Positron Emission Tomography ^{18}F-Fluorodeoxyglucose Uptake and Prognosis in Patients with Surgically Treated, Stage I Non-small Cell Lung Cancer:

A Systematic Review

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Background: ^{18}F-fluorodeoxyglucose (FDG) uptake holds potential as a noninvasive biomarker in patients with non-small cell lung cancer (NSCLC). We aimed to investigate the association between tumor FDG uptake and survival in patients with surgically resected, stage I NSCLC.

Methods: We used systematic methods to identify studies for inclusion, assess methodological quality, and abstract relevant data about study design and results.

Results: Our literature search identified 1578 citations, of which nine retrospective, cross-sectional studies met eligibility criteria. In all studies, higher degrees of FDG uptake in the primary tumor were associated with worse overall or disease free survival after 2 to 5 years of follow-up, but these differences were statistically significant in only five studies. Across studies, the median overall or disease free survival was 70% for patients with higher FDG uptake compared with 88% for patients with lower FDG uptake. In three studies that performed multivariable analysis, the adjusted hazard of death or recurrence was 1.9 to 8.6 times greater in patients with higher FDG uptake.

Conclusion: Current evidence suggests that increasing tumor FDG uptake is associated with worse survival in patients with stage I NSCLC. FDG uptake has the potential to be used as a biomarker for identifying stage I patients who are at increased risk of death or recurrence and therefore could identify candidates for participation in future trials of adjuvant therapy.

Key Words: Systematic review, Stage I, Non-small cell lung cancer, FDG uptake, Standard uptake value, Prognosis, Survival, Outcome.

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Lung cancer is the second most common cancer in both men and women in the United States, and it remains the number one cancer related cause of death, with over 160,000 people estimated to die of it during 2008 alone.[1] Non-small cell lung cancer (NSCLC) accounts for the majority of these cases, and to date prognosis and therapy have been guided chiefly by the Tumor, Node, Metastasis (TNM) staging system. Although surgically treated patients with localized disease have the best prognosis, 5-year survival after resection in patients with stage I disease approaches a modest 60%.[2–6]

^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging is widely used to determine TNM stage in patients with NSCLC, altering the stage designation and management in as many as 20 to 40% of patients.[7–9] It is based on the observation that metabolically active cells selectively take up and trap fluoridated glucose, which then undergoes nuclear decay that can be detected, localized, and quantified.[10] Furthermore, the intensity of FDG uptake has been shown to correlate with tumor growth rates.[11–14]

Methods for quantifying FDG uptake include calculating a standardized uptake value (SUV) or determining the metabolic rate of glucose (MRglu) by means of kinetic studies or Patlak analysis.[15,16] SUV can be quantified as a mean value (based on a region of interest [ROI], which circumscribes the given abnormality and is defined by a processing algorithm) or a maximum value. In either case, uptake is quantified numerically after making adjustments for injected dose, body weight, and background uptake. MRglu is used less commonly because of methodologic complexity.[15,16]

Given the imperfect nature of TNM staging, a number of investigators have examined tumor FDG uptake as a prognostic biomarker, with a recent review and meta-analysis concluding that FDG uptake is negatively correlated with prognosis in heterogeneous groups of patients with NSCLC.[17,18] However, studies included in these reviews were not limited to patients with localized disease, and several studies of FDG uptake and prognosis have been published in the interim. In theory, high FDG uptake may define a subgroup of patients with localized disease whose risk of recurrence and death might be large enough to justify enrollment in trials of adjuvant therapy after surgery. Accordingly, we performed a systematic review to identify, appraise, and synthesize results from published stud-

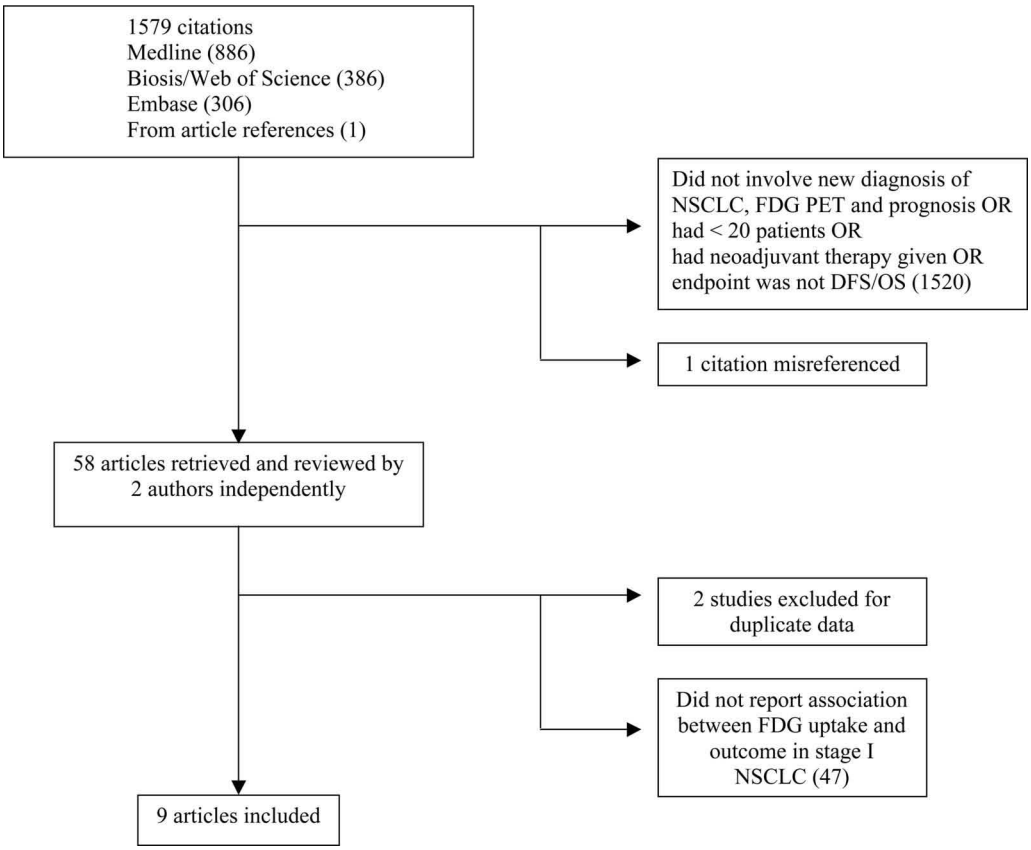

FIGURE 1. Flow chart of included and excluded studies.

ies that examined the association between tumor FDG uptake and prognosis in patients with stage I NSCLC.

METHODS

Patient Selection

We considered studies for inclusion if they examined the association between tumor FDG uptake and survival in newly diagnosed patients with a pathologic diagnosis of NSCLC, enrolled at least 20 patients, and had a defined endpoint of recurrence or death (Figure 1). Studies that included patients with small cell carcinoma were eligible if at least 90% of patients had NSCLC or separate results were reported for NSCLC patients. Studies that included patients who had received neoadjuvant therapy at the time of PET imaging were excluded.

Search Strategy

An unrestricted language search strategy was developed by the authors and a professional librarian that queried MEDLINE (from 1966 to August 2008), BIOSIS (from 1926 to August 2008), EMBASE (from 1947 to August 2008), and Web of Science (from 1900 to August 2008) using the following search terms:

Lung Cancer + FDG + Prognosis NOT Letter OR Case-Report OR Editorial OR Animal-Only Lung cancer* [tw] OR lung neoplasm* [tw] OR lung carcinoma* [tw] OR pulmonary neoplasm* [tw] OR pulmonary cancer* [tw] OR pulmonary carcinoma* [tw] OR ((lung* [tw] OR pulmonary [tw]) AND (cancer* [tw] OR carcinoma* [tw] OR malignan* [tw] OR eoplasm* [tw] OR tumors [tw] OR tumor [tw])) OR "Lung Neoplasms" [mesh] "18F-FDG" [tw] OR "FDG-F18" [tw] OR FDG [tw] OR F18 [tw] OR ((F18 [tw] OR "fluorine 18" [tw] OR "F 18" [tw] OR 18F [tw]) AND (fluorodeoxyglucose [tw] OR fludeoxyglucose [tw])) OR "2 Fluoro 2 deoxy D glucose" [tw] OR "2-Fluoro-2-deoxyglucose" [tw] prognos* [tw] OR predict* [tw] OR course [tw] OR "natural history" [tw] OR incidence [sh] OR death* OR "models, statistical" [mesh] OR cohort* [tw] OR diagnosed [tw] OR "first episode" [tw] OR occur* [tw] OR recur* [tw] OR "long term" [tw] OR prospective [tw] OR "mortality" [mesh] OR mortality [sh] OR "follow-up studies" [mesh].

We supplemented searches of electronic databases by reviewing the reference lists of retrieved articles.

Data Abstraction

One physician (V.S.N.) reviewed titles and abstracts of all reports. Reviews, editorials, and letters were excluded during the initial review process. All relevant citations were English in language. Two physicians (V.S.N., Y.K.) independently reviewed the full text of 58 potentially relevant articles to determine eligibility and study quality. In cases of discordance, a

third independent reviewer (M.K.G.) assessed eligibility. Quality criteria assessed study design, reporting of patient characteristics, PET protocols, clinical follow-up, and statistical analysis. Data abstraction was performed systematically with predetermined variables of interest recorded for each article including demographic characteristics, staging, histology, SUV acquisition methods and values, timing of events, and outcomes.

Data Synthesis

To describe study and patient characteristics, we report means, medians, and counts, depending on information provided in the primary studies. To describe outcomes, we report estimates of percent survival with *p* values comparing groups defined by high versus low degrees of FDG uptake. When available, we also report adjusted hazard ratios (HRs) with their 95% confidence intervals (CIs). Heterogeneity in study methods and reporting of results precluded quantitative synthesis. In some cases, time-to-event curves were analyzed by the author (V.S.N.) to obtain numerical data not provided in the study manuscript.

RESULTS

An initial search yielded 886 citations from MEDLINE, 386 citations from BIOSIS/Web of Science, and 306 citations from EMBASE (Figure 1). Fifty-eight abstracts required more thorough review to determine eligibility, and 30 of these articles examined FDG uptake and prognosis in patients with all stages of NSCLC. One article not initially retrieved from our search was included after reviewing references of included articles. One article was referenced incorrectly in the EMBASE database and therefore could not be identified.[19] Of these 30 eligible articles, we ultimately included nine studies that examined the association between tumor FDG uptake and survival in newly diagnosed patients with stage I NSCLC who had surgery with curative intent.[20–28]

A total of 1166 patients with resected stage I NSCLC were included in this analysis (Table 1). Only five of these patients received adjuvant therapy. Mean/median age ranged from 60 to 71 years, and women made up almost half of the samples. Median duration of follow-up ranged from 26 to 46 months. All studies reported results for patients with pathologic stage I NSCLC except for Port et al.[22] which reported results for patients with clinical stage I NSCLC.

Study quality was suboptimal in several domains (Table 2). None of the included studies enrolled participants prospectively and just over half reported consecutive enrollment. Patient characteristics were adequately described in most studies. Reporting of technical details about image acquisition, FDG uptake quantification, and statistical analysis were all highly variable. PET scanner type, dosing, time to acquisition, and serum glucose varied widely across included studies (see Appendix, Supplemental Digital Content 1, http://links.lww.com/JTO/A12). FDG uptake was quantified as a SUV in all studies, however, technical details of how this value was determined often were lacking (i.e., ROI processing algorithm and SUV formula for calculation). Statistical methods used to define threshold values for FDG uptake were highly variable. Of the included studies, only four described rigorous staging practices, varying from systematic nodal sampling and complete homolateral nodal dissection to hilar/mediastinal nodal sampling.[21,23,24,28] Many studies did not report methods used to document recurrence, i.e., computed tomography and/or PET, clinical status, or biopsy. Only a few studies performed multivariable analysis to adjust for confounding.

Average dose of injected tracer ranged from 5 to 15 mCi. Seven studies used dedicated PET imaging, one study used PET/computed tomography imaging, and one study did not report imaging modality (see Appendix, Supplemental Digital Content 1, http://links.lww.com/JTO/A12). Five studies used more than one scanner for their study and resolution was usually not reported. Fasting was standard for all studies and ranged from 4 to 12 hours, however, serum glucose concentration was reported before image acquisition in only one study. Time from injection dose to scan ranged from 40 to 60 minutes. Six studies reported the "brightest" pixel intensity

TABLE 1. Characteristics of Included Studies

Author	Country	Enrollment Period	n^a	Stage I[b]	Resected Stage I	Ia	Adjuvant Treatment	Age[a,c] (yr)	Gender M (%)	Median Follow-Up[a]
Higashi et al.[20]	Japan	1994–2000	57	46	46	38	None	64	54	34[d]
Cerfolio et al.[21]	United States	2001–2004	315	141	141	59	None	66	57	26
Port et al.[22]	United States	2001–2004	64	64	60	64	None	66	40	N/A
Ohtsuka et al.[23]	Japan	2001–2005	98	98	98	63	None	60	57	31[d]
Raz et al.[24]	United States	1998–2004	36	36[e]	36	16	5	71	39	31
Downey et al.[25]	United States	2000–2004	487	380	380	249	None	69	47	26
Gauger et al.[26]	United States	1992–2004	194	194[f]	194	125	None	67	44	33
Goodgame et al.[27]	United States	1999–2003	136	136	136	77	None	67	N/A	46
Hanin et al.[28]	Belgium	N/A–2006	96	75	75	34	None	65	76	45[d]
Totals:			1483	1170	1166	725				

[a] Represents data for all NSCLC from study, not just stage I NSCLC.
[b] All studies reported results of pathologic staging, except Port et al.
[c] Mean or median are reported depending on data that was provided and age for Ohtsuka was reported as follows: 66% of patients were 60 yr or older and 34% of patients were younger than 60 yr.
[d] Mean reported instead.
[e] All were BAC and were treated as stage I, however, 4/36 were "multifocal."
[f] Three patients were stage I "X" and only 173 of 194 of these patients had SUV data available for analysis.
N/A, not available; NSCLC, non-small cell lung cancer; SUV, standardized uptake value; BAC, bronchioloalveolar carcinoma.

TABLE 2. Quality Analysis of Included Studies

Study Criteria	Percent Studies
Study design	
Prospective enrollment	0
Consecutive enrollment	56
Representative sample of well-defined patients	100
Patient characteristics described	
Age	89
Gender	89
Smoking status	22
Histology	100
Stage	100
Staging methods	44
Systematic staging	22
Nonsystematic	22
Treatment	67
PET protocol	
PET model specified	67
Fasting specified	44
Adjusted for weight	44
Serum glucose reported	11
Injection dose reported	56
Acquisition time from injection reported	56
Volumetric "region of interest" defined	22
SUV formula described	33
Follow-up	
Survival/recurrence measured from date of PET scan	22
Time from PET to surgery/treatment specified	33
Fewer than 5% lost to follow-up	89
Reasons for lack of follow-up reported	11
Surveillance for disease recurrence described	44
Mean duration of follow-up at least 12 mo	100
Statistical analysis	
Statistical methods described	100
Multivariate analysis (with adjustment for)	33
Age	11
T stage	22
Histology	33
Treatment	33
Outcome clearly specified and objectively defined	100

SUV, standardized uptake value; PET, positron emission tomography.

of the given ROI to quantify measurement of FDG uptake (SUV_{max}). The remaining three studies used a ROI circumscribing the tumor to calculate an average SUV, although only two studies described their processing algorithm in detail.

The most common methods used to determine an SUV threshold were dichotomizing at the median (4 of 9) and the method of log ranks (3 of 9). Two studies used an arbitrary definition of PET positivity to dichotomize at a SUV_{max} of 2.5.[29] Accordingly, the threshold value for FDG uptake varied across studies from 2.5 to 10.

Methods for time-to-event analysis varied (Table 3). Five studies measured survival time from the date of operation, two from the date of PET scan, and two did not report this information. Five studies used overall survival (OS) as an endpoint and four studies used disease-free survival (DFS) as an endpoint with right censoring ranging from 2 to 5 years.

Five of nine studies reported that survival or disease free survival was significantly worse in patients with higher degrees of FDG uptake, including three of five studies that examined OS and two of four studies that examined DFS (Table 3). In the other four studies, there was a trend toward better outcomes in patients with lower FDG uptake that was not statistically significant in two of the studies and not formally tested in the two other studies. Median OS/DFS in the high FDG uptake groups was 70% (range 17–87%) compared with 88% (range 74–100%) in the low FDG uptake groups.

Three studies reported results of multivariable analyses for patients with stage I NSCLC (Table 3) after adjusting for histology (three studies), T stage (two studies), and age (one study). In these studies, the adjusted hazard of death or disease recurrence was 1.9 to 8.6 times greater in patients with high FDG uptake, although the results were not statistically significant in one study and the confidence intervals were very wide in two studies.

Four studies reported separate analyses for patients with stage Ia NSCLC, and survival was significantly worse for patients with higher FDG uptake in two of these studies (Table 4). Patients with higher degrees of FDG uptake had worse survival in two of three studies that reported separate results for patients with stage Ib NSCLC (Table 4). Two studies analyzed patients with resected, stage II NSCLC independently. One showed a significant difference in survival based on FDG uptake, whereas the other showed a nonsignificant trend toward improved survival with lower FDG uptake (Table 5).[21,28]

DISCUSSION

Identifying patients with localized NSCLC who have a poor prognosis remains a priority in clinical oncology given their high 5-year mortality despite resection. This review is the first to synthesize the existing data regarding the association between FDG uptake and prognosis in patients with surgically treated, stage I NSCLC. Although substantial heterogeneity across studies precluded us from performing a formal, quantitative synthesis, we found that higher FDG uptake in the primary tumor was significantly associated with a worse prognosis in five of nine studies that reported outcome for patients with resected, stage I NSCLC.

Although patients with higher degrees of FDG uptake had a worse prognosis in all included studies, the magnitude, and statistical significance of this finding varied across studies that appeared to be similar in design. For example, studies by Higashi et al. and Gauger et al. applied similar thresholds for FDG uptake, but Higashi et al. found large differences in DFS at 5 years, whereas Gauger et al. found differences in 5-year DFS that were small in magnitude and not statistically significant (Table 3). The study by Higashi et al. had more patients with stage Ia NSCLC (83% versus 55%) and more patients with bronchioloalveolar cell carcinoma (28% versus 5%), perhaps explaining a lower risk of recurrence in patients with low grade FDG uptake in this study. However, Raz et al. found large differences in OS stratified by FDG uptake at 3 years in a sample that was composed entirely of patients with bronchioloalveolar carcinoma. Downey et al. was the largest study included in our review, and although there was no significant difference in OS

TABLE 3. FDG Uptake and Survival for Stage I NSCLC

Study	*n*	Time Zero[a]	SUV Metric Measured	SUV Threshold	Survival Metric[b]	Percent Survival			Multivariable Analysis[c]
						High SUV	Low SUV	*p* value	
Higashi et al.	46	PET	Mean[d]	5	5 yr DFS	17	88[e]	0.001	
Cerfolio et al.	141	Surgery	Max	10	4 yr DFS	68	88[e]	N/A[f]	
Port et al.	64	N/A	Max	2.5	3 yr OS	87	100	0.46	
Ohtsuka et al.	98	N/A	Max	3.3	2 yr DFS	75	95[e]	0.008	4.2 (0.8–21.5)
Raz et al.	36	Surgery	Max	2.5	3 yr OS	49	95	0.005	8.6 (1.4–245)
Downey et al.	380	Surgery	Max	4.3	2 yr OS	76	87[e]	N/A	
Gauger et al.	173	PET	Mean[d]	4.1	5 yr DFS	70	77[g]	0.21	
Goodgame et al.	136	Surgery	Mean[d]	5.5	5 yr OS	53	74	0.006	1.9 (1.0–3.6)
Hanin et al.	75	Surgery	Max	7.8	2 yr OS	80	95[e]	0.001	

[a] Starting time point for survival analysis.
[b] Reported as OS (overall survival) or DFS (disease free survival).
[c] HR with 95% CI for 3 studies are shown: Ohtsuka adjusted for histology, Raz for histology and tumor size and Goodgame for histology, tumor size, and age.
[d] Determined from ROI (region of interest-an area circumscribing the area of FDG uptake but dependent on processing algorithm used).
[e] Extrapolated from survival curves provided within article.
[f] Reported a complete analysis for stage Ib NSCLC only, however, outcome for stage I NSCLC could be extrapolated from data provided.
[g] Calculated from data provided in Table 3 of this study.
N/A, not available; SUV, standardized uptake value; PET, positron emission tomography; FDG, ^{18}F-fluorodeoxyglucose; NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval.

TABLE 4. FDG Uptake and Survival in Stage Ia/Ib NSCLC

Stage	Study	*n*	Survival Metric	Percent Survival		
				High SUV	Low SUV	*p* value
Ia	Higashi et al.	38	5 yr DFS	25	85	0.001
	Cerfolio et al.	59	4 yr DFS	70	100	NS[a]
	Ohtsuka et al.	63	2 yr DFS	75	95	0.024
	Downey et al.	249	2 yr OS	85	90	0.91
Ib	Cerfolio et al.	82	4 yr OS	66	80	0.048[b]
	Ohtsuka et al.	35	2 yr DFS	85	100	0.001
	Downey et al.	131	2 yr OS	60	80	0.24

[a] Reported as not significant, however, full details of analysis not provided within text.
[b] Survival based on dichotomized median SUV_{max} of 10.3.
NS, not significant; SUV, standardized uptake value; FDG, ^{18}F-fluorodeoxyglucose; NSCLC, non-small cell lung cancer; OS, overall survival; DFS, disease free survival.

based on FDG uptake alone, the combination of adenocarcinoma, smaller tumor size, and low FDG uptake analyzed together identified a subgroup of patients with a favorable prognosis. Although reasons for discordant findings across the nine included studies are not readily apparent, heterogeneity in staging methods and histologic subtypes could be partly responsible.

We attempted to limit heterogeneity in study methods by restricting our analysis to patients with surgically treated, stage I NSCLC. *Posthoc*, we identified additional data from our search that examined the effect of FDG uptake on survival for patients with early-stage NSCLC who had surgical resection with curative intent (Table 5).[21,28,30–33] These data suggest similar between-group differences in survival for patients with low versus high FDG uptake.

A recent review by de Geus-Oei et al.[17] examined FDG uptake and prognosis in patients with all stages of NSCLC for 11 studies from 1998 to 2006. All 11 studies reported a significant association between FDG uptake and prognosis, although adjustments for potential confounders were not reported. A meta-analysis from 2008 by the European Lung Cancer Working Party identified 13 studies examining FDG uptake and prognosis for patients with NSCLC between 1998 and 2005.[18] In patients with stage I to III disease, they found that the hazard of death was twice as great in patients with high FDG uptake compared with those with low FDG uptake (HR 2.09, 95% CI 1.54–2.83). Neither study performed a separate analysis for patients with stage I disease.

Like our study, both the European Lung Cancer Working Party and de Geus-Oei et al. identified significant heterogeneity in methods across studies. PET scanner resolution, tumor volume, time to injection, and serum glucose are all thought to affect FDG uptake.[15,34–36] SUV_{max} may be more reproducible than average SUV[37] but much of the variability in measuring FDG uptake cannot be corrected for and standardized protocols are required. The use of FDG-PET as an additional determinant of prognosis in patients with NSCLC requires implemenation of recommendations for standardizing patient preparation, image acquisition, reconstruction, and processing. To facilitate these efforts, The European Organization for Research and Treatment of Cancer PET Study Group and the Cancer Imaging Program of the National Cancer Institute have developed guidelines for the use of FDG-PET imaging in determining prognosis.[15]

Studies included in this review had significant limitations. Two of nine studies included fewer than 50 patients with stage I NSCLC. All studies were retrospective and cross-sectional in design and four performed *posthoc* analyses for patients with stage I NSCLC. Six of nine studies did not adjust for potential confounders. Four of nine studies determined FDG uptake thresholds *posthoc* by selecting a favorable cutpoint, whereas the remaining studies used a prespecified definition of median SUV or "positive" FDG uptake as a threshold.

A critical question that remains unanswered in the treatment of NSCLC is who should receive adjuvant therapy after

TABLE 5. Studies Examining FDG Uptake and Prognosis in Patients with Early-Stage, Resected NSCLC

Study	Year	n^a	Stage	SUV Threshold[b]	Survival Metric	Percent Survival		
						High SUV	Low SUV	*p* value
Ahuja et al.	1998	69	Stage I/II	10	4 yr OS	40	40	NS
Sasaki et al.	2005	90[c]	Stage I/II	5	2 yr DFS	57	76	0.02
Cerfolio et al.	2005	57	Stage II	12.9	4 yr OS	32	64	0.028
van Baardwijk et al.	2007	102	Stage I/II[d]	8/11[e]	2 yr OS	59	91	0.001
Vesselle et al.	2007	103	Stages I–IIIA[f]	7	5 yr OS	N/A	N/A	NS[g]
Hanin et al.	2008	21	Stage II	7.8	2 yr OS	60	100	0.11

[a] All patients had resection.
[b] All values are for SUV_{max}.
[c] Eighteen patients received radiation therapy.
[d] Clinical staging.
[e] For two different PET scanners.
[f] Stage IIIA was T_3N_1 disease.
[g] Unadjusted HR for death in this group was 1.21, 95% CI 0.47–3.16.
NS, not significant; N/A, Not available; SUV, standardized uptake value; PET, positron emission tomography; FDG, ^{18}F-fluorodeoxyglucose; NSCLC, non-small cell lung cancer; OS, overall survival; DFS, disease free survival; HR, hazard ratio; CI, confidence interval.

resection. The recently released lung adjuvant cisplatin evaluation meta-analysis showed a 5.4% absolute overall survival benefit for patients with resected NSCLC (stages I–III) who received adjuvant chemotherapy.[38] However, early chemotherapy related mortality was substantial, with 342 of 2390 patients dying from "non-lung cancer deaths" (HR 2.41, 95% CI 1.64–3.55) within the first 6 months of follow-up. This translated to a 2% reduction in nonlung cancer survival for the chemotherapy arm within the first 6 months. In addition, adjuvant chemotherapy in patients with stage Ia NSCLC showed a trend toward harm (HR 1.40, 95% CI 0.95–2.06). Although treatment of patients with stage Ib NSCLC showed a nonsignificant trend toward benefit in this meta-analysis (HR 0.93, 95% CI 0.78–1.10), a recent follow-up of the CALGB 9633 trial showed a diminution of survival benefit over time for these patients.[39]

Clearly, we need additional markers of prognosis beyond that of TNM staging alone for risk stratification and selection of patients for adjuvant therapy. The degree of FDG uptake in the primary tumor may define a subgroup of patients with resected NSCLC and a poor prognosis who would be appropriate candidates for enrollment in future studies of adjuvant therapy. A "prognostic index" can be envisioned that would take into account not only known predictors of survival like TNM staging but also newer modalities including biomarkers and functional imaging.

CONCLUSION

We identified nine studies that examined FDG uptake and prognosis in patients with surgically treated, stage I NSCLC. Although significant heterogeneity existed across studies included in this review, we found substantial evidence that the degree of FDG uptake in the primary tumor is associated with prognosis in these patients. Future studies of FDG-PET and prognosis in patients with surgically treated, stage I NSCLC should enroll participants prospectively and consecutively, use standardized protocols for FDG PET acquisition and processing, adjust for potential confounders in the analysis (tumor size and histology), and determine the optimal threshold value of SUV_{max} that best identifies patients with an unfavorable prognosis who might benefit from adjuvant therapy. In addition, randomized trials of adjuvant chemotherapy seem to be justified in patients with resected, stage I NSCLC who are at increased risk of recurrence and death based on a high degree of FDG uptake in the primary tumor.

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