

Sistema de Estadiamento

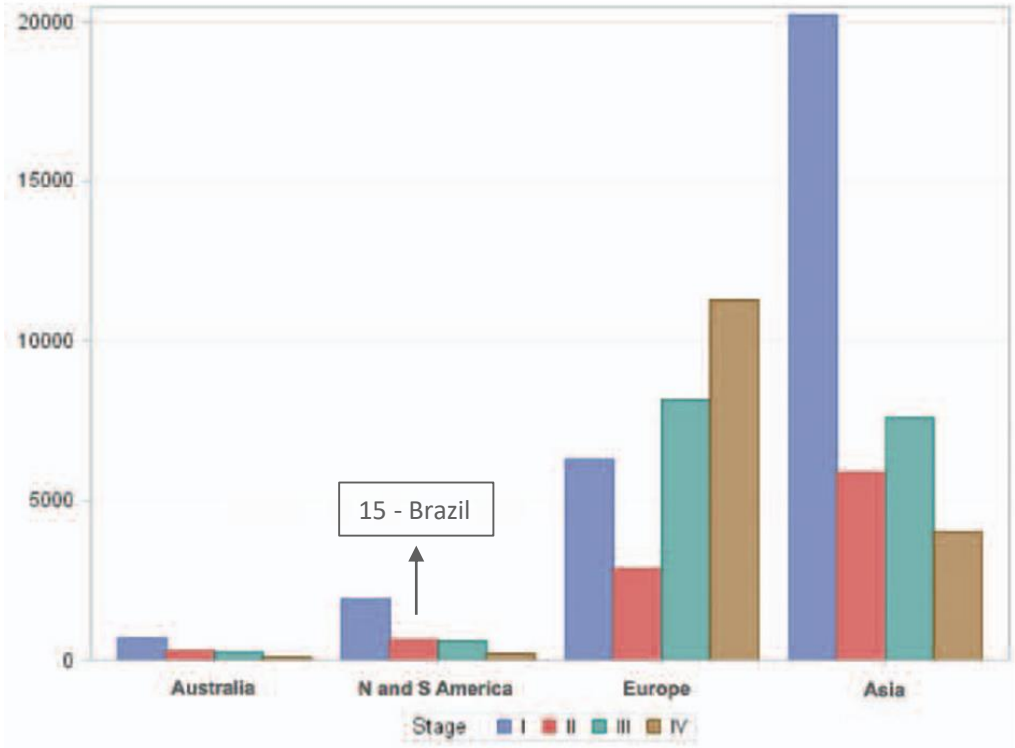
- Banco de dados IASLC para 8ª edição

Tumour	Number of Evaluable Patients
Lung cancer*	77,156
Malignant pleural mesothelioma*	2,460
Thymic malignancies**	8,145
Oesophageal cancer***	22,654

** Registered by the International Association for the Study of Lung Cancer (IASLC) and analysed by Cancer Research And Biostatistics (CRAB).*

*** Registered by the International Thymic Malignancies Interest Group and the IASLC, and analysed by CRAB.*

**** Registered by the World Wide Esophageal Cancer Collaboration and analysed at the Cleveland Clinic, Cleveland, OH, USA.*



Rami-Porta et al. J Thorac Oncol, 2014

Classificação TNM

T	tumor primário
N	acometimento linfonodal
M	metástases à distância

c	clínico
p	patológico
y	pós tratamento
a	autópsia

r	recidiva

Agrupamento por Estadios

- Denotados em algarismos romanos;
- Praticidade;
- Número relativamente balanceado de pacientes em cada categoria;
- Boa separação das curvas de sobrevida.

Apesar de o estadiamento auxiliar na determinação do prognóstico e harmonização de publicações, as estratégias diagnósticas e de tratamento devem obedecer a seleção de pacientes dos estudos originais e não a revisões do TNM que ocorrerem *a posteriori*

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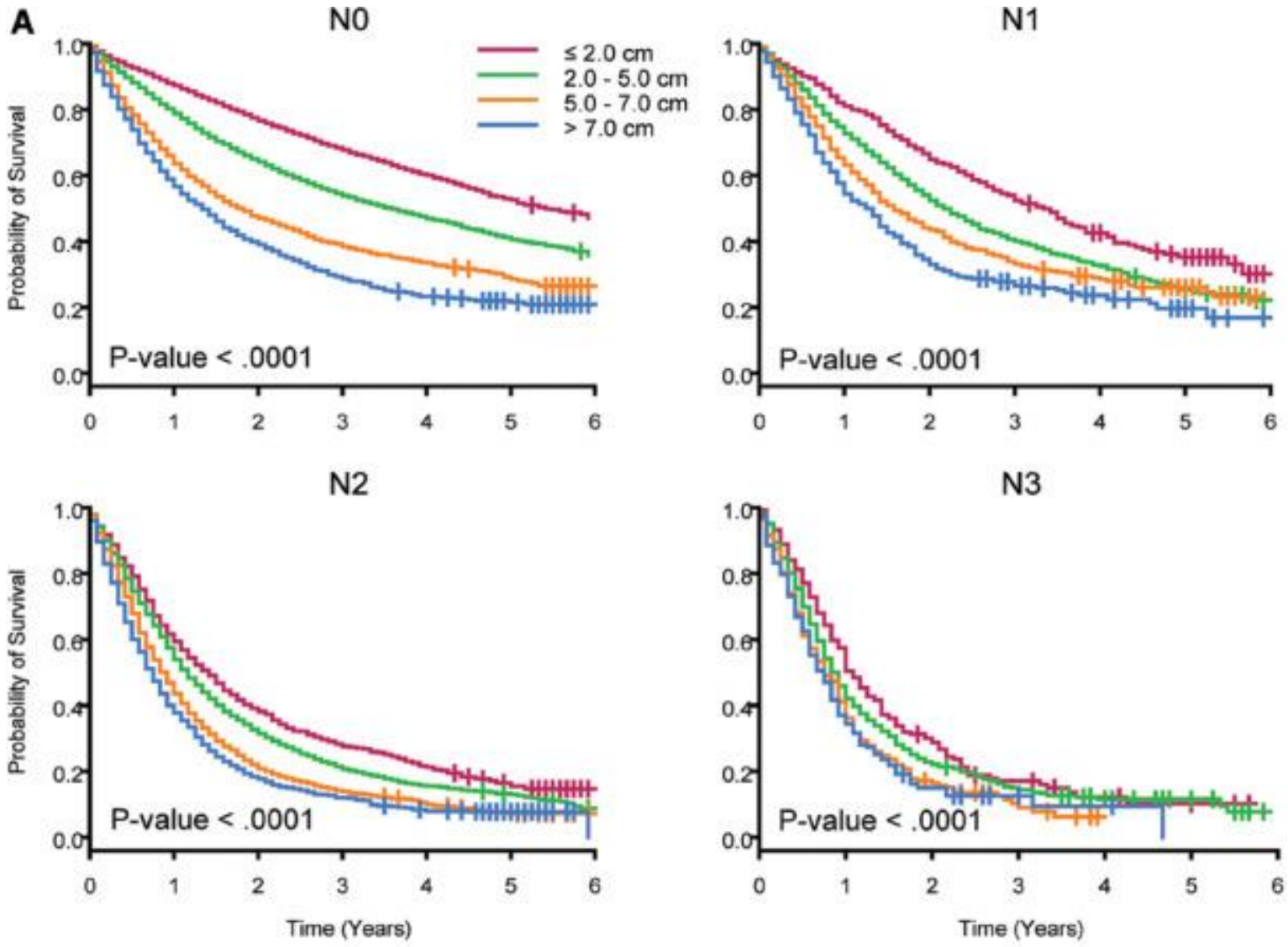
Descritor T – Principais Mudanças

- Definição de carcinoma in situ e minimamente invasivo;
- Valorização do tamanho do tumor;
- Acometimento de brônquio principal classificado como T2;
- Atelectasia parcial ou total ou pneumonite classificadas como T2;
- Atenção para classificação da invasão pleural;
- Reclassificação da invasão de diafragma como T4.

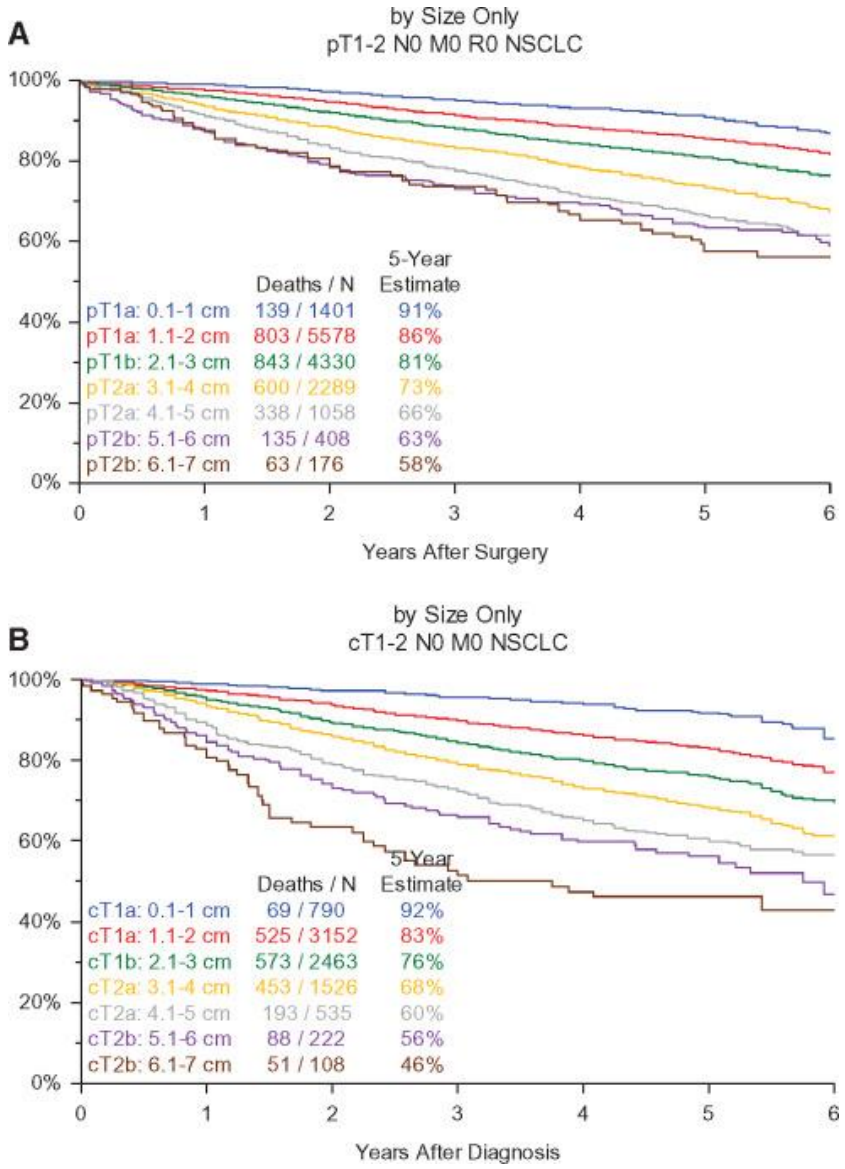
Descritor T – 8ª Edição

T		**Primary Tumor**
TX		Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0		No evidence of primary tumor
Tis		Carcinoma in situ Squamous cell carcinoma in situ (SCIS) Adenocarcinoma in situ (AIS): adenocarcinoma with pure lepidic pattern, ≤3 cm in greatest dimension
T1		Tumor ≤3 cm 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)
	T1mi	Minimally invasive adenocarcinoma: adenocarcinoma (≤3 cm in greatest dimension) with a predominantly lepidic pattern and ≤5 mm invasion in greatest dimension
	T1a	Tumor ≤1 cm in greatest dimension. A superficial, spreading tumor of any size whose invasive component is limited to the bronchial wall and may extend proximal to the main bronchus also is classified as T1a, but these tumors are uncommon.
	T1b	Tumor >1 cm but ≤2 cm in greatest dimension
	T1c	Tumor >2 cm but ≤3 cm in greatest dimension
T2		Tumor >3 cm but ≤5 cm or having any of the following features: (1) Involves the main bronchus, regardless of distance to the carina, but without involvement of the carina; (2) Invades visceral pleura (PL1 or PL2); (3) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung
	T2a	Tumor >3 cm but ≤4 cm in greatest dimension
	T2b	Tumor >4 cm but ≤5 cm in greatest dimension
T3		Tumor >5 cm but ≤7 cm in greatest dimension or directly invading any of the following: parietal pleura (PL3), chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or separate tumor nodule(s) in the same lobe as the primary
T4		Tumor >7 cm or tumor of any size invading one or more of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in a ipsilateral lobe different from that of the primary

Descritor T – Tamanho do Tumor

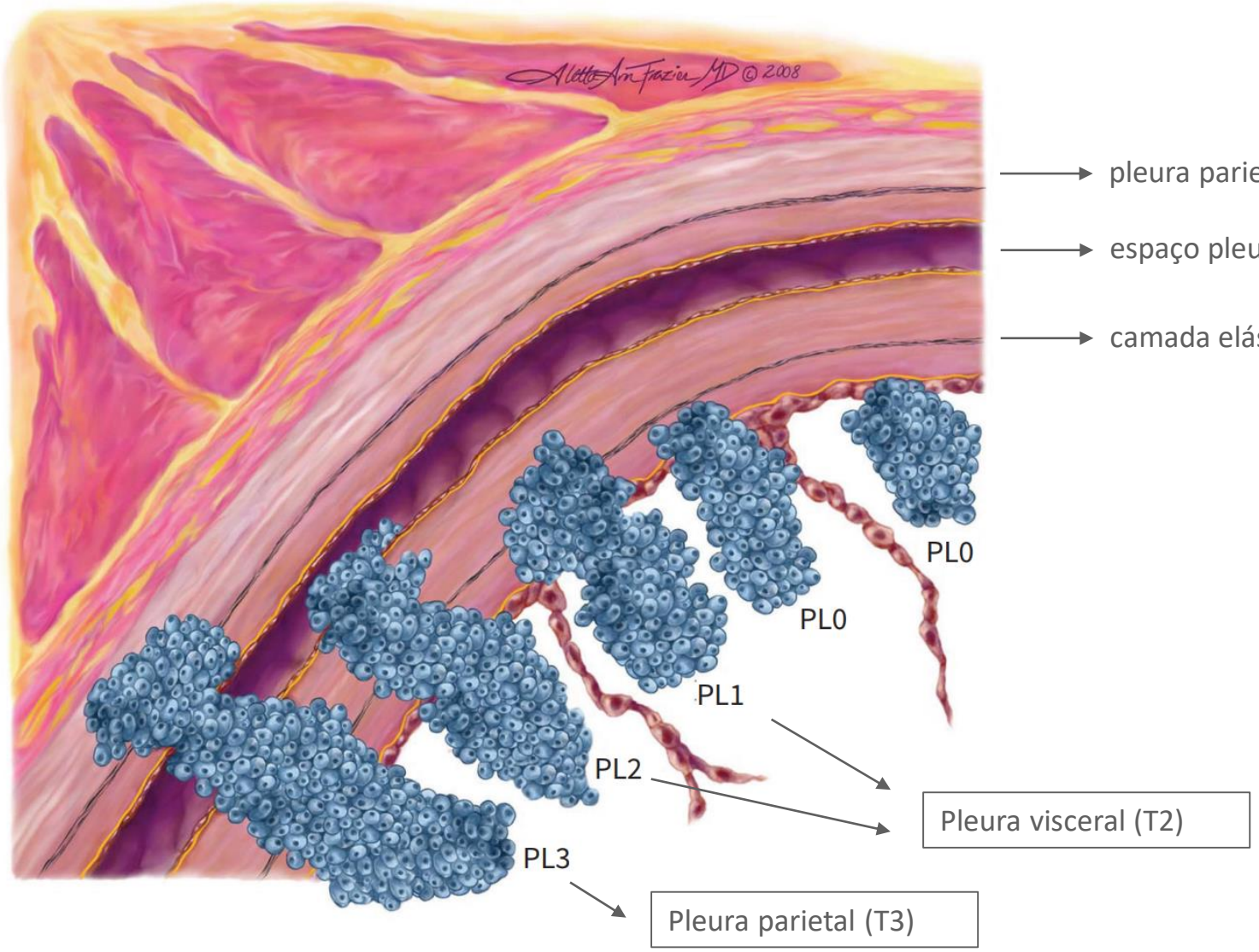


Descritor T – Tamanho do Tumor



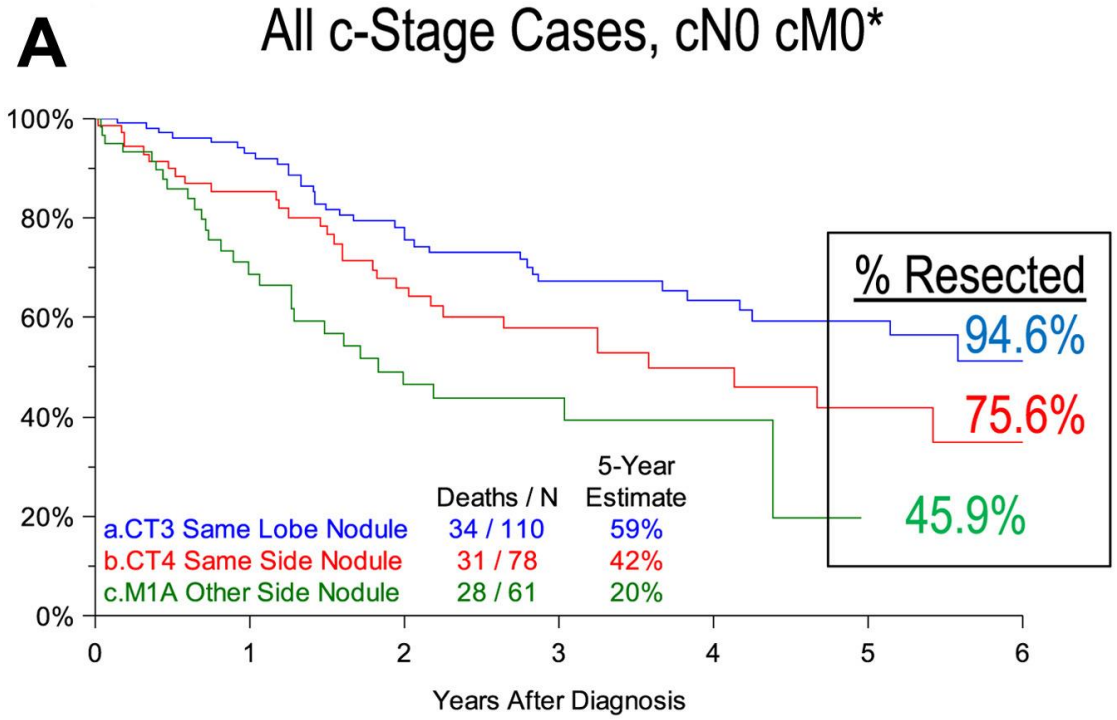
Rami-Porta et al. J Thorac Oncol, 2015

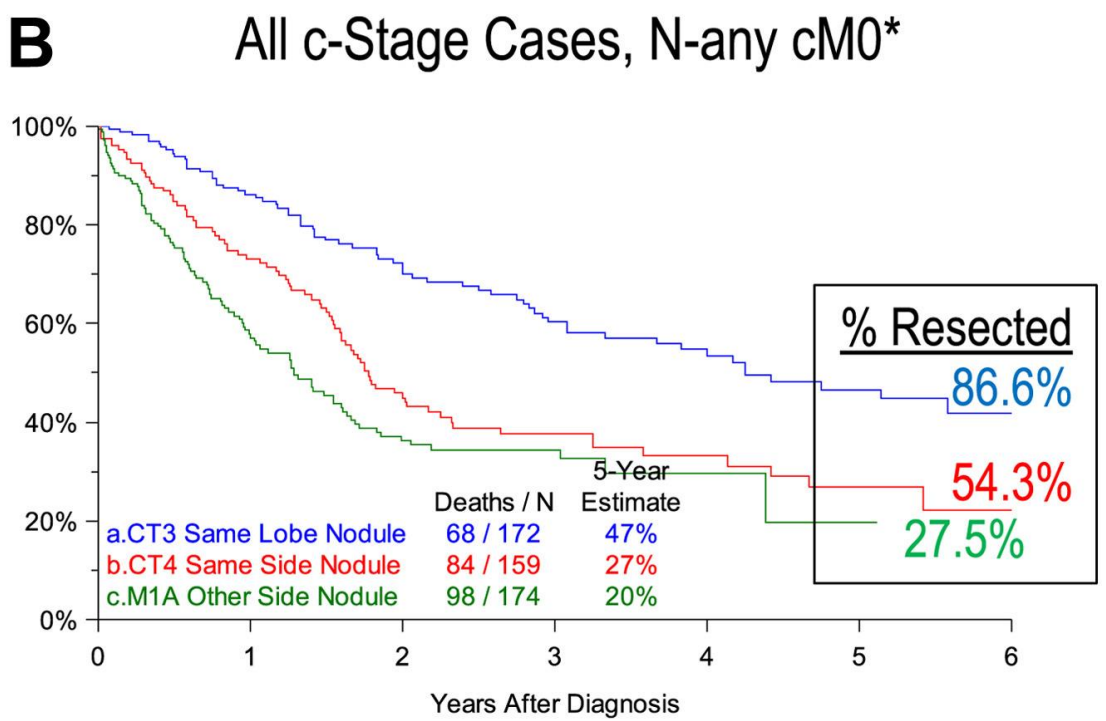
Descritor T – Invasão Pleural



Rami-Porta et al. J Thorac Oncol, 2015

Descritor T – Múltiplos Nódulos





Detterbeck et al. J Thorac Oncol, 2016

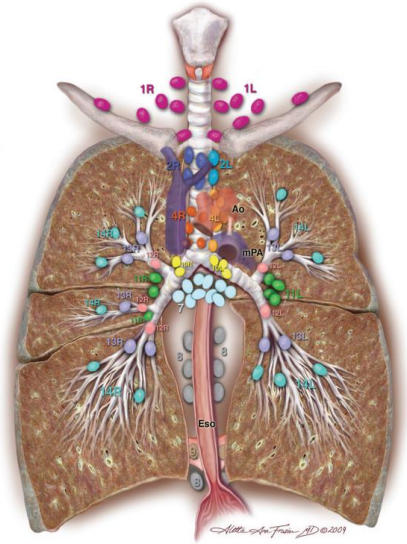
Pauta

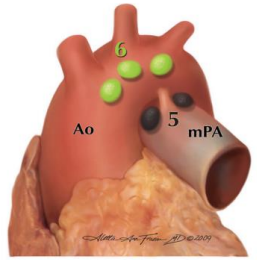
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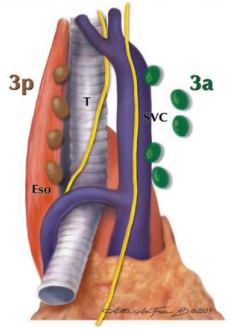
Descritor N – 8ª Edição

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)

Descritor N – Mapa Linfonodal







Supraclavicular zone
- 1 Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone
- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Prevascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

AORTIC NODES

AP zone
- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone
- 7 Subcarinal

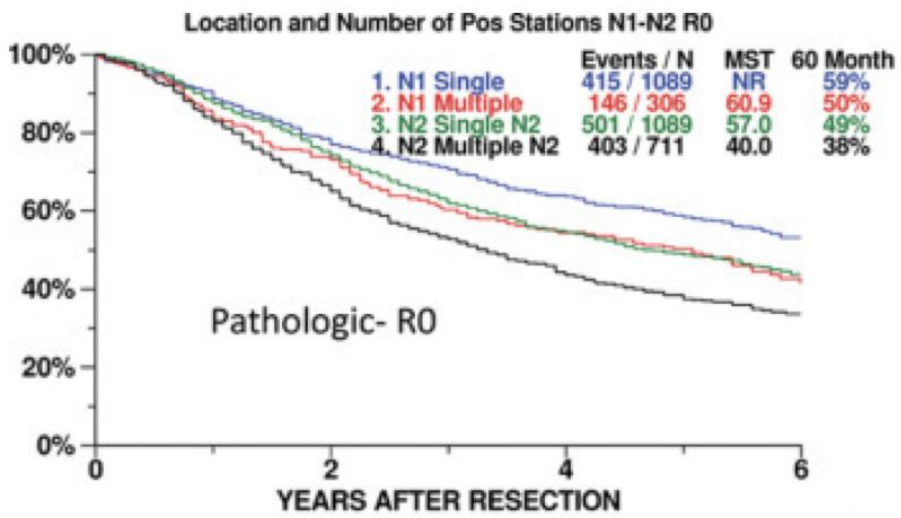
Lower zone
- 8 Paraesophageal (below carina)
- 9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone
- 10 Hilar
- 11 Interlobar

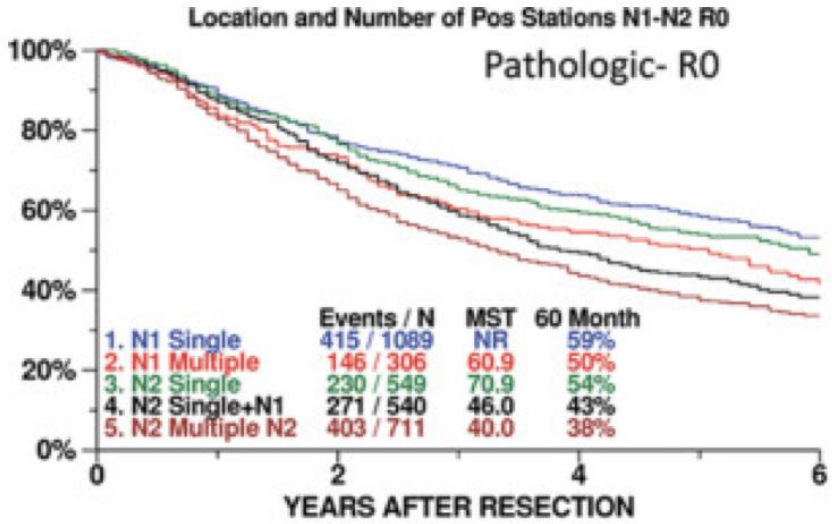
Peripheral zone
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Descritor N: mudanças em consideração para 9ª edição



N1a vs N1b vs N2a vs N2b Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+ , and Region. (Cox PH regression on R0 cases)		
comparison	HR	P
N1b vs N1a	1.40	0.0005
N2a vs N1b	1.04	0.6798
N2b vs N2a	1.47	<.0001

N1 Single = N1a
N1 Multiple = N1b
N2 Single N2 = N2a
N2 Multiple N2 = N2b



N1a vs N1b vs N2a1 vs N2a2 vs N2b Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+ , and Region. (Cox PH regression on R0 cases)		
comparison	HR	P
N1b vs N1a	1.39	0.0005
N2a1 (skip) vs N1b	0.89	0.2863
N2a2 vs N2a1 (skip)	1.35	0.0007
N2b vs N2a2	1.26	0.0028
N2a2 vs N1b	1.21	0.064

N1 Single = N1a
N1 Multiple = N1b
N2 Single N2 ("skip mets") = N2a1
N2 Single N2 + N1 = N2a2
N2 Multiple N2 = N2b

Asamura et al. J Thorac Oncol, 2015

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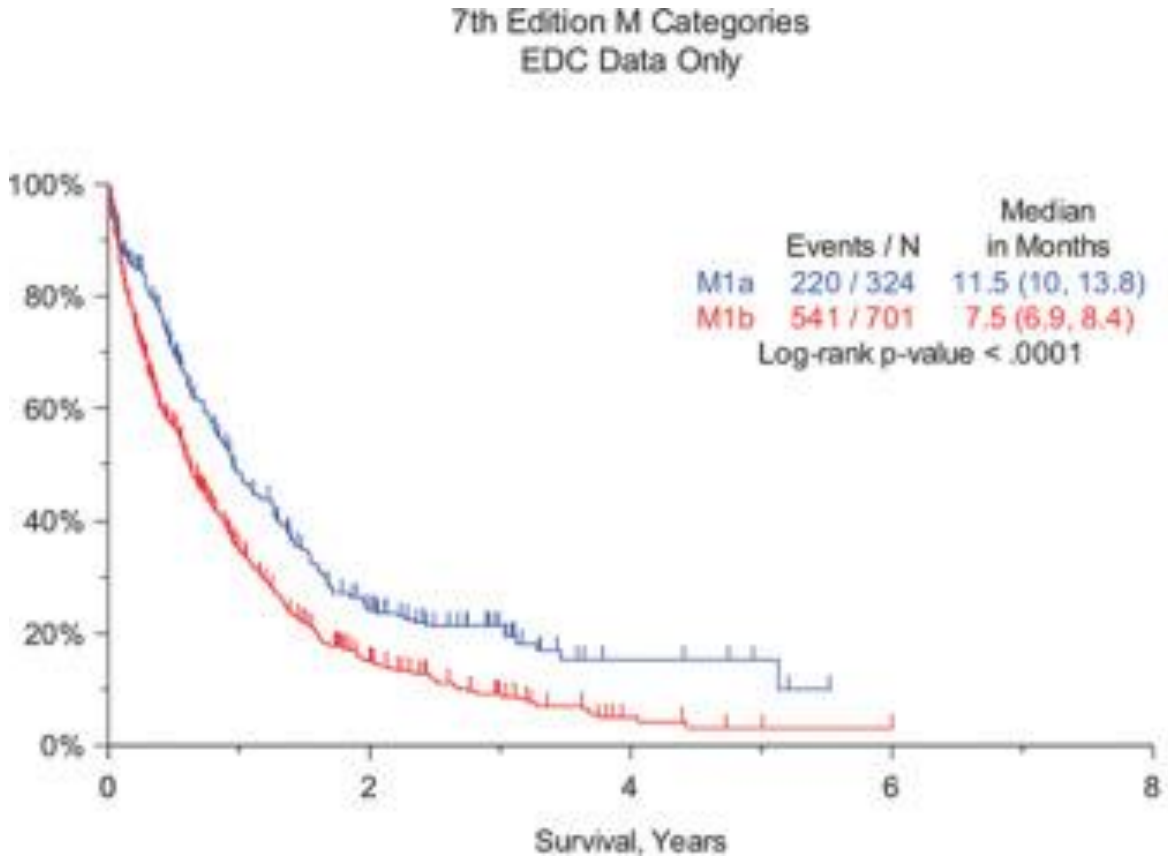
Descritor M – Principais Mudanças

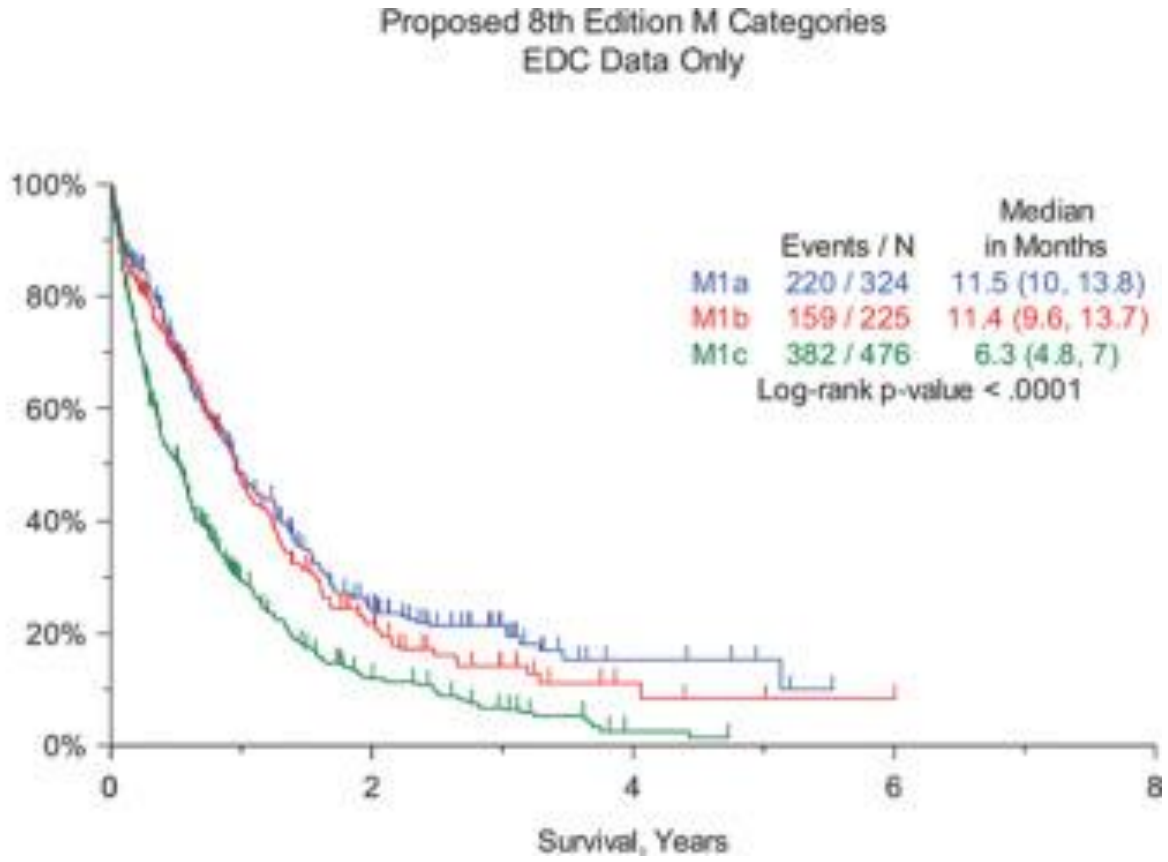
- Diferenciação de metástases extra-torácicas entre metástase única versus metástases múltiplas

Descritor M – 8ª Edição

M		**Distant Metastasis**
MX		Distant metastasis cannot be assessed
M0		No distant metastasis
M1		Distant metastasis
	M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion[a]
	M1b	Single extrathoracic metastasis in a single organ (including involvement of a single nonregional node)
	M1c	Multiple extrathoracic metastases in a single organ or in multiple organs

Descritor M: Metástase Extra-Torácica Única





Eberhardt et al. J Thorac Oncol, 2015

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Agrupamento TNM – Principais Mudanças

- Separação de estádios IA1, IA2, IA3
- Rearranjo de algumas categorias TNM
- Criação de estádio IIIC
- Separação de estádio IVA e IVB

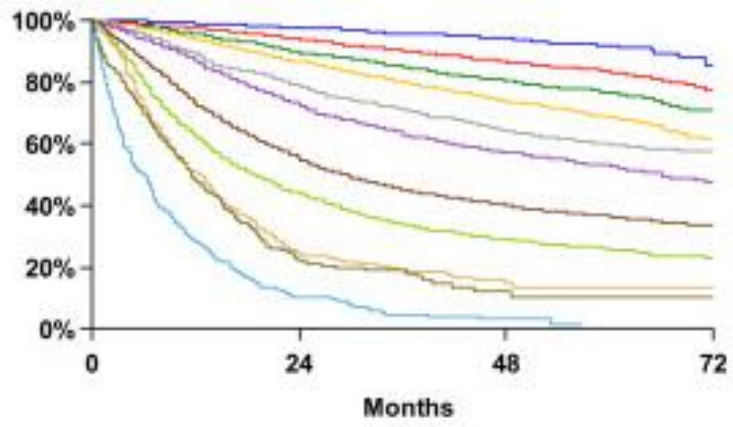
Agrupamento TNM – 8ª Edição

	T	N	M
Occult Carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	T1mi	N0	M0
	T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	T1a	N1	M0
	T1b	N1	M0
	T1c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
Stage 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

	T	N	M
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T1c	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N2	M0
	T4	N2	M0
Stage IIIC	T3	N3	M0
	T4	N3	M0
Stage IVA	Any T	Any N	M1a
	Any T	Any N	M1b
Stage IVB	Any T	Any N	M1c

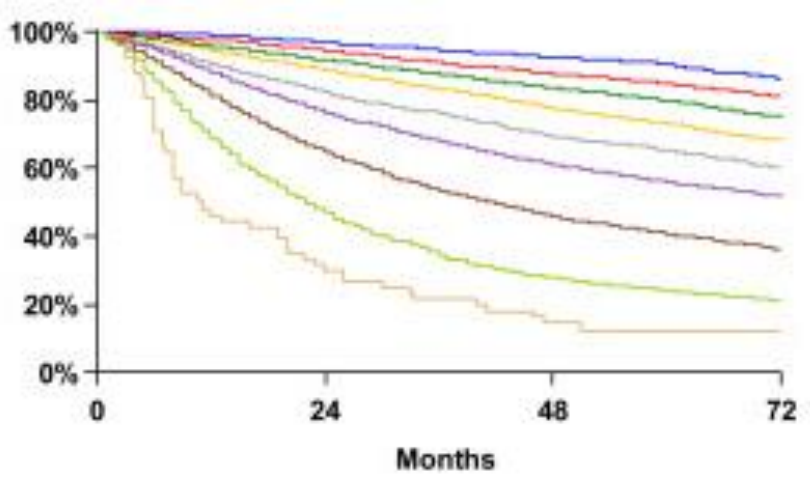
Agrupamento TNM – Prognóstico

Estadio Clínico



Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

Estadio Patológico



Proposed	Events / N	MST	24 Month	60 Month
IA1	139 / 1389	NR	97%	90%
IA2	823 / 5633	NR	94%	85%
IA3	875 / 4401	NR	92%	80%
IB	1618 / 6095	NR	89%	73%
IIA	556 / 1638	NR	82%	65%
IIB	2175 / 5226	NR	76%	56%
IIIA	3219 / 5756	41.9	65%	41%
IIIB	1215 / 1729	22.0	47%	24%
IIIC	55 / 69	11.0	30%	12%

Goldstraw et al. J Thorac Oncol, 2016

Conclusões

- Criação de banco de dados da IASLC permitiu refinamento do estadiamento do câncer de pulmão não pequenas células – aprimoramento constante;
- Valorização do tamanho do tumor como fator prognóstico importante;
- Descritor N possivelmente passará por mudanças na próxima edição;
- Reconhecimento da heterogeneidade do prognóstico da doença metastática.

Bibliografia

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3. Rami-Porta R, Bolejack V, Crowley J et al. The IASLC Lung Cancer Staging Project: proposals for the revisions of the T descriptors in the forthcoming 8th edition of the TNM classification for lung cancer. J Thorac Oncol 2015; 10: 990-1003.
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7. Goldstraw P, Chansky K, Crowley J et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the stage grouping in the forthcoming (8th) edition of the TNM classification of lung cancer. J Thorac Oncol 2016; 11: 39-51.

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