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Portuguesa
de São Paulo

Programa *Team Up* da Oncologia BP



Parceria: AstraZeneca

Estadiamento Invasivo do Mediastino

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Objetivos

- Discutir os princípios do estadiamento invasivo do mediastino
- Estabelecer conceitos e discutir áreas controversas.

Pauta

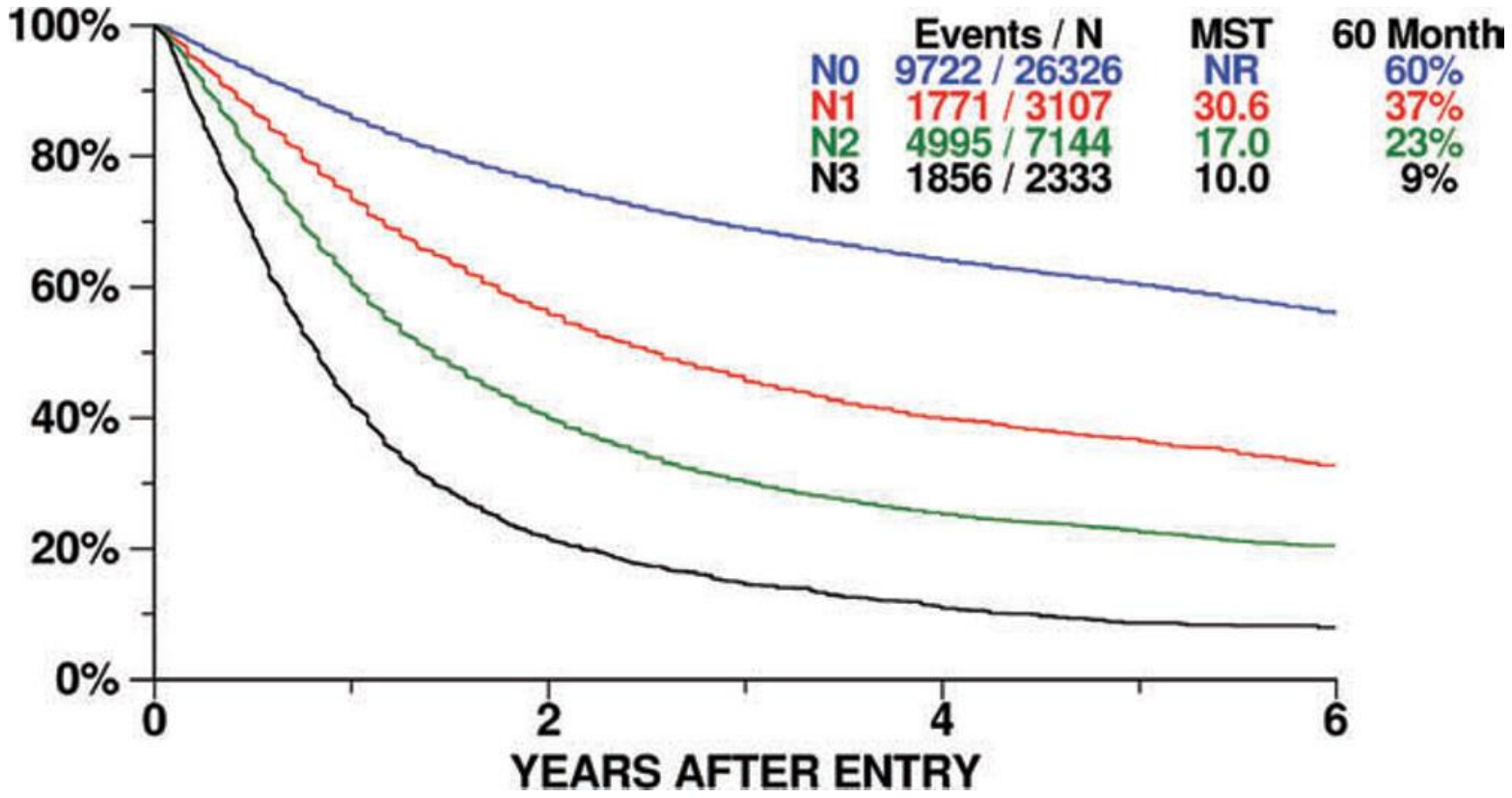
- Racional para estadiamento invasivo do mediastino
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Status N tem impacto prognóstico...

cT-qualquer M0



Asamura H et al. J Thorac Oncol 2015

Estadiamento mediastinal com TC de Tórax

First Author	Year	No.	Tech	Prev	Sens	Spec	PPV	NPV
Eggeling[137]	2002	73	CE	70	82	50	79	55
Wallace[143]	2001	121	CE	69	87	35	75	54
Marom[88]	1999	79	CE	56	59	86	84	63
Vansteenkiste[150]	1998	56	CE	50	86	79	80	85
Aaby[156]	1995	57	…	44	72	91	86	81
Schillaci[136]	2003	83	CE	42	69	75	67	77
Vansteenkiste[151]	1998	68	CE	41	75	63	58	78
Primack[157]	1994	159	CE	38	63	86	73	79
Turkmen[130]	2007	59	CE	36	43	66	41	68
Laudanski[141]	2001	92	CE	33	60	73	51	79
Yokoi1[58]	1994	113	CE	33	62	80	61	81
Gdeedo[153]	1997	100	CE	32	63	57	41	76
Bury[155]	1996	53	CE	32	71	81	63	85
McLoud[159]	1992	143	CE	31	64	62	44	79
Pieterman[90]	2000	102	CE	31	75	66	50	85
Yen[127]	2008	96	CE	31	47	80	52	77
Osada[146]	2001	335	CE	30	56	93	77	83
Jolly[160]	1991	336	CE	30	71	86	69	87
Subedi[67]	2009	91	CE	29	50	86	59	81
Buccheri[154]	1996	80	CE	28	64	74	48	84
Pozo-Rodriguez[24]	2004	132	CE	27	86	67	49	93
Kiernan[138]	2002	92	CE	27	64	94	80	88
Reed[19]	2003	302	CE	25	37	91	58	81
Nosotti[139]	2002	87	CE	25	64	88	64	88
Dunagan[144]	2001	72	CE	25	50	87	56	84
Kimura[135]	2003	203	CE	24	63	97	88	89
Yi1[29]	2007	143	CE	24	65	89	65	89
Suzuki[149]	1999	440	CE	23	33	92	56	82
Bury[152]	1997	64	CE	22	79	84	58	93
De Wever[44]	2007	50	CE	22	91	72	48	97
Webb[162]	1991	154	CE	21	52	69	31	84
Cole[161]	1993	150	…	21	26	81	26	81
Takamochi[132]	2005	71	CE	21	20	89	33	81
Kamiyoshihara[145]	2001	546	CE	20	33	90	46	84
Takamochi[147]	2000	401	CE	20	30	82	30	83
Lee[126]	2009	182	CE	20	36	79	30	83
Yang[128]	2008	122	CE	20	52	73	33	86
Kelly[134]	2004	69	CE	19	46	86	(43)*	87
Saunders[148]	1999	84	…	18	20	90	(30)*	84
Nomori[133]	2004	80	…	18	50	95	(70)*	90
Ebihara[131]	2006	205	CE	15	32	83	(26)*	87
Poncelet[142]	2001	62	CE	15	56	68	(23)*	90
Von Haag[140]	2002	52	CE	12	50	65	(16)*	91

- Revisão sistemática: 1980 - 2011
- 43 estudos; 7.368 pctes
- LN menor eixo > 10mm

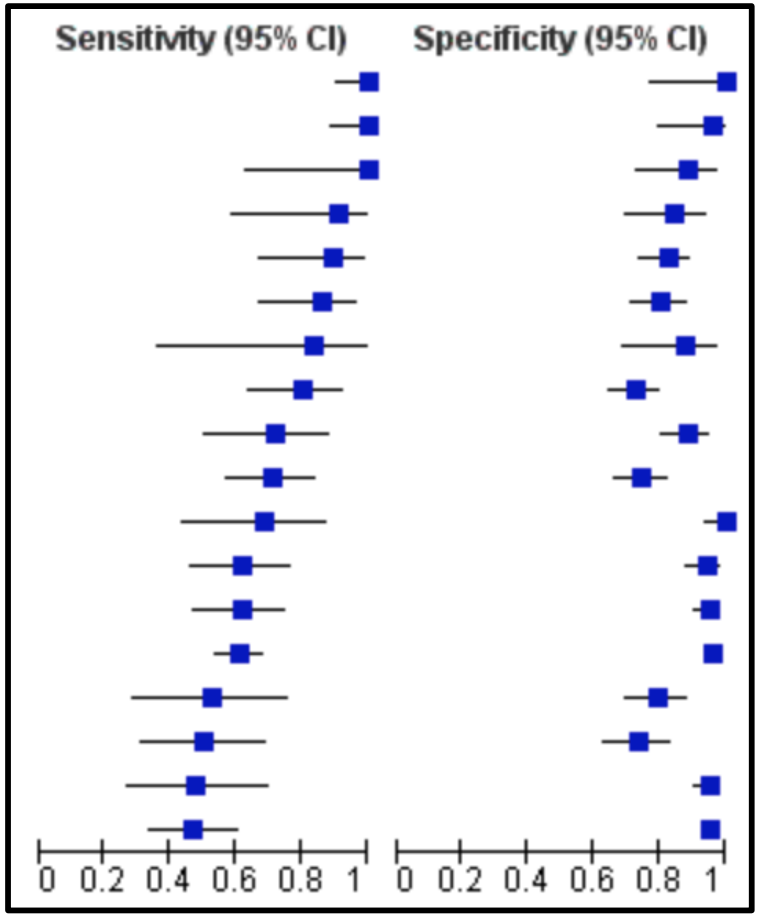
Prev N2	Sens	Espec	VPP	VPN
> 30%	67%	74%	62%	79%
21 – 30%	63%	87%	58%	84%
< 20%	41%	83%	30%	87%
Med 30%	**55%**	**81%**	**58%**	**87%**

Silvestri *et al*. ACCP Guideline 3rd Edition. CHEST, 2013

Estadiamento mediastinal com PET-CT

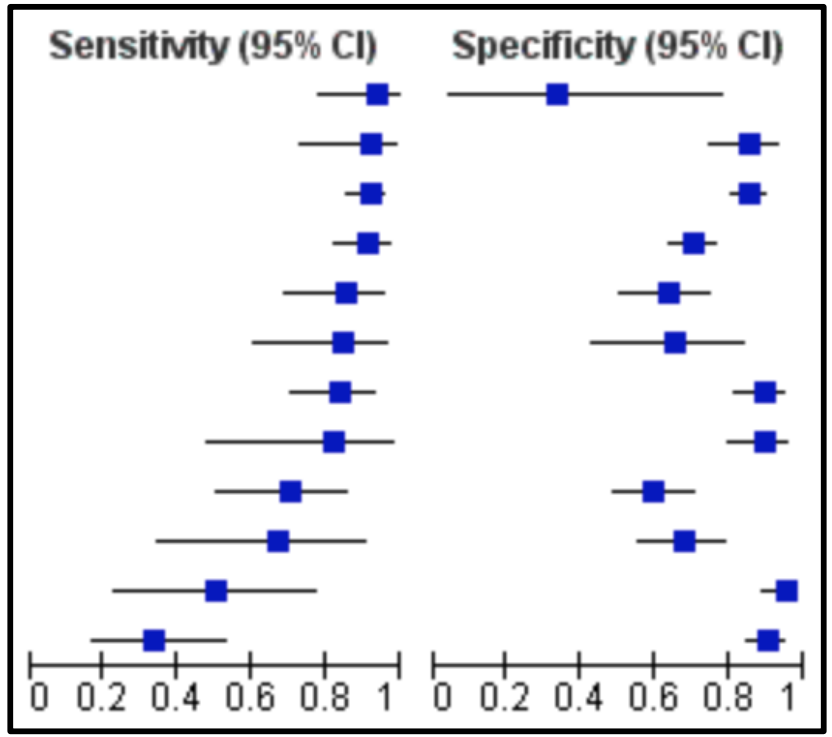
Revisão Sistemática Cochrane - 45 estudos

Atividade metabólica > *Blood Pool* Mediastinal (BPM)



	Sens	Espec
>BPM	77%	90%
SUV≥2.5	81%	80%

SUVmax ≥ 2.5



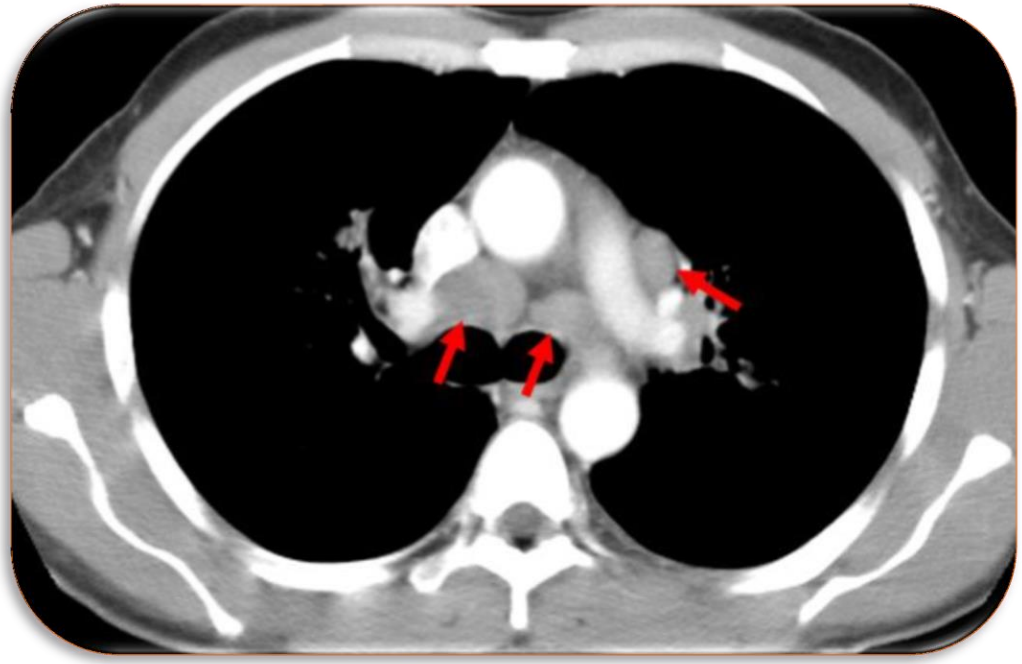
Schmidt-Hansen *et al*. Cochrane Database Syst Rev 2014

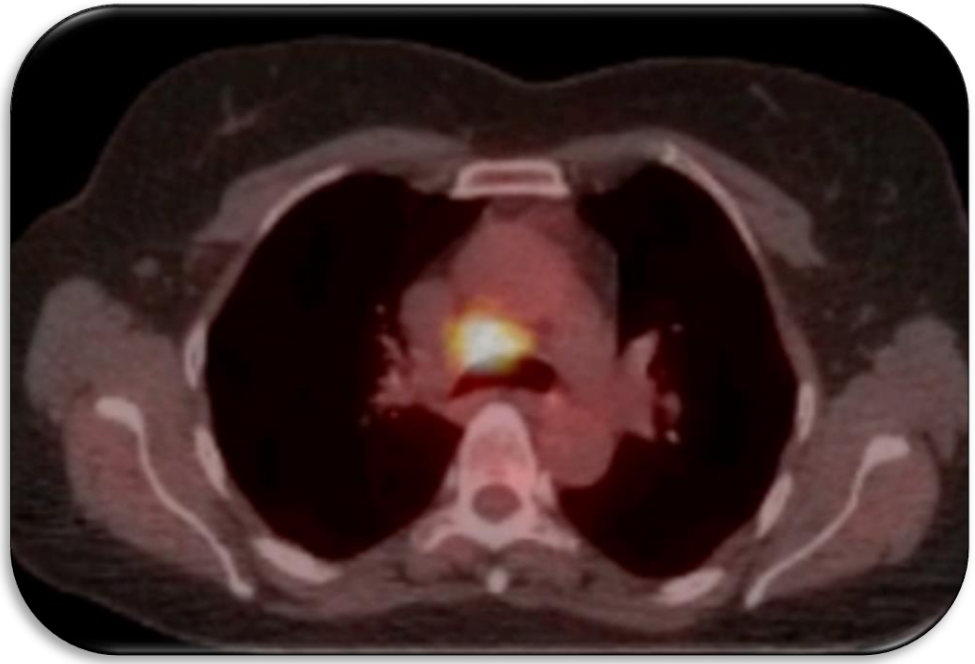
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Mediastino Anormal

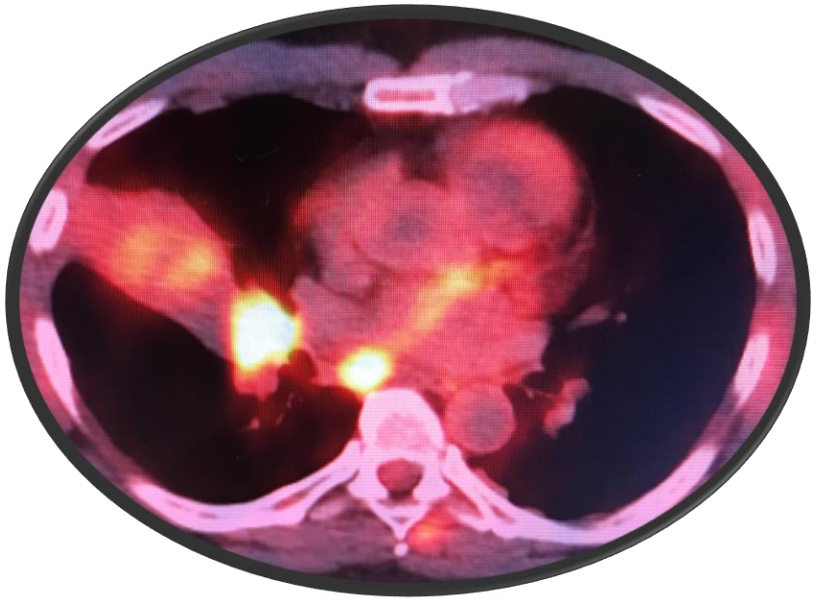
LN menor eixo > 10mm e/ou PET positivo





Confirmação histológica é necessária

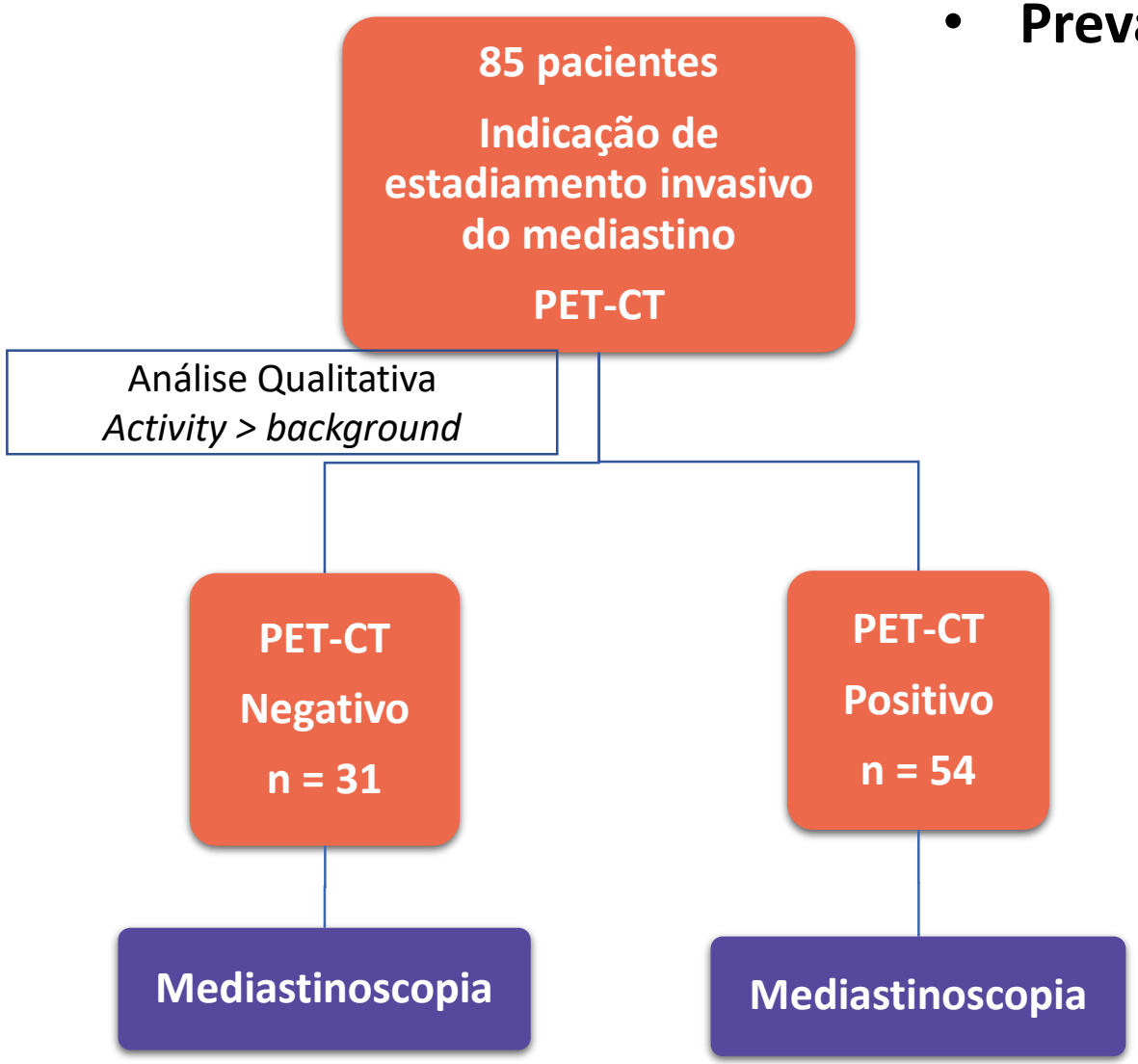
Causas de PET-CT falso-positivos



Fatores Independentes	*p*	95% CI
Artrite Reumatóide	0.048	0.071-0.99
História de TB	0.038	0.008-0.877
Pneumonia	0.012	0.087-0.735

Al-Sarraf N *et al*. Interactive CardioVascular and Thoracic Surgery, 2007.

Especificidade do PET-CT no Brasil



- **Prevalência pN2 = 27% (20 PET pos e 3 PET neg)**

SUV > 0

FALSO-POSITIVO	54%
ESPECIFICIDADE	45%
VPP	37%

SUV ≥ 5

FALSO-POSITIVO	21%
ESPECIFICIDADE	79%
VPP	54%

Werutsky et al. BMC Cancer. 2019

Mediastino Normal

CHEST AMERICAN COLLEGE of CHEST PHYSICIANS — ACCP, 2013

- Tumor central
- Suspeita de N1 (TC e/ou PET-CT)

EUROPEAN SOCIETY OF THORACIC SURGEONS · 1993 · — ESTS, 2014

NCCN National Comprehensive Cancer Network® — NCCN, 2019

- Tumor central
- Suspeita de N1 (TC e/ou PET-CT)
- Tumor > 3cm

N2 oculto: PET-CT falso-negativo

	pN2	VPN (PET-CT)
Peripheral T1N0	2.9% (1)	95% (2)
Tumor > 3cm	10.4% (3)	85% (2)
Central Tumor	21.6% (4)	78% (4)
cN1	24% (5)	76% (5)

1. Lee P et al. Ann Thorac Surg. 2007; 84:177–81
2. Wang J et al. Clin Lung Cancer 2012;13:81-9.
3. Uy et al. In Difficult Decisions in Lung Cancer, Ferguson 2007
4. Gómez-Caro A et al. Eur J Cardiothorac Surg 2012;42:93-100
5. Dooms C et al. CHEST 2015; 147(1): 209 - 215

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Métodos x Cadeias Linfonodais

	Cadeia Linfonodal
Endossonografia – EBUS/EUS	2R, 4R, 2L, 4L, 3p, 7, 8, 9, 5(1), 6(2), 10, 11
Mediastinoscopia	2R, 4R, 2L, 4L, 7, 8(3), 10(3)
Mediastinoscopia extendida	5(4), 6(4)
Mediastinotomia anterior	5(5), 6(5)
VATS	2R, 4R, 2L, 4L, 3a, 3p, 7, 8, 9, 5, 6, 10, 11

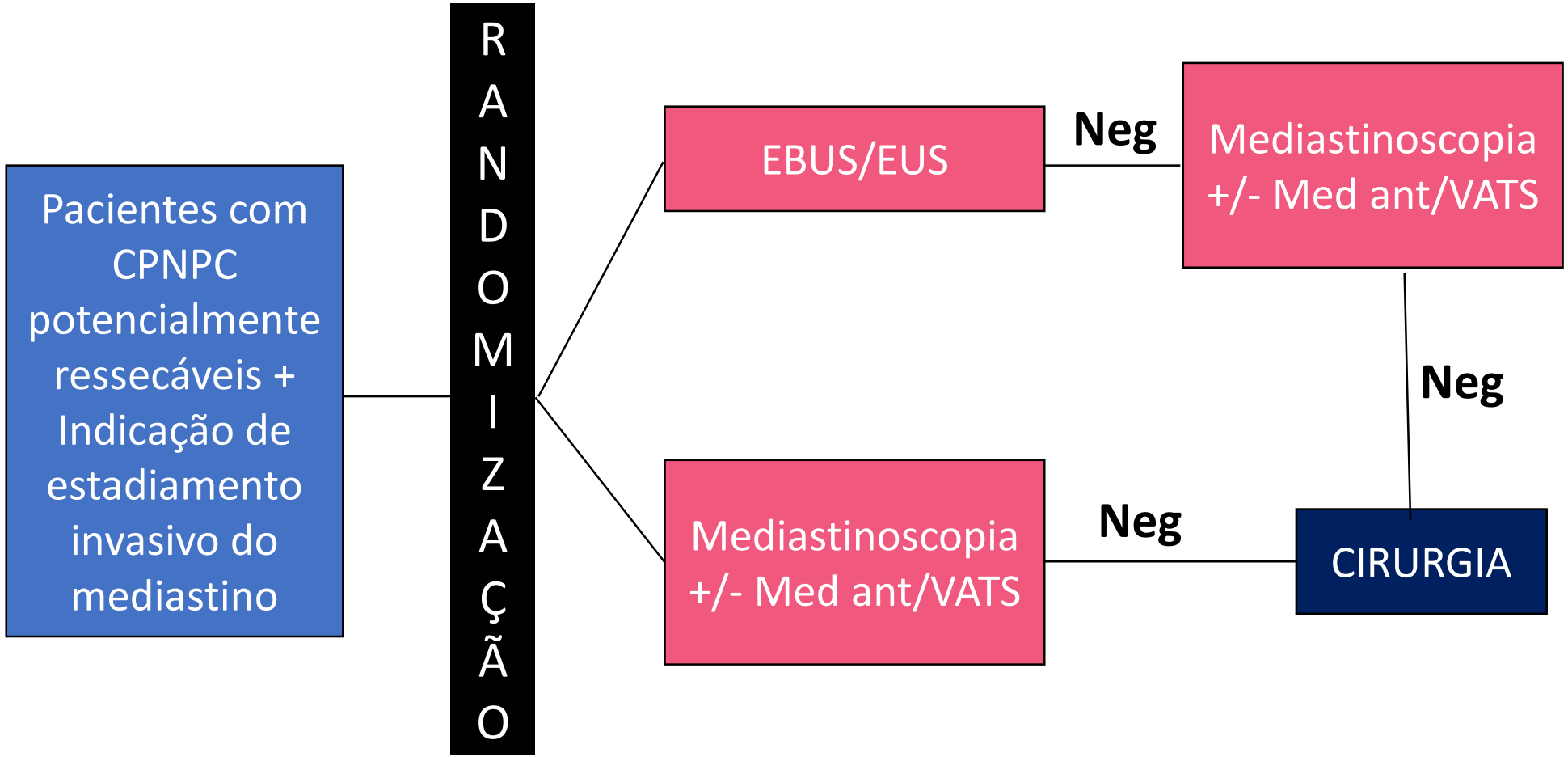
Needle-First Approach (ACCP, ESTS, NCCN *guidelines*)

1. Kazakov et al. Ann Thorac Surg. 2017
4. Witte et al. Eur J Cardiothorac Surg. 2014
5. Nechala et al. Ann Thorac Surg. 2006

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Assessment of Surgical sTaging vs Endoscopic Ultrasound in Lung Cancer: a Randomized Clinical Trial (ASTER Study)



Annema et al. JAMA. 2010

RESULTADOS

N = 241 EBUS/EUS = 123 / Mediastinoscopia = 117

	Sens	VPN	Acurácia
Mediastinoscopia	**79%**	**86%**	**91%**
EBUS-EUS +/- Med	**94%**	**93%**	**97%**
EBUS-EUS	**85%**	**85%**	**88%**

	Sens	VPN
Endossonografia +/- Med *vs.* Med	*p* =.02	*p* = .18
EBUS/EUS *vs.* Med	*p* = .47	*p* > .99

End-point Secundário	Endossonografia	Mediastinoscopia
Toracotomia fútil	7%	18% p = .02
Complicações*	1%	6% p = .03

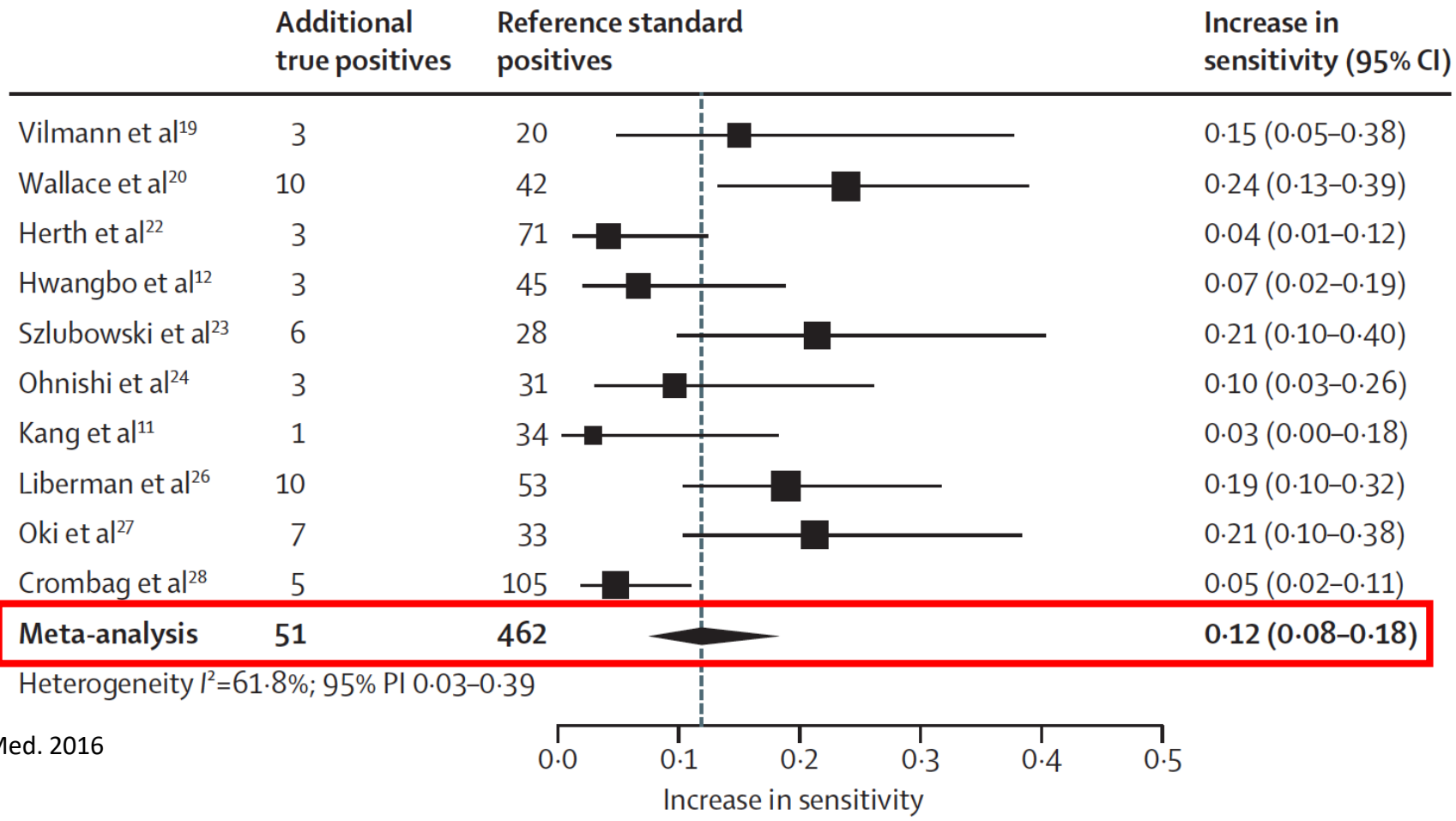
* EBUS/EUS apenas x Estadiamento Cirurgico

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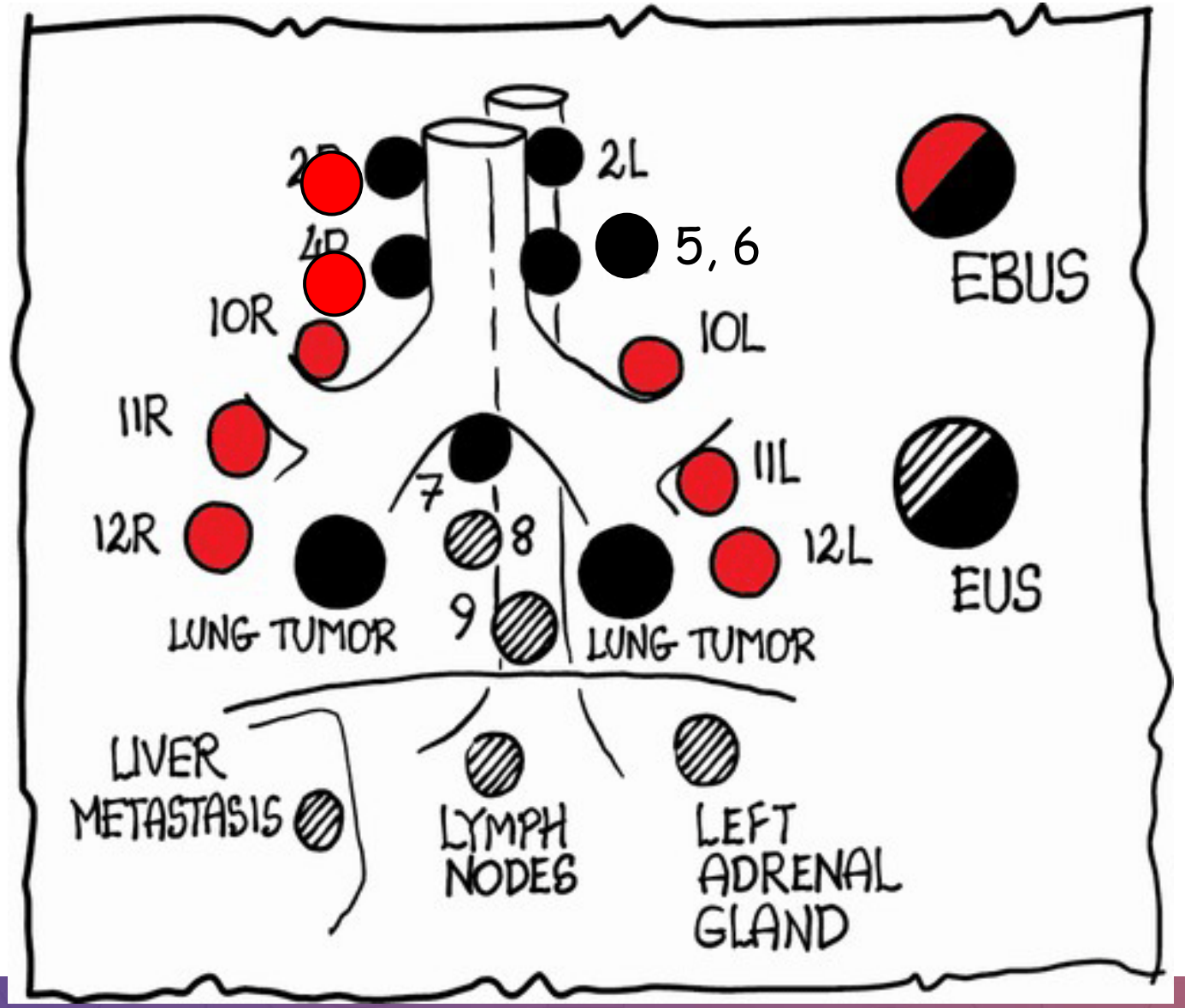
Added value of combined endobronchial and oesophageal endosonography for mediastinal nodal staging in lung cancer: a systematic review and meta-analysis

Ganho de Sensibilidade EBUS + EUS



Korevaar et al. Lancet Respir Med. 2016

EBUS e EUS são complementares

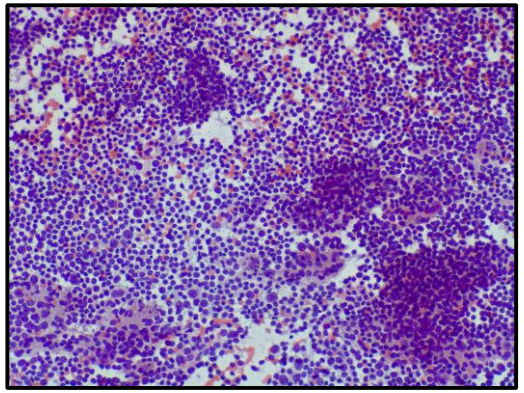


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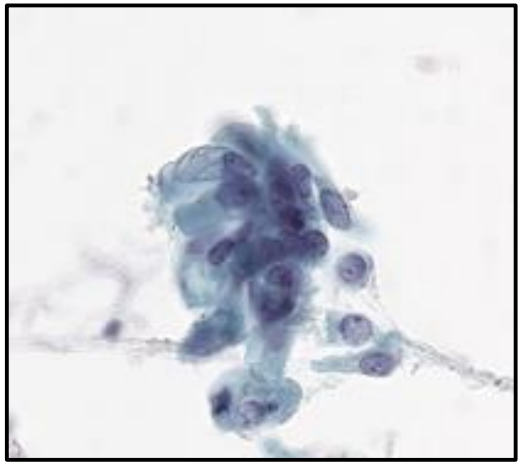
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Em caso de EBUS negativo...

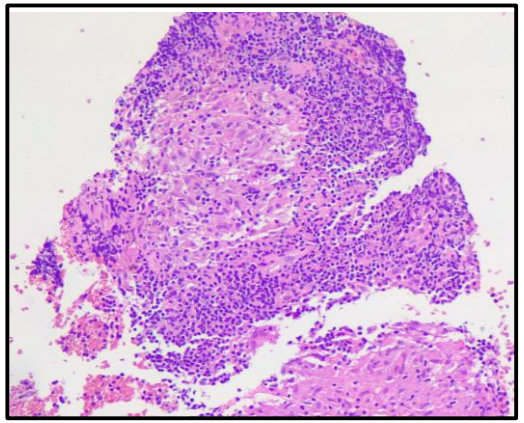
- As amostras foram de qualidade satisfatória? Inconclusiva ≠ Negativa



- Densidade Linfocitos > 40/campo x40



- Células Neoplásicas



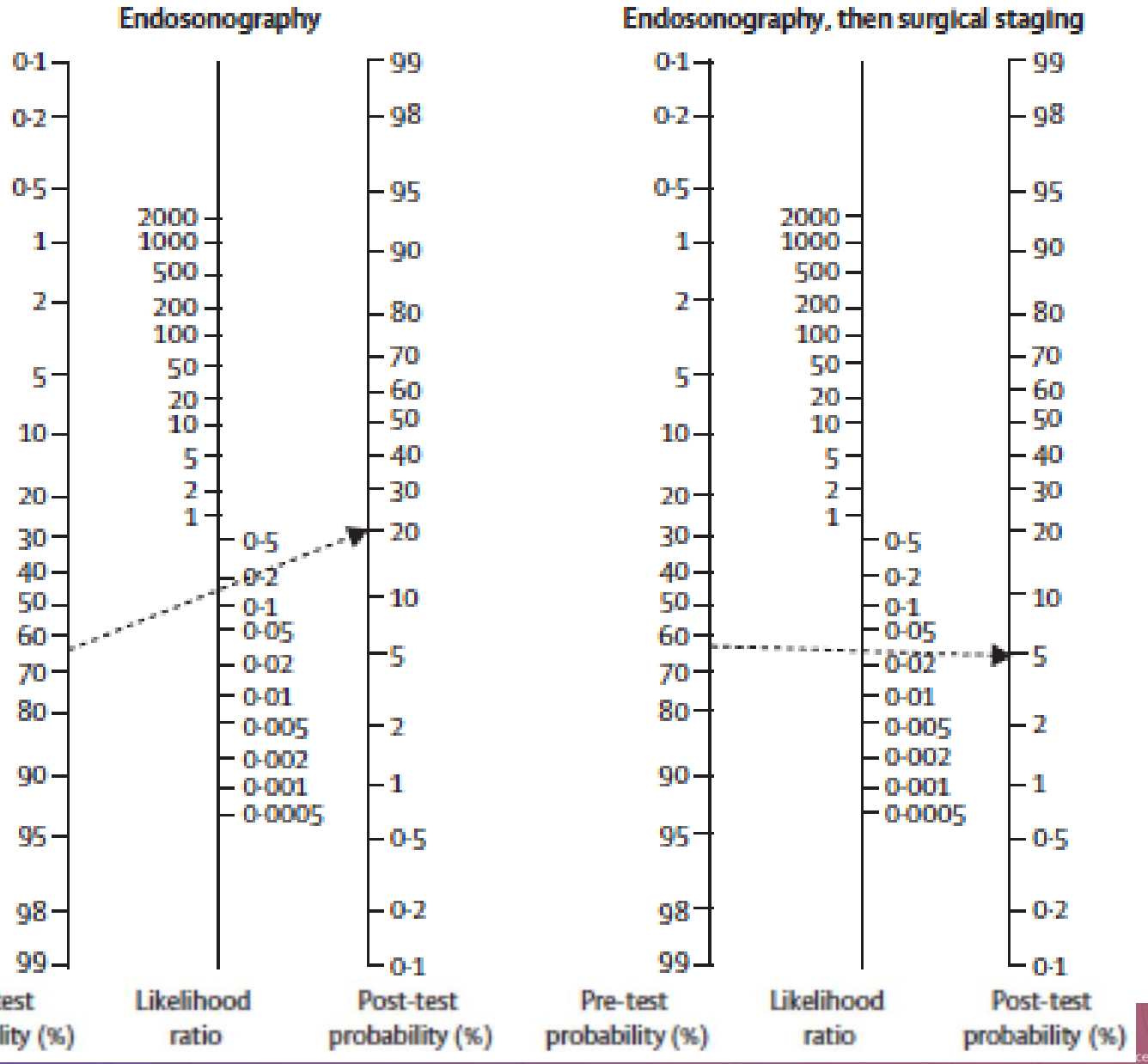
- Presença de granuloma e/ou pigmentos de antracose



- CIRTORAX
- Santa Casa - BA

Impacto da mediastinoscopia após EBUS negativo

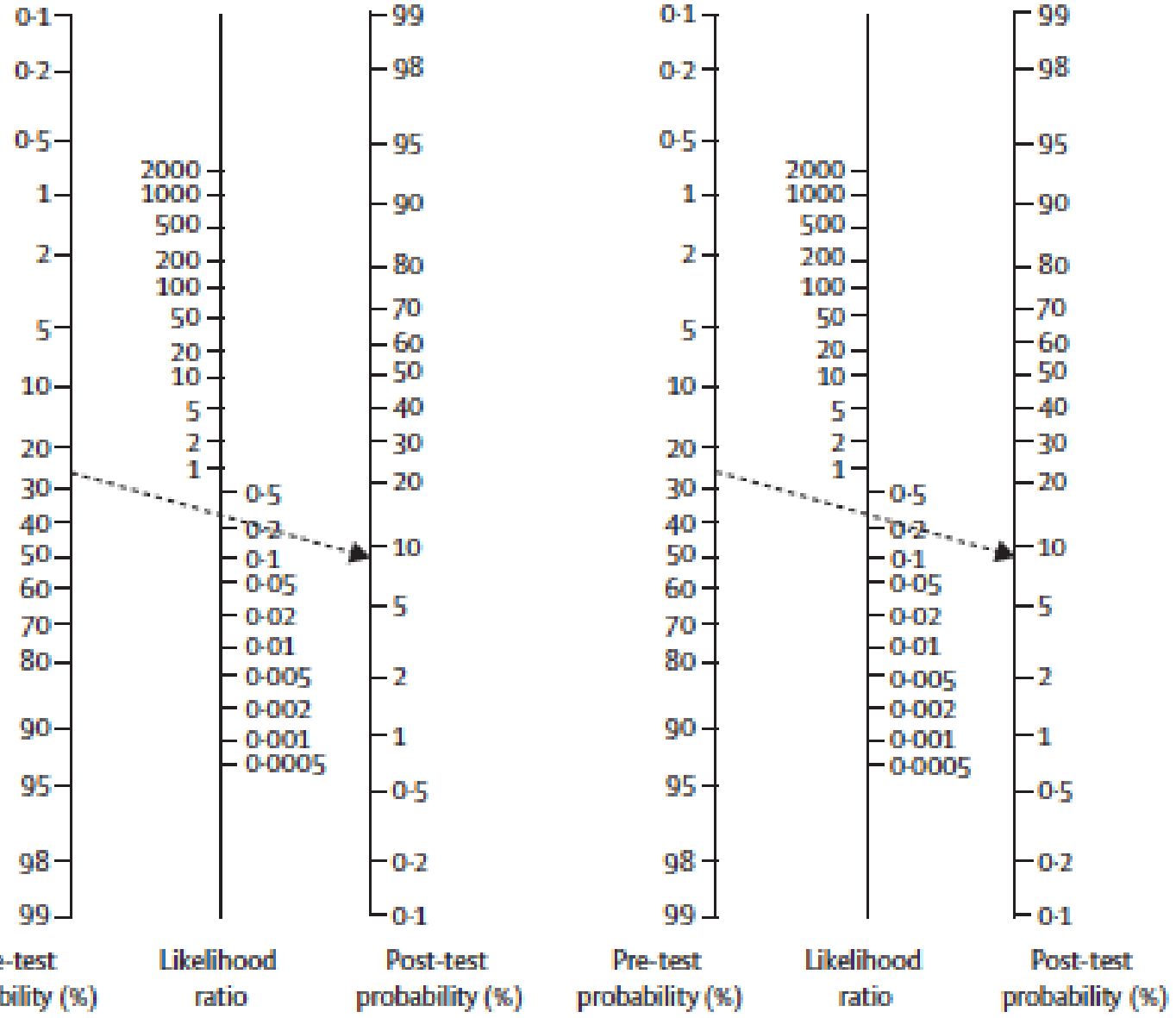
Mediastino Anormal - cN2 (CT/PET)



Tournoy et al. Lancet Oncol. 2012

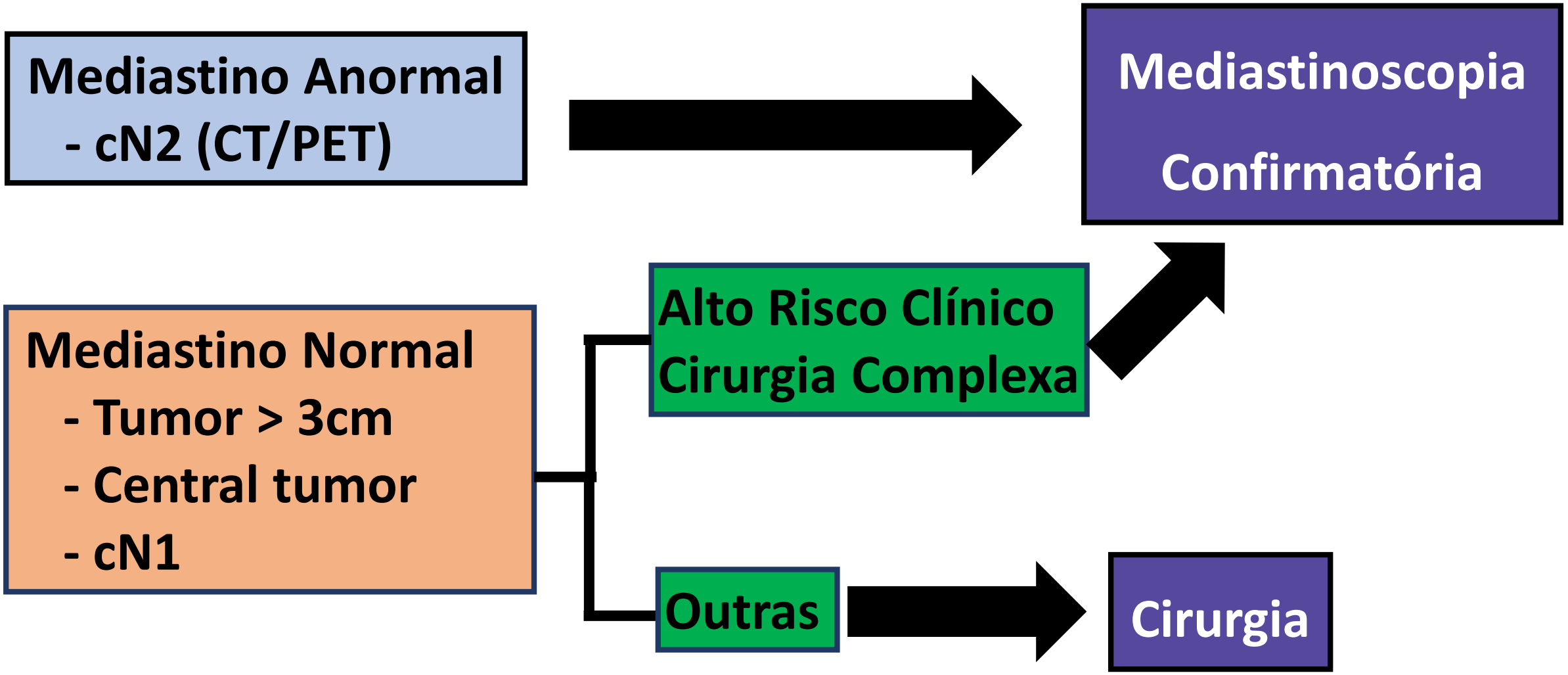
Impacto da mediastinoscopia após EBUS negativo

Mediastino Normal
- **Tumor > 3cm**
- **Tumor central**
- **cN1**



Tournoy et al. Lancet Oncol. 2012

Como eu faço


Mediastino Anormal
- cN2 (CT/PET)
Mediastinoscopia
Confirmatória
Mediastino Normal
- Tumor > 3cm
- Central tumor
- cN1
Alto Risco Clínico
Cirurgia Complexa
Outras
Cirurgia

Conclusões

- Estadiamento invasivo do mediastino está indicado em casos suspeitos de N2 na TC e/ou PET-CT (MEDIASTINO ANORMAL).
- A suspeita de N2 na TC e/ou PET-CT deve ser seguida de confirmação histológica.
- Na ausência de suspeita de N2, o estadiamento invasivo do mediastino está indicado em tumores centrais, cN1 e tumores > 3cm (MEDIASTINO NORMAL).
- Se disponível, é recomendado iniciar estadiamento invasivo do mediastino com EBUS + EUS, com resultados comparáveis à mediastinoscopia.
- O acréscimo do EUS ao EBUS está associado a aumento de Sensibilidade no estadiamento mediastinal.
- Em caso de EBUS negativo em pacientes com risco elevado de N2 (LN > 10mm e/ou PET+), deve-se realizar mediastinoscopia confirmatória.
- Em caso de EBUS negativo em pacientes com risco intermediário de N2 (tumor central, cN1, tumor > 3cm), a indicação de mediastinoscopia confirmatória é controversa e deve ser ponderada.

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Obrigado

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Parceria:

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