

# Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis

*David E. Ost, MD, MPH; Jiangong Niu, MS; Hui Zhao, PhD; Horia B. Grosu, MD; and Sharon H. Giordano, MD*

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## **e-Appendix 1.**

### **Methods**

SEER and TCR algorithms for determining stage:

We used `dajccstg1` to define AJCC stage, and `dajccm1`, `dajccn1` (2004+) for M0 and N1,N2,N3 stages. We used `dajcct1` to remove T4 patients. So in summary, for all SEER and TCR patients we had detailed information on their complete TNM stage (T1-T3, N1-3, and M0).

Participants and rationale for algorithm criteria

Patients in HMO's were excluded since detailed claims data were required for the analysis.

Patients with known T4 disease were excluded since patients with direct mediastinal invasion on imaging would be at least stage IIIA and lymph node sampling might not be required in such cases.<sup>1-3</sup> In the original and subsequent ACCP lung cancer guidelines, specifically the 2007 version, they describe patterns of mediastinal involvement and lymph node involvement.<sup>3,10,11</sup> When the CT or MRI shows T4 disease in this characteristic pattern staging per se is not required, rather only a tissue diagnosis. The wording in the 2007 guidelines by Detterbeck, et al. is as follows: "...In this case, it does not matter whether tissue is obtained from the primary tumor or from a mediastinal site". In the 2007 ACCP guidelines on invasive staging by Detterbeck, et al., the summary recommendation number 1 is:

For patients with extensive mediastinal infiltration of **tumor** (and no distant metastases), radiographic (CT scan) assessment of the mediastinal stage is usually sufficient without invasive confirmation. Grade of recommendation, 2C

Because staging is mainly relevant for treatment planning patients were only included if they received some form of treatment. Treatment was defined as any chemotherapy, radiation or surgery. The type of treatment received was determined by analyzing CPT codes (e-Table 1).

Test sequencing definitions, categories, and rationale

If mediastinal lymph node sampling was performed on the same day as surgical resection, this was categorized as mediastinal lymph node sampling first. Bronchoscopy without TBNA was considered as a biopsy of the peripheral lesion without mediastinal lymph node sampling. While CT-guided needle biopsy of mediastinal lymph nodes can be performed, this is rarely done since it is associated with a much higher complication rate than EBUS-TBNA and as such it represents an inferior technique. Therefore, CT-guided needle biopsy was considered as inconsistent with guidelines when done as a first procedure.

## Results:

After propensity matching, we compared survival for stage II and III patients, according to whether guideline consistent care was provided (e-Figure 1). Survival was similar whether mediastinal sampling was performed first or later for stage II disease (log-rank test  $p=0.99$ ). For patients with stage III disease patients that had mediastinal sampling done 2<sup>nd</sup> or later lived longer (log-rank test  $p<0.001$ , e-figure 1b). Note that propensity matching did not control for the type of treatment, and there were significant differences between groups in terms of whether surgery was part of the treatment. For stage III patients that had mediastinal sampling performed first, only 32% of guideline consistent care patients had surgery. Conversely, 59% of guideline inconsistent care, mediastinal sampling done 2<sup>nd</sup> or later patients had surgery.

## References:

1. Rivera MP, Mehta AC. Initial Diagnosis of Lung Cancer\*. *Chest*. 2007;132(3 suppl):131S-148S.
2. Detterbeck FC, Jantz MA, Wallace M, Vansteenkiste J, Silvestri GA. Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest*. 2007;132(3 Suppl):202S-220S.
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**e-Table 1. ICD9 and CPT codes for determining diagnostic testing, treatments, and outcomes**

Procedures	ICD-9 Diagnosis Codes	ICD-9 Procedure Codes	CPT/HCPCS codes
Diagnostic Tests			
CT-guided Biopsy			32405, 10022, 10021
Bronch without TBNA			31622, 31623, 31624, 31625, 31627, 31628, 31632, 31645, no 31629
Bronch with TBNA			31629 but no 31620
Bronch with TBNA+EBUS			31629 and 31620 and 31633 for additional nodes
Mediastinotomy or Mediastinoscopy			39000,39010,39220,39400,32662
Endoscopy with ultrasound			43232
Thoracotomy			19272, 31786, 32095, 32100, 32440, 32442, 32445, 32480, 32482, 32484, 32486, 32488, 32500, 32503, 32504, 32520, 32522, 32525, 32602, 32606, 32657, 32662, 32663,38746, 32686, 32096, 32097, 32098, 32505, 32506, 32507, 32601, 32602, 32606, 32607, 32608, 32609, 32657, 32662, 32663, 32666, 32667, 32668, 32669, 32605, 32674, 38746
Complications			
Pneumothorax	512		
Pneumothorax requiring a chest tube	512	34.04	32002,32020
Hemorrhage requiring blood transfusion	998.1	99.03, 99.04	36430
Respiratory failure		96.04 plus 96.7	31500
Treatments			
Radiation Therapy			77371-77373, 77401-77525, 77761-77799, G0251, G0339, G0340, G0174
Chemotherapy			96400 – 96549, J9000 – J9999, Q0083 – Q0085, J8520, J8521, J8530, J8540, J8560, J8597, J8610, J8999; EXCLUDE ALL OF THE FOLLOWING CODES: J9003, J9165, J9175, J9202, J9209, J9212-J9226, J9240, J9395
Surgery			19272, 32440, 32442, 32445, 32480, 32482, 32484, 32486, 32488, 32500, 32503, 32504, 32520, 32522, 32525, 32657, 32662, 32663,38746, 32671, 32670, 32669, 32095, 32096, 32097, 32505, 32506, 32507, 32602, 32607, 32608, 32666, 32667, 32668

**e-Table 2. Surgery codes details and classification**

Code	Description	Major resection: Involves at least segmentectomy, lobectomy, pneumonectomy, tracheal resection or chest wall resection	Wedge resection	Suitable for assessing complications due to diagnosis and/or staging in stage II patients
19272	Excision of chest wall tumor involving ribs	Yes	No	No
31786	Excision of tracheal tumor or carcinoma	Yes	No	No
32098	Thoracotomy with biopsy of pleura	No	No	Yes if not combined with another code involving lung resection
32440	Pneumonectomy	Yes	No	No
32442	Pneumonectomy	Yes	No	No
32445	Pneumonectomy	Yes	No	No
32480	Lobectomy	Yes	No	No
32482	Bilobectomy	Yes	No	No
32484	Segmentectomy	Yes	No	No
32486	Sleeve lobectomy	Yes	No	No
32488	Completion pneumonectomy	Yes	No	No
32500	Wedge resection, single or multiple	No	Yes	Yes if not combined with another code involving lung resection
32503	Resection of apical lung tumor (eg, Pancoast tumor), including chest wall resection, rib(s) resection(s), neurovascular dissection, when performed; without chest wall reconstruction(s)	Yes	No	No
32504	Resection of apical lung tumor (eg, Pancoast tumor), including chest wall resection, rib(s) resection(s), neurovascular dissection, when performed; with chest wall reconstruction	Yes	No	No
32520	Resection of lung with resection of chest wall	Yes	No	No
32525	Resection of lung with reconstruction chest wall without prosthesis	Yes	No	No
32605	Thoracoscopy, diagnostic mediastinal space without biopsy	No	No	Yes if not combined with another code involving lung resection

32606	Thoracoscopy, diagnostic mediastinal space with biopsy	No	No	Yes if not combined with another code involving lung resection
32609	Thoracoscopy, diagnostic with biopsy of pleura	No	No	Yes if not combined with another code involving lung resection
32657	Thoracoscopy, wedge resection, single or multiple	No	Yes	Yes if not combined with another code involving lung resection
32662	Thoracoscopy, surgical; with excision of mediastinal cyst, tumor, or mass	Yes	No	No
32663	Thoracoscopy, surgical; with lobectomy (single lobe)	Yes	No	No
38746	Thoracic lymphadenectomy by thoracotomy, mediastinal and regional lymphadenectomy	No	No	Yes if not combined with another code involving lung resection
32671	Thoracoscopy with pneumonectomy	Yes	No	No
32670	Thoracoscopy with bilobectomy	Yes	No	No
32669	Thoracoscopy with segmentectomy	Yes	No	No
32095	Thoracotomy limited for biopsy of lung or pleura, (wedge incisional)	Yes	No	No
32096	Thoracotomy with dx bx of lung infiltrates, wedge, incisional	Yes	No	No
32097	Thoracotomy with dx bx of lung nodule or masses, wedge, incisional	Yes	No	No
32505	Thoracotomy with therapeutic wedge, initial	No	Yes	Yes if not combined with another code involving lung resection
32506	Thoracotomy with therapeutic wedge resection (nodule or mass), each additional resection, ipsilateral, list in addition to primary code	No	Yes	Yes if not combined with another code involving lung resection
32507	Thoracotomy with diagnostic wedge followed by anatomic lung resection (list in addition to primary code: 32440, 32442, 32445, 32484, 32488, 32503, 32504)	Yes	No	No
32602	Thoracoscopy, diagnostic, lungs and pleural space	No	No	Yes if not combined with another code involving lung resection



32607	Thoracoscopy, with dx biopsies of infiltrates (wedge, incisional, unilateral)	No	No	Yes if not combined with another code involving lung resection
32608	Thoracoscopy, with dx bx of lung nodules or masses, unilateral	No	No	Yes if not combined with another code involving lung resection
32666	Therapeutic wedge resection, initial unilateral	No	No	Yes if not combined with another code involving lung resection
32667	Therapeutic wedge resection, each addition resection, ipsilateral	Yes	No	No
32668	Thoracoscopy with wedge resection, diagnostic wedge followed by anatomic lung resection	Yes	No	No
32100	Thoracotomy with exploration and biopsy	No	No	Yes if not combined with another code involving lung resection
32522	Remove lung & revise chest	Yes	No	No
32601	Thoracoscopy, diagnostic (separate procedure); lungs, pericardial sac, mediastinal or pleural space, without biopsy	No	N	Yes if not combined with another code where this column says No
32674	with mediastinal and regional lymphadenectomy (List separately in addition to code for primary procedure)	No	No	Yes if not combined with another code where this column says No

**e-Table 3. Patient characteristics of propensity score matched cohorts**

<b>Variables</b>	<b>Evaluation consistent with guidelines, mediastinal sampling done first</b>	<b>Evaluation inconsistent with guidelines, mediastinal sampling performed on the 2<sup>nd</sup> or later biopsy</b>	<b>Total</b>	<b>p value</b>
	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	
All subjects	3048 (100)	3048 (100)	6096 (100)	
Age				0.925
66-70	1036 (34)	1058 (34.7)	2094 (34.4)	
71-75	934 (30.6)	924 (30.3)	1858 (30.5)	
76-80	689 (22.6)	689 (22.6)	1378 (22.6)	
>80	389 (12.8)	377 (12.4)	766 (12.6)	
Gender				0.898
Female	1476 (48.4)	1481 (48.6)	2957 (48.5)	
Male	1572 (51.6)	1567 (51.4)	3139 (51.5)	
Race				0.979
Non-Hispanic White	2609 (85.6)	2604 (85.4)	5213 (85.5)	
Hispanic	134 (4.4)	141 (4.6)	275 (4.5)	
Non-Hispanic Black	198 (6.5)	196 (6.4)	394 (6.5)	
Non-Hispanic Other	107 (3.5)	107 (3.5)	214 (3.5)	
Year of Diagnosis				0.990
2004	268 (8.8)	268 (8.8)	536 (8.8)	
2005	319 (10.5)	314 (10.3)	633 (10.4)	
2006	306 (10)	308 (10.1)	614 (10.1)	
2007	312 (10.2)	330 (10.8)	642 (10.5)	
2008	334 (11)	307 (10.1)	641 (10.5)	
2009	314 (10.3)	314 (10.3)	628 (10.3)	
2010	283 (9.3)	285 (9.4)	568 (9.3)	
2011	279 (9.2)	282 (9.3)	561 (9.2)	
2012	332 (10.9)	325 (10.7)	657 (10.8)	
2013	301 (9.9)	315 (10.3)	616 (10.1)	
SEER/TCR Region				0.997
California	530 (17.4)	538 (17.7)	1068 (17.5)	
Connecticut	174 (5.7)	181 (5.9)	355 (5.8)	
Detroit	194 (6.4)	186 (6.1)	380 (6.2)	
Georgia	387 (12.7)	387 (12.7)	774 (12.7)	
Hawaii	22 (0.7)	26 (0.9)	48 (0.8)	
Iowa	132 (4.3)	131 (4.3)	263 (4.3)	
Kentucky	230 (7.6)	241 (7.9)	471 (7.7)	

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Louisiana	115 (3.8)	115 (3.8)	230 (3.8)	
New Jersey	430 (14.1)	404 (13.3)	834 (13.7)	
New Mexico	33 (1.1)	27 (0.9)	60 (1)	
Seattle	144 (4.7)	148 (4.9)	292 (4.8)	
Texas	631 (20.7)	641 (21)	1272 (20.9)	
Utah	26 (0.9)	23 (0.8)	49 (0.8)	
Comorbidities				0.477
0	1325 (43.5)	1372 (45)	2697 (44.2)	
1	988 (32.4)	964 (31.6)	1952 (32)	
2+	735 (24.1)	712 (23.4)	1447 (23.7)	
T stages				0.747
T0/T1	944 (31)	936 (30.7)	1880 (30.8)	
T2	1649 (54.1)	1666 (54.7)	3315 (54.4)	
T3	260 (8.5)	272 (8.9)	532 (8.7)	
Unknown	195 (6.4)	174 (5.7)	369 (6.1)	
N stages				0.905
N1	962 (31.6)	949 (31.1)	1911 (31.4)	
N2	1846 (60.6)	1863 (61.1)	3709 (60.8)	
N3	240 (7.9)	236 (7.7)	476 (7.8)	
Cancer type				0.911
NSCLC	2879 (94.5)	2881 (94.5)	5760 (94.5)	
Small cell	169 (5.5)	167 (5.5)	336 (5.5)	

NSCLC: Non-small cell lung cancer

**e-Table 4. Procedure utilization and incidence of complications per procedure in patients with mediastinal sampling done**

Invasive diagnostic test and associated complications	Mediastinal Sampling done as 1st test				Mediastinal Sampling done as 2nd test or later			
	TBNA/ EBUS	Surgical	Frequency of test use p-value‡	Incidence of complication s p-value*	TBNA/ EBUS	Surgical	Frequency of test use p-value‡	Incidence of complications p-value*
	N	N			N	N		
Total Patients	2140	1904			502	3752		
Procedures								
CT guided biopsy (%)†	324 (15)	68 (4)	<0.001		380 (76)	2791 (74)	0.1953	
Complications within 1d								
Pneumothorax, n (%)*	62 (19)	16 (24)		0.407	75 (20)	713 (26)		0.014
Pneumothorax requiring chest tube, n (%)*	11 (3)	<11(<16 )		0.718	11 (3)	140 (5)		0.072
Hemorrhage, n (%)*	<11 (<3)	0 (0)		1.00	<11 (<3)	30 (1)		1.00
Respiratory failure, n (%)*	<11 (<3)	<11 (<16)		0.317	<11 (<3)	<11 (<0.4)		.318
Bronch without TBNA (%)†	79 (4)	22 (1)	<0.001		286 (57)	1938 (52)	0.7013	
Complications within 1d								
Pneumothorax, n (%)	<11 (<14)	0 (0)		0.342	11 (4)	49 (3)		0.237
Pneumothorax requiring chest tube, n (%)	<11 (<14)	0 (0)		1.00	<11 (<4)	<11 (<1)		0.660
Hemorrhage, n (%)	<11 (<14)	0 (0)		1.00	<11 (<4)	23 (1)		0.352
Respiratory failure, n (%)	<11 (<14)	0 (0)		1.00	<11 (<4)	11 (1)		0.679



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Bronch with TBNA (%)†	2383 (111)	<11 (<0.6)	<0.001		521 (104)	<11 (<0.3)	<0.001	
Complications within 1d								
Pneumothorax, n (%)	39 (2)	<11		0.155	<11 (<2)	0 (0)		1.00
Pneumothorax requiring chest tube, n (%)	<11 (<0.5)	<11		0.041	<11 (<2)	0 (0)		1.00
Hemorrhage, n (%)	17 (1)	0 (0)		1.00	<11 (<2)	0 (0)		1.00
Respiratory failure, n (%)	25 (1)	0 (0)		1.00	<11 (<2)	0 (0)		1.00
Mediastinoscopy alone (no thoracotomy) (%)†	200 (9)	1028 (5)	<0.001		34 (7)	1397 (37)	<0.001	
Complications within 14d								
Pneumothorax, n (%)	14 (7)	51 (5)		0.230	<11 (<32)	81 (6)		0.718
Pneumothorax requiring chest tube, n (%)	0 (0)	<11 (<1)		0.367	0 (0)	<11 (<0.8)		1.00
Hemorrhage, n (%)	<11 (<6)	12 (1)		0.024	<11 (<32)	44 (3)		1.00
Respiratory failure, n (%)	11 (6)	<11 (<1)		<0.001	0 (0)	22 (2)		1.00
Thoracotomy (%)†	322 (15)	1205 (6)	<0.001		91 (18)	2938 (78)	<0.001	
Complications within 14 d								
Hemorrhage, n (%)	20 (6)	68 (6)		0.687	<11 (<12)	142 (5)		0.322
Respiratory failure, n (%)	11 (3)	38 (3)		0.859	<11 (<12)	110 (4)		0.259

† Strata with 10 or less patients were suppressed as per National Cancer Institute policy and are reported as "< 11" to ensure confidentiality. . \* Fisher's exact test p-value comparing complication rates between TBNA/EBUS and surgical groups. † p-value using chi-square test compares the frequency of testing utilization between groups on a per patients basis.

**e-Figure 1.** Survival in patients with NSCLC according to stage and diagnostic strategy after propensity matching. A) Patients with stage II NSCLC. B) Patients with stage III NSCLC. Diagnostic strategy is shown for each stage as follows: guideline consistent care with mediastinal sampling performed first (solid blue line), guideline inconsistent care with mediastinal sampling performed 2<sup>nd</sup> or later (solid red line). For figure 1B, log-rank p-value <0.001.

