Appendix A. Search Strategy

Search Strategies

The strategy below is presented in EMBASE syntax; the search was simultaneously conducted across EMBASE and MEDLINE. A similar strategy was used to search the databases comprising the Cochrane Library, and PubMed.

EMBASE/MEDLINE (2000–2014)

Set Number	Concept	Search Statement
1	Small cell lung cancer	'small cell lung carcinoma'/exp OR 'small cell lung carcinoma' OR 'carcinoma small cell'/exp OR 'carcinoma small cell' OR 'lung small cell cancer':de
2		'small-cell lung cancer' OR 'small cell lung cancer' OR 'oat cell' OR sclc
3		#1 OR #2
4		#3 NOT ('non-small cell':ti OR 'non-small-cell':ti OR 'non small cell':ti OR 'nonsmall cell':ti OR nsclc:ti)
5	Lung Symptoms	'lung disease'/mj OR 'lung tumor'/mj
6		lung*:ti OR pulmonary:ti OR bronch*:ti OR chest:ti AND (age*:ab,ti OR smok*:ab,ti OR symptom*:ab,ti OR wheez*:ab,ti OR cough*:ab,ti OR edema:ab,ti OR fibrosis:ab,ti OR asthma:ab,ti OR 'shortness of breath':ab,ti OR pain*:ab,ti OR nodule*:ab,ti)
7		#5 OR #6
8		#7 NOT ('non-small cell':ti OR 'non-small-cell':ti OR 'non small cell':ti OR 'nonsmall cell':ti OR nsclc:ti)
9	Imaging	'computer assisted tomography'/exp OR 'emission tomography'/de OR 'nuclear magnetic resonance imaging'/exp OR 'diagnostic imaging'/exp OR 'tomography'/de OR 'respiratory-gated imaging' OR ‘bone scintiscanning’
10		pet NEXT/1 ct OR sdct:ab,ti OR mdct:ab,ti OR mri:ab,ti OR ct:ab,ti OR cat:ab,ti OR pet:ab,ti OR fdg NEAR/1 pet OR 'computed tomography':ab,ti OR 'positron emission':ab,ti OR 'magnetic resonance':ab,ti OR multislice:ab,ti OR 'multi slice':ab,ti OR bone NEXT/2 scan*
11		'endosonography'/exp OR 'endosonography' OR 'eus' OR endoscop* NEXT/1 (ultrasound OR ultrasonography* OR echograph*)
12		'endobronchial ultrasonography'/exp OR 'endobronchial echography' OR 'endobronchial ultrasound' OR ‘ebus’/exp OR 'ebus' OR endobronch* NEXT/1 (ultrasound OR ultrasonography* OR echograph*)
13		#9 OR #10 OR #11 OR #12
14	Pretreatment staging and planning	'cancer classification'/mj OR 'cancer classification' OR 'cancer staging'/exp OR cancer NEAR/2 stag*
15		(cancer OR tumor* OR tumour* OR mass* OR neoplasm*) NEAR/2 (stage OR staging OR class*)
16		‘pre-treatment’:ab,ti OR pretreatment:ab,ti OR ‘pretreatment’ NEXT/2 staging OR ‘pre-treatment’ NEXT/2 plan*
17		#14 OR #15 OR #16
18	Prognosis	cancer prognosis'/exp OR 'cancer prognosis' OR prognos* OR predict* OR outcome* OR 'survival'/de OR survival OR 'quality of life'/de OR 'quality of life' OR qol
19	Combine Small Cell Lung Cancer AND Imaging	#4 AND #13

EMBASE/MEDLINE (2000–2014) (continued)

Set Number	Concept	Search Statement
20	Combine Lung Symptoms AND Imaging	#8 AND #13
21	Combine SCLC AND Imaging AND Pretreatment staging and planning (KQ 1)	#17 AND #19
22	Combine Lung Symptoms AND Imaging AND Pretreatment staging and planning (KQ 1)	#17 AND #20
23	Combine SCLC AND Imaging AND Pretreatment staging and planning AND prognosis (KQ 2)	#17 AND #18 AND #19
24	Combine Lung Symptoms AND Imaging AND Pretreatment staging and planning AND prognosis (KQ 2)	#17 AND #18 AND #20
25	Combine final sets	#21 OR #22 OR #23 OR #24
26	Apply limits	#25 AND [humans]/lim AND [2000-2014]/py
27	Limit by publication and study type	#26 AND ('clinical article'/exp OR 'clinical article' OR 'clinical trial'/exp OR 'clinical trial' OR 'controlled study'/exp OR 'controlled study' OR 'intermethod comparison'/exp OR 'intermethod comparison' OR 'major clinical study'/exp OR 'major clinical study' OR 'retrospective study'/exp OR 'retrospective study')
28	Guidelines	#26 AND ('practice guideline'/exp OR 'practice guideline' OR 'professional standard':de OR 'practice parameter' OR 'position statement' OR 'position paper' OR 'policy statement' OR standard*:ti OR guideline*:ti OR 'white paper' OR 'clinical pathway'/exp OR 'clinical pathway' OR 'clinical guideline' OR 'consensus development'/exp OR 'consensus development')
29	Systematic Reviews	#26 AND ('research synthesis' OR pooled OR 'systematic review'/de OR 'meta analysis'/de OR ('evidence base' OR 'evidence based' OR methodol* OR systematic OR quantitative* OR studies OR search* AND ('review'/de OR review/it)))
30	Remove unwanted publication types	#26 NOT ('conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'case report'/de)
31	Combine final sets	#27 OR #28 OR #29 OR #30

EMBASE.com Syntax:

*	=	truncation character (wildcard)
NEAR/*n*	=	search terms within a specified number (*n*) of words from each other in any order
NEXT/*n*	=	search terms within a specified number (*n*) of words from each other in the order specified
/	=	search as a subject heading
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
mj	=	denotes a term that has been searched as a major subject heading
:de	=	search in the descriptors field
:lnk	=	floating subheading
:it,pt.	=	source item or publication type
:ti.	=	limit to title
:ti,ab.	=	limit to title and abstract fields

PUBMED (PreMEDLINE)

Set Number	Concept	Search Statement
1	Small cell lung cancer	(('small-cell' OR 'small cell') AND (lung OR bronch*)) OR 'oat cell' OR sclc
2		2 NOT ('non-small cell'[ti] OR 'non-small-cell'[ti] OR 'non small cell'[ti] OR 'nonsmall cell'[ti] OR nsclc[ti])
3	Lung Symptoms	(lung*[ti] OR pulmonary[ti] OR bronch*[ti] OR chest[ti]) AND (age* OR smok* OR symptom* OR wheez* OR cough* OR edema OR fibrosis OR asthma OR 'shortness of breath' OR pain* OR nodule*)
4	Imaging	sdct OR mdct OR mri OR ct OR (cat AND scan*) OR pet OR (fdg AND pet) OR 'computed tomography' OR 'positron emission' OR 'magnetic resonance' OR 'multislice' OR 'multi slice' OR "bone scan" OR "bone scintigraphy" OR (bone AND scan*)
5		'endosonography' OR 'eus' OR (endoscop* AND (ultrasound OR ultrasonography* OR echograph*))
6		'endobronchial echography' OR 'endobronchial ultrasound' OR 'ebus' OR (endobronch* AND (ultrasound OR ultrasonography* OR echograph*))
7		#4 OR #5 OR #6
8	Pretreatment staging and planning	(cancer OR tumor* OR tumour* OR mass* OR neoplasm*) AND (stage OR staging OR class*)
9		(cancer[tiab] OR neoplasm[tiab] OR tumor*[tiab] OR tumour*[tiab]) AND (care[tiab] OR treatment[tiab] OR therapy[tiab] OR pretreatment[tiab] OR 'pre-treatment'[tiab] OR plan[tiab])
10		#8 OR #9
11	Prognosis	'cancer prognosis' OR prognos* OR predict* OR outcome* OR survival OR 'quality of life' OR qol
12	Combine SCLC OR Lung Symptoms	#2 OR #3
13	Combine SCLC OR Lung Symptoms with imaging	#7 AND #12
14	Combine SCLC OR Lung Symptoms with imaging and pretreatment planning	#10 AND #13
15	Combine with prognosis	#11 AND #14
16	In process	#15 AND (pubmednotmedline[sb] OR inprocess[sb] OR [publisher[sb])
17	English	#16 AND English[la]

PubMed Syntax:

* = truncation character (wildcard)

[ti] = limit to title field

[tiab] = limit to title and abstract fields

[tw] = text word

Appendix B. List of Excluded Full Articles

Alatas F, Dundar E, Yildirim H, et al. Role of real-time endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis and mediastinal staging of lung cancer. Turk Klin J Med Sci. 2012;32(2):407-14. PMID: ***One test of interest, but no data on SCLC staging accuracy.***

Al-Kadi OS, Watson D. Texture analysis of aggressive and nonaggressive lung tumor CE CT images. IEEE Trans Biomed Eng. 2008 Jul;55(7):1822-30. PMID: 18595800. ***Unclear whether any patients had SCLC.***

Allen-Auerbach M, Yeom K, Park J, et al. Standard PET/CT of the chest during shallow breathing is inadequate for comprehensive staging of lung cancer. J Nucl Med. 2006 Feb 1;47(2):298-301. PMID: 16455636. ***Not SCLC.***

An YS, Sheen SS, Oh YJ, et al. Nonionic intravenous contrast agent does not cause clinically significant artifacts to 18F-FDG PET/CT in patients with lung cancer. Ann Nucl Med. 2007 Dec;21(10):585-92. Epub 2007 Dec 25. PMID: 18092135. ***Fewer than 10 patients with SCLC.***

Anantham D, Koh MS. Endobronchial Ultrasound-guided Tranbronchial Needle Aspiration (EBUS-TBNA) in the diagnosis and staging of lung cancer. Chin J Lung Cancer. 2010 May;13(5):418-23. PMID: 20677635. ***Not a study (e.g., review, opinion).***

Andrade RS, Groth SS, Rueth NM, et al. Evaluation of mediastinal lymph nodes with endobronchial ultrasound: the thoracic surgeon's perspective. J Thorac Cardiovasc Surg. 2010 Mar;139(3):578-83. PMID: ***Fewer than 10 patients with SCLC.***

Annema JT, Versteegh MI, Veselic M, et al. Endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of lung cancer and its impact on surgical staging. J Clin Oncol. 2005;23(33):8357-61. PMID: 16219935. ***No separate SCLC data.***

Aquino SL, Fischman AJ. Does whole-body 2-[18F]-fluoro-2-deoxy-D-glucose positron emission tomography have an advantage over thoracic positron emission tomography for staging patients with lung cancer? Chest. 2004 Sep;126(3):755-60. PMID: 15364753. ***Not SCLC.***

Araz O, Demirci E, Ucar EY, et al. Roles of Ki-67, p53, transforming growth factor-β and lysyl oxidase in the metastasis of lung cancer. Respirology. 2014 Oct;19(7):1034-9. Epub 2014 Jul 3. PMID: 24995672. ***One test of interest, but no data on SCLC staging accuracy.***

Ardengh JC, Bammann RH, de Giovani M, et al. Endoscopic ultrasound-guided biopsies for mediastinal lesions and lymph node diagnosis and staging. Clinics. 2011;66(9):1579-83. PMID: 22179163. ***Fewer than 10 patients with SCLC.***

Arslan N, Tuncel M, Kuzhan O, et al. Evaluation of outcome prediction and disease extension by quantitative 2-deoxy-2-[18F] fluoro-D-glucose with positron emission tomography in patients with small cell lung cancer. Ann Nucl Med. 2011 Jul;25(6):406-13. PMID: 21409347. ***One test of interest, but no data on SCLC staging accuracy.***

Azad A, Chionh F, Scott AM, et al. High impact of 18F-FDG-PET on management and prognostic stratification of newly diagnosed small cell lung cancer. Mol Imaging Biol. 2010 Aug;12(4):443-51. PMID: 19921339. ***None of the modalities of interest.***

Bae W, Kim H, Kim YA, et al. Diagnostic concordance rate between histologic and cytologic specimens of endobronchial ultrasound-guided transbronchial needle aspiration in lung cancer: a single institution experience. Thorac Cancer. 2014 Mar;5(2):174-8. PMID: ***No separate SCLC data.***

Bayrak SB, Ceylan E, Serter M, et al. The clinical importance of bone metabolic markers in detecting bone metastasis of lung cancer. Int J Clin Oncol. 2012 Apr;17(2):112-8. PMID: 21691728. ***None of the modalities of interest.***

Bayram N, Borekci S, Uyar M, et al. Transbronchial needle aspiration in the diagnosis and staging of lung cancer. Indian J Chest Dis Allied Sci. 2008 Jul-Sep;50(3):273-6. PMID: 18630793. ***Fewer than 10 patients with SCLC.***

Behrendt FF, Temur Y, Verburg FA, et al. PET/CT in lung cancer: Influence of contrast medium on quantitative and clinical assessment. Eur Radiol. 2012 Nov;22(11):2458-64. Epub 2012 Jun 4. http://dx.doi.org/10.1007/s00330-012-2515-1. PMID: 22661058. ***Unclear whether any patients had SCLC.***

Benveniste H, Zhang S, Reinsel RA, et al. Brain metabolomic profiles of lung cancer patients prior to treatment characterized by proton magnetic resonance spectroscopy. Int J Clin Exp Med. 2012;5(2):154-64. PMID: 22567176. ***Not SCLC.***

Biersack HJ, Bender H, Ruhlmann J, et al. Clinical PET in oncology. Rev Esp Med Nucl. 2000 Jun 1;19(3):219-24. PMID: ***Not SCLC.***

Bilaceroglu S, Chhajed P, Mavis A, et al. Computed tomography-guided transthoracic needle aspiration in diagnosing and staging hilar and mediastinal masses of lung cancer after negative bronchoscopy. J Bronchol. 2007 Jul;14(3):149-55. PMID: ***None of the modalities of interest.***

Block MI. Transition from mediastinoscopy to endoscopic ultrasound for lung cancer staging. Ann Thorac Surg. 2010 Mar;89(3):885-90. PMID: 20172149. ***Fewer than 10 patients with SCLC.***

Blum R, MacManus MP, Rischin D, et al. Impact of positron emission tomography on the management of patients with small-cell lung cancer: preliminary experience. Am J Clin Oncol. 2004 Apr;27(2):164-71. PMID: 15057156. ***None of the modalities of interest.***

Bocchino M, Valente T, Somma F, et al. Detection of skeletal muscle metastases on initial staging of lung cancer: a retrospective case series. Jpn J Radiol. 2014 Mar;32(3):164-71. PMID: 24452325. ***Fewer than 10 patients with SCLC.***

Bolton WD, Johnson R, Banks E, et al. Utility and accuracy of endobronchial ultrasound as a diagnostic and staging tool for the evaluation of mediastinal adenopathy. Surg Endosc. 2013 Apr;27(4):1119-23. PMID: 23239294. ***Fewer than 10 patients with SCLC.***

Bradley JD, Dehdashti F, Mintum MA, et al. Positron emission tomography in limited-stage small-cell lung cancer: a prospective study. J Clin Oncol. 2004;22(16):3248-54. PMID: 15310768. ***One test of interest, but no data on SCLC staging accuracy.***

Brakel K, Van Overhagen H, Heijenbrok MW, et al. Detection and diagnosis of supraclavicular lymph node metastases in patients with symptoms of lung cancer by palpation, ultrasound and CT. Nederlands Tijdschrift Voor Geneeskunde. 2005 Jan 22;149(4):189-95. PMID: ***No separate SCLC data.***

Buchbender C, Hartung-Knemeyer V, Beiderwellen K, et al. Diffusion-weighted imaging as part of hybrid PET/MRI protocols for whole-body cancer staging: does it benefit lesion detection? Eur J Radiol. 2013 May;82(5):877-82. Epub 2013 Feb 18. PMID: 23428414. ***Not SCLC.***

Buck AK, Herrmann K, Schreyogg J, et al. PET/CT for staging lung cancer: costly or cost-saving? Eur J Nucl Med Mol Imaging. 2011 May;38(5):799-801. Epub 2011 Mar 26. PMID: 21442260. ***Not a study (e.g., review, opinion).***

Bugalho A, Ferreira D, Barata R, et al. Endobronchial ultrasound-guided transbronchial needle aspiration for lung cancer diagnosis and staging in 179 patients. Rev Port Pneumol. 2013 Sep/Oct;19(5):192-9. PMID: 23850376. ***Fewer than 10 patients with SCLC.***

Chan WL, Freund J, Pocock NA, et al. Coincidence detection FDG PET in the management of oncological patients: attenuation correction versus non-attenuation correction. Nucl Med Commun. 2001;22(11):1185-92. PMID: ***Not SCLC.***

Chin R Jr, McCain TW, Miller AA, et al. Whole body FDG-PET for the evaluation and staging of small cell lung cancer: a preliminary study. 2002;37(1):1-6. PMID: 12057859. ***One test of interest, but no data on SCLC staging accuracy.***

Cho AR, Lim I, Na II, et al. Evaluation of adrenal masses in lung cancer patients using F-18 FDG PET/CT. Nucl Med Mol Imaging. 2011 Mar;45(1):52-8. PMID: ***Fewer than 10 patients with SCLC.***

Chong S, Lee KS, Kim BT, et al. Integrated PET/CT of pulmonary neuroendocrine tumors: diagnostic and prognostic implications. AJR Am J Roentgenol. 2007 May;188(5):1223-31. PMID: 17449764. ***One test of interest, but no data on SCLC staging accuracy.***

Chooi WK, Matthews S, Bull MJ, et al. Multislice computed tomography in staging lung cancer: the role of multiplanar image reconstruction. J Comput Assist Tomogr. 2005 May/Jun;29(3):357-60. PMID: 15891507. ***Unclear whether any patients had SCLC.***

Chou PC, Lin SM, Lo CY, et al. Endobronchial mucosa invasion predicts survival in patients with small cell lung cancer. PLoS ONE. 2012 Oct 4;7(10):e47613. Epub 2012 Oct 4. PMID: 23056644. ***No outcomes of interest.***

Claessens NJ, Maas KW, Kummer JA, et al. [Lung cancer staging by endobronchial ultrasound with transbronchial needle aspiration]. Nederlands Tijdschrift Voor Geneeskunde. 2012;156(46);A4741. PMID: 23151327. ***Other: Full article no obtainable.***

Cucuruz B, Dango S, Jurinovic V, et al. MAGE qPCR improves the sensitivity and accuracy of EBUS-TBNA for the detection of lymphatic cancer spread. J Thorac Oncol. 2012 Apr;7(4):690-7. PMID: 22237266. ***Fewer than 10 patients with SCLC.***

Cullen JP, Glynn C, Murtagh E, et al. Auditing a new lung cancer service. Ir Med J. 2004 Oct;97(9):281-3. PMID: 15568588. ***No separate SCLC data.***

Dane F, Turk HM, Sevinc A, et al. The markers of bone turnover in patients with lung cancer. J Natl Med Assoc. 2008 Apr;100(4):425-8. PMID: 18481482. ***No outcomes of interest.***

Dango S, Cucuruz B, Mayer O, et al. Detection of disseminated tumour cells in mediastinoscopic lymph node biopsies and endobronchial ultrasonography-guided transbronchial needle aspiration in patients with suspected lung cancer. 2010 Jun;68(3):383-8. PMID: 19733415. ***One test of interest, but no data on SCLC staging accuracy.***

Debevec L, Erzen J, Debeljak A, et al. Exploratory thoracotomy and its influence on the survival of patients with lung cancer. Wiener Klinische Wochenschrift. 2006 Aug;118(15):479-84. PMID: 16957979. ***Fewer than 10 patients with SCLC.***

DeLappe E, Dunphy M. 18F-2-Deoxy-d-Glucose positron emission tomography-computed tomography in lung cancer. Semin Roentgenol. 2011 Jul;46(3):208-23. PMID: 21726705. ***Not a study (e.g., review, opinion).***

Delattre C, Fournier C, Bouchindhomme B, et al. Endoscopic ultrasound guided transbronchial fine needle aspiration: a French Department of Pathology's 4-year experience. J Clin Pathol. 2011 Dec;64(12):1117-22. Epub 2011 Sep 30. PMID: 21965831. ***No separate SCLC data.***

Dubey S, Powell CA. Update in lung cancer 2006. Am J Respir Crit Care Med. 2007 May 1;175(9):868-74. PMID: 17446343. ***Not a study (e.g., review, opinion).***

Evison M, Crosbie PA, Martin J, et al. EBUS-TBNA in elderly patients with lung cancer: safety and performance outcomes. J Thorac Oncol. 2014 Mar;9(3):370-6. PMID: 24518088. ***No separate SCLC data.***

Farjah F, Flum DR, Ramsey SD, et al. Multi-modality mediastinal staging for lung cancer among medicare beneficiaries. J Thorac Oncol. 2009 Mar;4(3):355-63. PMID: 19156000. ***Not SCLC.***

Feller-Kopman D, Yung RC, Burroughs F, et al. Cytology of endobronchial ultrasound-guided transbronchial needle aspiration: a retrospective study with histology correlation. Cancer Cytopathol. 2009 Dec 25;117(6):482-90. PMID: 19834962. ***Fewer than 10 patients with SCLC.***

Flechsig P, Kratochwil C, Schwartz LH, et al. Quantitative volumetric CT-histogram analysis in N-staging of 18F-FDG-equivocal patients with lung cancer. J Nucl Med. 2014 Apr 1;55(4):559-64. Epub 2014 Feb 13. PMID: 24525209. ***Fewer than 10 patients with SCLC.***

Fournel P. Criteria of choice for 1(st) line CT. Rev Pneumol Clin. 2004 Nov;60(5). PMID: 15687986. ***Not SCLC.***

Fujiwara T, Yasufuku K, Nakajima T, et al. The utility of sonographic features during endobronchial ultrasound-guided transbronchial needle aspiration for lymph node staging in patients with lung cancer: a standard endobronchial ultrasound image classification system. Chest. 2010 Sep 1;138(3):641-7. PMID: 20382710. ***No separate SCLC data.***

Fusaroli P, Caletti G. Endoscopic ultrasonography. Endoscopy. 2007 Jan;39(1):17-20. PMID: 17252454. ***Not a study (e.g., review, opinion).***

Garcia-Olive I, Monso E, Andreo F, et al. Sensitivity of linear endobronchial ultrasonography and guided transbronchial needle aspiration for the identification of nodal metastasis in lung cancer staging. Ultrasound Med Biol. 2009 Aug;35(8):1271-7. PMID: 19540652. ***No separate SCLC data.***

Go SI, Song HN, Kang JH, et al. The clinical impact of the sum of the maximum standardized uptake value on the pretreatment with F-FDG-PET/CT in small-cell lung cancer. Oncology. 2014 Jan;86(1):1-9. Epub 2013 Dec 10. PMID: 24335538. ***One test of interest, but no data on SCLC staging accuracy.***

Gomez DR, Gladish GW, Wei X, et al. Prognostic value of positron emission tomography/computed tomography findings in limited-stage small cell lung cancer before chemoradiation therapy. Am J Clin Oncol. 2014 Feb;37(1):77-80. PMID: ***One test of interest, but no data on SCLC staging accuracy.***

Graeter TP, Hellwig D, Hoffmann K, et al. Mediastinal lymph node staging in suspected lung cancer: comparison of positron emission tomography with F-18-fluorodeoxyglucose and mediastinoscopy. Ann Thorac Surg. 2003 Jan 1;75(1):231-6. PMID: 12537221. ***Fewer than 10 patients with SCLC.***

Grahek D, Tofighi M, Montravers F, et al. 18FDG CDET in staging of lung cancer. Med Nucl. 2000;24(2):99-106. PMID: ***Fewer than 10 patients with SCLC.***

Gregory DL, Brennan SM, Stillie A, et al. Impact of 18F-fluorodeoxyglucose positron emission tomography in the staging and treatment response assessment of extra-pulmonary small-cell cancer. J Med Imaging Radiat Oncol. 2010 Apr;54(2):100-7. PMID: ***Not SCLC.***

Halter G, Buck AK, Schirrmeister H, et al. Lymph node staging in lung cancer using [18F]FDG-PET. Thorac Cardiovasc Surg. 2004 Apr;52(2):96-101. PMID: 15103582. ***Not SCLC.***

Halter G, Buck AK, Schirrmeister H, et al. [18F] 3-deoxy-3'-fluorothymidine positron emission tomography: alternative or diagnostic adjunct to 2-[18f]-fluoro-2-deoxy-D-glucose positron emission tomography in the workup of suspicious central focal lesions? J Thorac Cardiovasc Surg. 2004 Apr;127(4):1093-9. PMID: 15052207. ***Fewer than 10 patients with SCLC.***

Han TJ, Kim HJ, Wu HG, et al. Comparison of treatment outcomes between involved-field and elective nodal irradiation in limited-stage small cell lung cancer. Jpn J Clin Oncol. 2012 Oct;42(10):948-54. PMID: 22811409. ***Other: Did not separate data of standalone PET patients from PET/CT patients.***

Harders SW. Lucis: Lung Cancer Imaging Studies. Dan Med J. 2012;59(11):1-30. PMID: ***Not a study (e.g., review, opinion).***

Hashizume T, Yamada K, Suzuki R, et al. Correlation between clinical characteristics, radiological findings, pathological findings, and prognosis in patients with a peripheral lung adenocarcinoma less than 15 mm in diameter. Jpn J Lung Cancer. 2005 Aug;45(4):311-7. PMID: ***Not SCLC.***

Hattori A, Suzuki K, Maeyashiki T, et al. The presence of air bronchogram is a novel predictor of negative nodal involvement in radiologically pure-solid lung cancer. Eur J Cardiothorac Surg. 2014 Apr;45(4):699-702. PMID: 24135955. ***Not SCLC.***

Hattori A, Suzuki K, Matsunaga T, et al. Tumour standardized uptake value on positron emission tomography is a novel predictor of adenocarcinoma in situ for c-Stage IA lung cancer patients with a part-solid nodule on thin-section computed tomography scan. Interact Cardiovasc Thorac Surg. 2014 Mar;18(3):329-34. PMID: ***Not SCLC.***

Hauber HP, Bohuslavizki KH, Lund CH, et al. Positron emission tomography in the staging of small-cell lung cancer: a preliminary study. Chest. 2001;119(3):950-4. PMID: 11243980. ***Fewer than 10 patients with SCLC.***

Henschke CI, Yankelevitz DF, Miettinen OS. Computed tomographic screening for lung cancer: the relationship of disease stage to tumor size. Arch Intern Med. 2006 Feb 13;166(3):321-5. PMID: 16476872. ***One test of interest, but no data on SCLC staging accuracy.***

Herth FJ, Becker HD, Ernst A, et al. Ultrasound-guided transbronchial needle aspiration: an experience in 242 patients. Chest. 2003 Feb 1;123(2):604-7. PMID: 12576386. ***No separate SCLC data.***

Herth FJF, Krasnik M, Vilmann P. EBUS-TBNA for the diagnosis and staging of lung cancer. Endoscopy. 2006 Jun;38 Suppl 1:S101-5. PMID: 16802239. ***Not a study (e.g., review, opinion).***

Herth FJF, Schuler H, Gompelmann D, et al. Endobronchial ultrasound-guided lymph node biopsy with transbronchial needle forceps: a pilot study. Eur Respir J. 2012 Feb 1;39(2):373-7. PMID: 21700609. ***Fewer than 10 patients with SCLC.***

Herth R, Becker HD, Manegold C, et al. Endobronchial ultrasound (EBUS)--assessment of a new diagnostic tool in bronchoscopy for staging of lung cancer. Onkologie. 2001 Apr;24(2):151-4. PMID: 11441295. ***Unclear whether any patients had SCLC.***

Hillner BE, Tosteson AN, Tosteson TD, et al. Intended versus inferred care after PET performed for initial staging in the national oncologic PET registry. J Nucl Med. 2013 Dec 1;54(12):2024-31. PMID: 24221994. ***One test of interest, but no data on SCLC staging accuracy.***

Hochstenbag MMH, Twijnstra A, Wilmink JT, et al. Asymptomatic brain metastases (BM) in small cell lung cancer (SCLC): MR-imaging is useful at initial diagnosis. J Neurooncol. 2000;48(3):243-8. PMID: 11100822. ***One test of interest, but no data on SCLC staging accuracy.***

Hsu LH, Ko JS, You DL, et al. Transbronchial needle aspiration accurately diagnoses subcentimetre mediastinal and hilar lymph nodes detected by integrated positron emission tomography and computed tomography. Respirology. 2007 Nov;12(6):848-55. PMID: 17986113. ***Not SCLC.***

Hu Y, Puri V, Crabtree TD, et al. Attaining proficiency with endobronchial ultrasound-guided transbronchial needle aspiration. J Thorac Cardiovasc Surg. 2013 Dec;146(6):1387-1392.e1. PMID: 24075565. ***No separate SCLC data.***

Huang D, Zhang Y, Zhao F, et al. Clinical significance of (99m)Tc-tetrofosmin SPECT in the diagnosis of lung neoplasms and mediastinal lymph node involvement. Chin J Lung Cancer. 2007 Feb 20;10(1):25-8. PMID: ***No separate SCLC data.***

Huang GJ, Zhang DC, Mao YS, et al. Comparison of clinical and surgico-pathological TNM stage of 2007 lung cancer patients. Zhonghua Zhong Liu Za Zhi. 2005 Sep;27(9):551-3. PMID: 16438855. ***No separate SCLC data.***

Huellner MW, Collen TD, Gut P, et al. Multiparametric PET/CT-perfusion does not add significant additional information for initial staging in lung cancer compared with standard PET/CT. EJNMMI Res. 2014;4(1):6. PMID: 24450990. ***Fewer than 10 patients with SCLC.***

Igdem T, Alco G, Ercan T, et al. The application of positron emission tomography/computed tomography in radiation treatment planning: effect on gross target volume definition and treatment management. Clin Oncol (R Coll Radiol). 2010 Apr;22(3):173-8. PMID: ***Fewer than 10 patients with SCLC.***

Imamura F, Kuriyama K, Seto T, et al. Detection of bone marrow metastases of small cell lung cancer with magnetic resonance imaging: early diagnosis before destruction of osseous structure and implications for staging. 2000 Mar;27(3):189-97. PMID: 10699692. ***Other: Authors analyzed only a component of the full MR imaging procedure.***

Ippolito D, Capraro C, Guerra L, et al. Feasibility of perfusion CT technique integrated into conventional 18FDG/PET-CT studies in lung cancer patients: clinical staging and functional information in a single study. Eur J Nucl Med Mol Imaging. 2013 Jan;40(2):156-65. Epub 2012 Nov 10. PMID: 23143661. ***Fewer than 10 patients with SCLC.***

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Appendix C. Evidence Tables

Table C-1. General study information of included studies

Study	Country	Name of Clinic(s)	Range of Dates When Patients Received Imaging Tests	Prospective or Retrospective	Funding Source and Disclosed Potential Conflicts of Interest
Lee et al. (2012)[1]	South Korea	Soonchunhyang University	Jan 2006–Oct 2011	Retrospective	Funding NR, No conflicts to disclose
Munoz et al. (2012)[2]	Spain	Ciudad Real	Jul 2008–Dec 2009	Retrospective	NR
Sohn et al. (2012)[3]	South Korea	Asan Medical Center	Jan 2002–Dec 2007	Retrospective	NR, but no conflicts to disclose
Wada et al. (2010)[4]	Japan	Chiba University	Nov 2002–Sep 2008	Retrospective	NR
Fischer et al. (2006)[5]	Denmark	Copenhagen University Hospital	Feb 2003–Dec 2004	Prospective	NR
Brink et al. (2004)[6]	Germany	Freiburg University Hospital	1999–2003	Prospective	Funded by German Cancer Foundation, conflicts NR
Shen et al. (2002)[7]	Taiwan	China Medical College	NR	Prospective	NR

NR=Not reported

Table C-2. Patient characteristics of included studies

Study	Patient Enrollment Criteria	Number of Patients Included	% Female	Age (Mean, Range)	Consecutivity
Lee et al. (2012)[1]	Diagnosed with SCLC, no treatment, no history of previous malignancy	95	25% (24/95)	Mean 68, SD 9, range NR	Did not report whether enrollment was consecutive
Munoz et al. (2012)[2]	Diagnosed with SCLC, had pre-treatment PET/CT, no neurologic symptoms	21	14% (3/21)	Mean 66.57 (range 45–83)	Excluded patients followed up less than 6 months. Does not explicitly say consecutive.
Sohn et al. (2012)[3]	Diagnosed with SCLC, no treatment, had initial CT and bone scan or neuro imaging	73	18% (13/73)	Mean NR, SD NR, median 62, range 27–83	Does not explicitly say consecutive.

Table C-2. Patient characteristics of included studies (continued)

Study	Patient Enrollment Criteria	Number of Patients Included	% Female	Age (Mean, Range)	Consecutivity
Wada et al. (2010)[4]	Limited disease SCLC patients who underwent EBUS-TBNA for lymph node staging because they were being considered for surgical resection	40	15% (6/40)	Mean 66.0, SD NR, range 37–79	Did not report whether enrollment was consecutive. Of note, although the demographic data describe 40 pts, only 36 were included in the denominator for sen, spec, calcs, since 4 patients who were considered "negative" by EBUS could not undergo surgery and confirmation of "negative" status. However, the demographics for these 4 are not provided separately.
Fischer et al. (2006)[5]	Patients with pathologically proven SCLC	34	62% (21/34)	Mean 63, range 47–77	Consecutive enrollment
Brink et al. (2004)[6]	Histologically confirmed SCLC, exclusion criteria not reported	120	25% (30/120)	Mean 60.8, SD 8.9	Consecutive enrollment
Shen et al. (2002)[7]	Diagnosed with SCLC, no treatment	25	28% (7/25)	Mean 56.4, SD 7.2, median 57, range 45–68	Did not report whether enrollment was consecutive.

NR=Not reported

Table C-3. General test details of included studies

Study	Number of SCLC Patients in This Study Who Received This Test	Imaging Test	Test Details	Order of Multiple Tests Performed	Elapsed Time Between Tests
Lee et al. (2012)[1]	95	Bone scintigraphy	Tc99m-MDP, 740-925 MBq 3 hours prior, GE Xeleris dual-head camera, continuous acquisition mode (12 cm/min), 20% symmetric window about 140 keV, whole-body and spot imaging	NR	Median 5 days, max 20 days
Lee et al. (2012)[1]	95	FDG PET/CT	FDG, 5.18 MBq/kg 1 hour prior, Philips Gemini scanner, 128 matrix, 3D reformatting	NR	Median 5 days, max 20 days
Munoz et al. (2012)[2]	21	FDG PET/CT of the brain	FDG, methods reported in previous article, GE Discovery DSTE 16 scanner	NA	NA
Sohn et al. (2012)[3]	73	FDG PET/CT	FDG, 550 MBq 1 hour prior, Siemens Biograph Sensation, 2 minutes per position	Conventional first	NR
Sohn et al. (2012)[3]	73	Standard staging	History, physical exam, chest x-ray, chest CT, bone scan, bone marrow aspiration, MRI or CT of the brain)	Conventional first	NR

Table C-3. General test details of included studies (continued)

Study	Number of SCLC Patients in This Study Who Received This Test	Imaging Test	Test Details	Order of Multiple Tests Performed	Elapsed Time Between Tests
Wada et al. (2010)[4]	40	EBUS	Convex probe EBUS (BF-UC260F-OL8; Olympus, Tokyo, Japan) integrated with convex transducer (7.5 MHz); ultrasound images processed with ultrasound scanner (EU-C2000;Olympus); a dedicated 22-gauge needle was used to perform transbronchial needle aspiration (NA-201SX-4022; Olympus)	NA	NA
Fischer et al. (2006)[5]	29	Standard staging	Any of the following: Clinical exam, blood test, chest x-ray, bronchoscopy, and bone marrow biopsy	NR	All exams performed within one week
Fischer et al. (2006)[5]	29	FDG PET/CT	400 MBq 18-F-FDG was given, scan performed on integrated PET/CT system (GE Discovery LS; General Electric Medical Systems, Milwaukee, WI). A standardized CT protocol (80–120 mAs, 140 kV, tube rotation time 0.5 s per rotation, pitch 6, and slice thickness of 5 mm) was applied followed by PET scan (3 or 5 min emission scan per table position)	Radiologist first read CT (blinded to PET), then nuclear medicine physician read PET (blinded to CT findings); then "fused PET/CT images were evaluated in consensus afterwards"	CT result was derived from PET/CT, thus no time lapse between PET/CT and CT. Bone scan was at most six days after PET/CT
Fischer et al. (2006)[5]	29	Bone scintigraphy	Whole body scan with dual head gamma camera (Geor ADAC) with high resolution low energy collimator was performed 2 hr after injection with 500-700 MBq 99m Tc-oxydronate (TechneScan HDP; Malinkrodt, Hazelwood, MO, USA)	NR	All exams performed within one week
Fischer et al. (2006)[5]	29	CT	Was performed using PET/CT scanner	Radiologist first read CT (blinded to PET), then nuclear medicine physician read PET (blinded to CT findings); then "fused PET/CT images were evaluated in consensus afterwards"	CT result was derived from PET/CT, thus no time lapse between PET/CT and CT. Bone scan was at most six days after PET/CT

Table C-3. General test details of included studies (continued)

Study	Number of SCLC Patients in This Study Who Received This Test	Imaging Test	Test Details	Order of Multiple Tests Performed	Elapsed Time Between Tests
Brink et al. (2004)[6]	120	CT	NR	NA	NA
Brink et al. (2004)[6]	76	Bone scintigraphy	Tc99m-MDP, 700 MBq 3 hours prior, dual-head camera, mfr. not reported, some SPECT as well	NR	NR
Shen et al. (2002)[7]	25	Standard staging	Standard staging assessment, which included history and physical exam, chest x-ray, possibly chest CT, brain CT, abdominal CT, possibly hepatic sonography, Tc-99m MDP bone scan, unilateral iliac crest bone marrow exam.	NA	NA

Note: This table includes details of only the imaging tests for which data met our inclusion criteria.

NA=Not applicable; NR=not reported

Table C-4. Imaging test readers and reference standards

Study	Imaging Test	Number of Test Readers Per Scan	Prior Experience of These Readers With This Imaging Test	Other Reported Details About the Readers	Reference Standard
Lee et al. (2012)[1]	Bone scintigraphy	2	Experienced	NM specialist, used 4-point scale. Consensus or independent reading NR, blinding NR	Positive biopsy OR CT or MRI confirmation OR progression seen on subsequent scan (any one sufficient to diagnose)
Lee et al. (2012)[1]	FDG PET/CT	2	Experienced	NM specialist, used 4-point scale. Consensus or independent reading NR, blinding NR	Positive biopsy OR CT or MRI confirmation OR progression seen on subsequent scan (any one sufficient to diagnose)
Munoz et al. (2012)[2]	FDG PET/CT of the brain	NR	Nuclear medicine experts	NR	Minimum 6 month clinical follow-up including contrast CT, brain MRI.
Sohn et al. (2012)[3]	FDG PET/CT	2 (consensus)	Experienced	Not blinded to other results	Clinical follow-up
Sohn et al. (2012)[3]	Standard staging	NR	NR	Not blinded to other results	Clinical follow-up
Wada et al. (2010)[4]	EBUS	1	NR	Blinded to patient details	Negative nodes: surgical path; positive nodes: EBUS results

Table C-4. Imaging test readers and reference standards (continued)

Study	Imaging Test	Number of Test Readers Per Scan	Prior Experience of These Readers With This Imaging Test	Other Reported Details About the Readers	Reference Standard
Fischer et al. (2006)[5]	Standard staging	NR	NR	NR	Reference standard based on four things: 1) histology if available; 2) concordance between different imaging modalities; 3) results of MRI or ultrasound; 4) clinical follow-up
Fischer et al. (2006)[5]	FDG PET/CT	2	Experienced	NR	See above
Fischer et al. (2006)[5]	Bone scintigraphy	1	"Experienced" nuclear medicine physician	NR	See above
Fischer et al. (2006)[5]	CT	1	"An experienced radiologist, blinded to PET findings interpreted the CT scan"	NR	See above
Brink et al. (2004)[6]	CT	NR	NR	NR	Consensus achieved by committee of 4 (2 clinicians, 2 nuclear medicine specialists)
Brink et al. (2004)[6]	Bone scintigraphy	Not reported	Not reported	NR	Committee decision
Shen et al. (2002)[7]	Standard staging (multiple tests)	NR	NR	NR	Based on several considerations including surgical findings, other imaging results, and one year clinical follow-up

Note: This table includes details of only the imaging tests for which data met our inclusion criteria.

NA=Not applicable; NR=not reported

Table C-5. Concordance data for tests of interest in included studies (Fischer et al. [2006])

Staging Determination	Test 1 Versus Test 2	Number With Both Tests Positive	Number With Both Tests Negative	Number With Where Test 1 Positive But Test 2 Negative	For These Discrepancies, How Many Were Stated by the Authors to be True Positives?	Number With Where Test 2 Positive and Test 1 Negative	For These Discrepancies, How Many Were Stated by the Authors to be True Positives?	% Agreement Between Tests	Comments
Tumor stage (T)	CT vs. PET/CT	28	0	1	NR	0	NR	97%	Out of 29 patients, CT and PET/CT agreed on T staging for 28. For 1 patient, CT found stage =3, while PET/CT found stage =2. PET/CT was assessed in consensus by two people (one who had previously viewed just the CT portion of PET/CT, and the other who previously viewed just the PET portion of PET/CT), whereas CT was assessed without reference to PET/CT.
N stage (N) Lymph nodes	CT vs. PET/CT	25	0	2	NR	2	NR	86%	Out of 29 patients CT and PET/CT agreed for 25 patients; for 2 patients CT had higher stage (Stages 3 vs. 2, Stage 2 vs. 0); for 2 patients PET/CT had higher stages (Stage 3 vs. 2 and Stage 3 vs. 2)
Pleural effusion	CT vs. PET/CT	9	20	0	NA	0	NA	100%	Out of 29 patients, complete agreement
Metastasis to ipsilateral lung	CT vs. PET/CT	4	23	2	NR	0	NR	93%	Out of 29 patients, 2 patients for whom CT found ipsilateral mets, but PET/CT did not
Metastasis to contralateral lung	CT vs. PET/CT	3	26	0	NR	0	NR	100%	Our of 29 patients there was complete agreement between these 2 tests

Table C-5. Concordance data for tests of interest in included studies (Fischer et al. [2006]) (continued)

Staging Determination	Test 1 Versus Test 2	Number With Both Tests Positive	Number With Both Tests Negative	Number With Where Test 1 Positive But Test 2 Negative	For These Discrepancies, How Many Were Stated by the Authors to be True Positives?	Number With Where Test 2 Positive and Test 1 Negative	For These Discrepancies, How Many Were Stated by the Authors to be True Positives?	% Agreement Between Tests	Comments
Metastasis to the liver	CT vs. PET/CT	10	16	1	NR	2	NR	90%	
Metastasis to adrenals	CT vs. PET/CT	3	24	2	NR	0	NR	93%	
Metastasis to extra-thoracic lymph nodes	CT vs. PET/CT	5	22	1	NR	1	NR	93%	
Metastasis to osseous structures	CT vs. PET/CT	3	21	0	NA	5	5	83%	All five discrepancies were called corrected by PET/CT and incorrectly by CT
Metastasis to osseous structures	CT vs. bone scint.	1	12	1	1	14	7	46%	Counting equivocal as + for Bone scan. The 14 includes 4 times where bone scintigraphy was positive and CT was negative. 10 times where bone scintigraphy was equivocal and CT was negative. Out of 15 total discrepancies, PET/CT was correct in 8 and bone scintigraphy was correct in 7.

Table C-5. Concordance data for tests of interest in included studies (Fischer et al. [2006]) (continued)

Staging Determination	Test 1 Versus Test 2	Number With Both Tests Positive	Number With Both Tests Negative	Number With Where Test 1 Positive But Test 2 Negative	For These Discrepancies, How Many Were Stated by the Authors to be True Positives?	Number With Where Test 2 Positive and Test 1 Negative	For These Discrepancies, How Many Were Stated by the Authors to be True Positives?	% Agreement Between Tests	Comments
Metastasis to osseous structures	FDG PET/CT vs. bone scint.	5	11	2	2	10	2	57%	Counting equivocal as + for Bone scan. The 10 includes 4 times where bone scintigraphy was positive and PET/CT was negative, and 6 times where bone scintigraphy was equivocal and PET/CT was negative. Out of 12 total discrepancies, PET/CT was correct in 10 and bone scintigraphy was correct in 2.

All included concordance data are from Fischer et al. (2006).[5]

NA=Not applicable; NR=not reported

Table C-6. Accuracy data for tests of interest in included studies

Study	Staging Determination	Test(s) of Interest (Test 1 vs. Test 2)	Test 1, True Positives	Test 1, False Positives	Test 1, False Negatives	Test 1, True Negatives	Test 2, True Positives	Test 2, False Positives	Test 2, False Negatives	Test 2, True Negatives	No Internal Discrepancies in Reported Data?	Comments
Fischer et al. (2006)[5]	LD/ED	Standard staging vs. FDG PET/CT	19	0	3	6	21	0	1	6	OK	
Shen et al. (2002)[7]	LD/ED	Standard staging only	14	1	1	9	NA	NA	NA	NA	OK	Data are from Table III in the article

Table C-6. Accuracy data for tests of interest in included studies (continued)

Study	Staging Determination	Test(s) of Interest (Test 1 vs. Test 2)	Test 1, True Positives	Test 1, False Positives	Test 1, False Negatives	Test 1, True Negatives	Test 2, True Positives	Test 2, False Positives	Test 2, False Negatives	Test 2, True Negatives	No Internal Discrepancies in Reported Data?	Comments
Lee et al. (2012)[1]	Metastasis to osseous structures	FDG PET/CT vs. Bone scintigraphy	30	0	0	65	11	5	19	60	OK	These data are on a per-patient basis
Fischer et al. (2006)[5]	Metastasis to osseous structures	CT vs. Bone scintigraphy	2	0	7	19	7	8	2	11	OK	These data treat equivocal bone scintigraphy results as positives
Fischer et al. (2006)[5]	Metastasis to osseous structures	CT vs. Bone scintigraphy	2	0	7	19	2	3	7	16	OK	These data treat equivocal bone scintigraphy results as negatives
Fischer et al. (2006)[5]	Metastasis to osseous structures	CT vs. FDG PET/CT	3	0	7	19	8	0	2	19	OK	
Fischer et al. (2006)[5]	Metastasis to osseous structures	FDG PET/CT vs. Bone scintigraphy	7	0	2	19	7	8	2	11	OK	These data treat equivocal bone scintigraphy results as positives
Fischer et al. (2006)[5]	Metastasis to osseous structures	FDG PET/CT vs. Bone scintigraphy	7	0	2	19	2	3	7	16	OK	These data treat equivocal bone scintigraphy results as negatives
Brink et al. (2004)[6]	Metastases to osseous structures	Bone scintigraphy only	14	2	9	51	NA	NA	NA	NA	OK	Subset of patients who had bone scan
Wada et al. (2010)[4]	Metastasis to mediastinal and hilar lymph nodes	EBUS only	27	0	1	8	NA	NA	NA	NA	OK	
Brink et al. (2004)[6]	Metastasis to lymph node(s)	CT only	37	4	16	61	NA	NA	NA	NA	OK	Excluded two cases where CT and PET disagreed and no reference diagnosis was obtained
Brink et al. (2004)[6]	Metastases to adrenal glands	CT only	15	4	9	92	NA	NA	NA	NA	OK	

Table C-6. Accuracy data for tests of interest in included studies (continued)

Study	Staging Determination	Test(s) of Interest (Test 1 vs. Test 2)	Test 1, True Positives	Test 1, False Positives	Test 1, False Negatives	Test 1, True Negatives	Test 2, True Positives	Test 2, False Positives	Test 2, False Negatives	Test 2, True Negatives	No Internal Discrepancies in Reported Data?	Comments
Brink et al. (2004)[6]	Metastases to liver	CT only	23	2	3	92	NA	NA	NA	NA	OK	
Brink et al. (2004)[6]	Metastases to spleen	CT only	3	0	1	116	NA	NA	NA	NA	OK	
Sohn et al. (2012)[3]	Distant metastasis	Standard staging vs. FDG PET/CT	12	0	14	47	24	2	2	45	Discrepancies	The two false positives were termed by authors as positives tests at first, but then termed equivocal tests; these data treat them as false positives
Munoz et al. (2012)[2]	Metastases to brain	FDG PET/CT of the brain only	3	0	2	16	NA	NA	NA	NA	OK	

NA=Not applicable; NR=not reported

Table C-7. Analyses of accuracy data for tests of interest in included studies

Study	Staging Determination	Test(s)	Sensitivity Test 1 (95% CI)	Sensitivity Test 2 (95% CI)	Specificity Test 1 (95% CI)	Specificity Test 2 (95% CI)	95% CI Around the Difference in Logit Sensitivities	95% CI Around the Difference in Logit Specificities
Fischer et al. (2006)[5]	LD/ED	Standard staging vs. FDG PET/CT	86% (66% to 95%) (19/22)	95% (78% to 99%) (21/22)	100% (60% to 100%) (6/6)	100% (60% to 100%) (6/6)	-3 to 1.1	-3.6 to 3.6
Shen et al. (2002)[7]	LD/ED	Standard staging only	93% (70% to 99%) (14/15)	NA	90% (59% to 98%) (9/10)	NA	NA	NA
Lee et al. (2012)[1]	Metastasis to osseous structures	FDG PET/CT vs. Bone scintigraphy	100% (88% to 100%) (30/30)	37% (22% to 55%) (11/30)	100% (94% to 100%) (65/65)	92% (83% to 97%) (60/65)	2.2 to 7.1 Favors FDG PET/CT	-0.1 to 4.9

Table C-7. Analyses of accuracy data for tests of interest in included studies (continued)

Study	Staging Determination	Test(s)	Sensitivity Test 1 (95% CI)	Sensitivity Test 2 (95% CI)	Specificity Test 1 (95% CI)	Specificity Test 2 (95% CI)	95% CI Around the Difference in Logit Sensitivities	95% CI Around the Difference in Logit Specificities
Fischer et al. (2006)[5]	Metastasis to osseous structures	CT vs. Bone scintigraphy (treating equivocals as positive)	22% (7% to 55%) (2/9)	78% (45% to 93%) (7/9)	100% (83% to 100%) (19/19)	58% (36% to 77%) (11/19)	-4.4 to -0.3 Favors bone scint.	0.8 to 5.9 Favors CT.
Fischer et al. (2006)[5]	Metastasis to osseous structures	CT vs. Bone scintigraphy (treating equivocals as negative)	22% (7% to 55%) (2/9)	22% (7% to 55%) (2/9)	100% (83% to 100%) (19/19)	84% (62% to 94%) (16/19)	-1.9 to 2.2	-0.7 to 4.6
Fischer et al. (2006)[5]	Metastasis to osseous structures	CT vs. FDG PET/CT	30% (11% to 60%) (3/10)	80% (49% to 94%) (8/10)	100% (83% to 100%) (19/19)	100% (83% to 100%) (19/19)	-3.9 to -0.1 Favors FDG PET/CT	-3.4 to 3.4
Fischer et al. (2006)[5]	Metastasis to osseous structures	FDG PET/CT vs. Bone scintigraphy (treating equivocals as positive)	78% (45% to 93%) (7/9)	78% (45% to 93%) (7/9)	100% (83% to 100%) (19/19)	58% (36% to 77%) (11/19)	-2.2 to 1.9	0.8 to 5.9 Favors FDG PET/CT.
Fischer et al. (2006)[5]	Metastasis to osseous structures	FDG PET/CT vs. Bone scintigraphy (treating equivocals as negative	78% (45% to 93%) (7/9)	22% (7% to 55%) (2/9)	100% (83% to 100%) (19/19)	84% (62% to 94%) (16/19)	0.3 to 4.4 Favors FDG PET/CT	-0.7 to 4.6
Brink et al. (2004)[6]	Metastases to osseous structures	Bone scintigraphy only	61% (41% to 78%) (14/23)	NA	96% (87% to 99%) (51/53)	NA	NA	NA
Wada et al. (2010)[4]	Metastasis to mediastinal and hilar lymph nodes	EBUS only	96% (82% to 99%) (27/28)	NA	100% (67% to 100%) (8/8)	NA	NA	NA
Brink et al. (2004)[6]	Metastasis to lymph node(s)	CT only	70% (56% to 80%) (37/53)	NA	94% (85% to 97%) (61/65)	NA	NA	NA

Table C-7. Analyses of accuracy data for tests of interest in included studies (continued)

Study	Staging Determination	Test(s)	Sensitivity Test 1 (95% CI)	Sensitivity Test 2 (95% CI)	Specificity Test 1 (95% CI)	Specificity Test 2 (95% CI)	95% CI Around the Difference in Logit Sensitivities	95% CI Around the Difference in Logit Specificities
Brink et al. (2004)[6]	Metastases to adrenal glands	CT only	63% (43% to 79%) (15/24)	NA	96% (90% to 98%) (92/96)	NA	NA	NA
Brink et al. (2004)[6]	Metastases to liver	CT only	88% (71% to 96%) (23/26)	NA	98% (92% to 99%) (92/94)	NA	NA	NA
Brink et al. (2004)[6]	Metastases to spleen	CT only	75% (30% to 95%) (3/4)	NA	100% (97% to 100%) (116/116)	NA	NA	NA
Sohn et al. (2012)[3]	Distant metastasis	Standard staging vs. FDG PET/CT	46% (29% to 65%) (12/26)	92% (76% to 98%) (24/26)	100% (86% to 99%) (47/47)	96% (92% to 100%) (45/47)	-4.1 to -1.1 Favors FDG PET/CT	-1.2 to 4.1
Munoz et al. (2012)[2]	Metastases to brain	PET/CT of the brain only	60% (23% to 88%) (3/5)	NA	100% (80% to 100%) (16/16)	NA	NA	NA

NA=Not applicable; NR=not reported

Appendix D. Risk of Bias Assessments

Figure D-1. Risk of bias assessments of comparative accuracy studies

Item	Lee et al. (2012)[1]	Fischer et al. (2006)[5]	Sohn et al. (2012)[3]
1. Did the study enroll all, consecutive, or a random sample of patients?	NR	Yes	Yes
2. Was the study unaffected by spectrum bias (e.g., patients with known status before the study, or patients selected for being difficult to diagnose/stage)?	NR	NR	No
3. Was prior experience with the test (technicians, readers) similar for the two imaging tests being compared in the study?	Yes	Yes	Yes
4. Were the imaging tests performed within one month of each other (to avoid the possibility that the patient's true condition changed between tests)?	Yes	Yes	Yes
5. Was knowledge of the other test complementary (either both tests were read with knowledge of the other results, or neither test was read with knowledge of the other)?	NR	Yes	No
6. Did the interpreters have the same other information available at the time of interpretation for the two imaging tests (other clinical information, 3rd test results)?	NR	NR	No
7. Was each test's accuracy measuring using the same reference standard (or a similar proportion of patients who underwent different reference standards such as clinical follow-up and surgical findings)?	Yes	Yes	Yes
8. Were readers of both tests of interest blinded to the results of the reference standard (or the reference standard was unknowable until after the tests were read)?	Yes	Yes	Yes
9. Were the people determining the reference standard unaware of the diagnostic test results?	No	No	No
Risk of Bias Category	**Moderate**	**Moderate**	**High**

Figure D-2. Risk of bias assessments of single test accuracy studies

Item	Wada et al. (2010)[4]	Brink et al. (2004)[6]	Shen et al. (2002)[7]	Munoz et al. (2012)[2]
1. Did the study enroll all, consecutive, or a random sample of patients?	Yes	Yes	NR	NR
2. Were more than 85 percent of the approached/eligible patients enrolled?	Yes	NR	NR	NR
3. Were the patient inclusion and exclusion criteria applied consistently to all patients?	Yes	Yes	NR	NR
4. Was the study unaffected by obvious spectrum bias?	Yes	Yes	Yes	Yes
5. Did the study account for inter-reader differences?	No	Yes	No	No
6. Were readers of the diagnostic test of interest blinded to the results of the reference standard?	NR	Yes	Yes	Yes
7. Were readers of the reference standard blinded to the results of the diagnostic test of interest?	No	No	NR	Yes
8. Were readers of the diagnostic test of interest blinded to all other clinical information?	Yes	Yes	NR	NR
9. Were readers of the reference standard blinded to all other clinical information?	NR	No	No	No
10. Were patients assessed by a reference standard regardless of the test's results?	No	Yes	Yes	Yes
11. Were all patients assessed by the same reference standard regardless of the test's results?	No	Yes	Yes	Yes
12. If the study reported data for a single diagnostic threshold, was the threshold chosen a priori?	NA	NA	NA	NA
13. Were the study results unaffected by intervening treatments or disease progression/regression?	Yes	Yes	Yes	No
14. Were at least 85 percent of the enrolled patients accounted for?	Yes	No	Yes	Yes
Risk of Bias Category	**Moderate**	**Moderate**	**Moderate**	**Moderate**

Appendix E. Appendix References

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