Pattern of Failure Following Chemoradiation for Locally Advanced Non-small Cell Lung Cancer: Potential Role for Stereotactic Body Radiotherapy

NAM P. NGUYEN[1], MARIA BISHOP[2], THOMAS J. BOROK[3], JAMES WELSH[4], RUSS HAMILTON[1], DEIRDRE COHEN[1], LY M. NGUYEN[5] and VINH-HUNG VINCENT[6]

[1]Department of Radiation Oncology, and [2]Division of Hematology Oncology, University of Arizona, Tucson, AZ, U.S.A.;
[3]Borok-M.D.P.A, Dallas, TX, U.S.A.;
[4]Department of Radiation Oncology, University of Texas at M.D. Anderson, Houston, TX, U.S.A.;
[5]School of Public Health, University of Michigan, Ann Arbor, MI, U.S.A.;
[6]Department of Radiation Oncology, University of Geneva, Geneva, Switzerland

Abstract. *Standard of care for locally advanced non-small cell lung cancer has been concurrent chemoradiation. However, optimal chemotherapy regimen, radiation therapy dose and treatment volume have not been clearly defined despite 30 years of controlled clinical trials. This review analyzes survival and failure pattern reported from randomized studies of chemoradiation for non-small cell lung cancer. Despite introduction of new chemotherapy agents, survival remained poor; rates of both locoregional failures and distant metastasis remained high. The current radiation dose appears insufficient to reliably establish local control. Stereotactic body radiotherapy may allow radiation dose escalation and should be tested in future clinical trials.*

It is estimated that over 200,000 patients will develop bronchogenic carcinoma in the United States with non-small cell lung cancer (NSCLC) the predominant histologic cell type (1). One third of these patients will present with locally advanced stages. Radiation alone has poor outcome compared to combined modality of chemotherapy and radiation (2-5). Median survival was significantly improved with the addition of chemotherapy. Improvement in survival was attributed to the reduced rate of distant metastasis in the combined therapy as local control remained poor with or without chemotherapy (4). Concurrent chemoradiation provides improved survival and local control compared to sequential chemotherapy and radiation with higher toxicity (6). Traditional chemotherapy agents have been based on platinum moiety agents combined with radiation (7-10). Newer agents (gemcitabine and paclitaxel) thought to be superior radiation sensitizers were subsequently introduced into combination programs with prospects of superior therapeutic ratio (11-14). It remains unclear which chemotherapy regimen or radiation therapy dose fractionation are optimal for locally advanced NSCLC. Thus, further analysis of local failure/survival patterns from randomized chemoradiation trials for locally advanced NSCLC may clarify these unanswered questions and help design future clinical trials. If locoregional failures rates remain a significant issue, radiotherapy dose escalation may improve survival. The introduction of stereotactic body radiotherapy (SBRT) allows significant improvement in survival of early stages NSCLC and may have an impact on locally advanced stages (15). However, if a high rate of distant metastasis is responsible for poor survival, the addition of selective target agents to conventional chemotherapy may be considered based on molecular predictors of response to these agents (16).

Correspondence to: Nam P. Nguyen, MD, Associate Professor of Radiation Oncology, Department of Radiation Oncology, University of Arizona, 1501 N. Campbell Ave, Tucson, AZ 85724-5081, U.S.A. Tel: +1 5206947236, Fax: +1 5206947236, e-mail: NamPhong.Nguyen@yahoo.com

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Patients and Methods

This systematic review was designed to investigate locoregional control, survival and complications rate from reported randomized chemoradiation trials for locally advanced NSCLC. The search was based on PubMed, Embase, and Google Scholar electronic data bases. The following terms were explored and used for each data base search: non-small cell lung carcinoma, locally advanced (stage IIIA and IIIB), concurrent chemotherapy and radiation. Reference lists of relevant papers were then secondarily searched for additional

publications. Data was extracted to analyze each article for: tumor stage, chemotherapy regimen, radiation therapy dose fractionation, radiation therapy technique and treatment volume, locoregional control, distant metastasis rate and complications. Using these criteria, we identified 20 valid relevant randomized trials delivering concurrent chemoradiation (6-14, 17-27).

Results

Randomized trials with conventional chemotherapy agents. Conventional chemotherapy agents used concurrently with radiation for NSCLC were cisplatin or carboplatin either alone or combined with etoposide, mitomycin, vinblastine and vinorelbine. Radiation dose to the tumor ranged from 60-74 Gy for once daily fractionation (*qd*) or 69.6 Gy for twice daily fractionation (*bid*). Radiation therapy technique varied with institutional preference. Except for one study (5), ipsilateral mediastinum was treated to 40-45 Gy. Ipsilateral supraclavicular and lower mediastinum lymph node regions were treated prophylactically when tumor involved upper and lower lobe respectively. In selective institutions, contralateral hilum was irradiated (22-24). Despite delivering radiotherapy to a large mediastinal volume which significantly increased the rates of severe pneumonitis (grade 3 to 5), locoregional failures remained high and accounted in part to the poor survival observed in these studies. Three and five-year survival ranged from 10-29% and 5%-25% respectively (6-10, 17-25, 27). Locoregional failures ranged from 31-100%. In studies which reported regional failures separately from local failures, mediastinal lymph node recurrences ranged from 4% to 56% (8, 18, 21, 23). High rates of distant metastasis were also observed ranging from 18% to 71%. It was unclear whether the poor locoregional control contributed to the high rates of distant metastasis or these patients may have had micrometastases at diagnosis. Mediastinal radiation also induced significant damage to the esophagus as the full length and circumference of the thoracic esophagus were included in the radiation fields. Severe esophagitis required treatment interruption to allow patient recovery and may compromise outcome because of tumor re-growth during radiotherapy. However, treatment breaks during radiotherapy were not specified in most studies. Thus, acute toxicity during chemoradiation were predominantly grade 3-4 hematologic, esophagitis and pneumonitis with fatal pneumonitis reported in two studies (21, 24). Tables I and II summarize survival and failure pattern respectively for concurrent chemoradiation with conventional chemotherapy agents for locally advanced non-small cell lung cancer.

Randomized trials with new chemotherapy agents. Five randomized trials reported survival associated with newer chemotherapy agents (paclitaxel, docetaxel, gemcitabine and vinorelbine) and radiation for locally advanced non-small cell lung cancer. Four trials used induction chemotherapy followed by concurrent chemoradiation (11-14). Radiation therapy technique and tumor dose (60-66 Gy) was similar to the studies using conventional chemotherapy (platinum-based) chemotherapy agents. Three-year survival ranged from 18.6% to 29% which was not different from the ones reported in studies with conventional chemotherapy agents (12-14, 26). One study reported 5-year survival 25% (11). Locoregional recurrence remained high ranging from 30% to 85%. One study reported regional recurrence rates of 36% to 40% with gemcitabine, paclitaxel and vinorelbine (12). Distant metastasis rates were also elevated ranging from 20% to 60%. Thus, induction chemotherapy with new chemotherapy agents did not seem to decrease distant metastasis rates which raised the possibility that poor locoregional control was the cause of distant failures. The acute toxicity profile was comparable to conventional chemotherapy agents with grade 3-4 hematologic toxicity, predominantly esophagitis and pneumonitis with fatal pneumonitis reported in one study (12). Despite introduction of new chemotherapy agents, there was no change in survival and failure pattern which suggested that unless radiation dose escalation can be safely delivered in future clinical trials, there will be little improvement in patient outcome. In order for radiotherapy to be effective, treatment toxicity should be reduced to avoid treatment breaks and late pneumonitis related to radiation of a significant lung volume. Stereotactic body radiotherapy is particularly suitable for that purpose because the rapid radiotherapy dose fall off with current image-guided radiotherapy technique. At a distance of 1.4 cm from the tumor, radiation dose fell rapidly from 174 Gy to 10 Gy (28).

Tables III and IV summarize survival and failure pattern following concurrent chemotherapy and radiation using new chemotherapy agents for locally advanced non-small cell lung cancer. Table V summarizes acute grade 3-4 toxicity reported from all randomized trials for locally advanced non-small cell lung cancer.

Discussion

To our knowledge, this is the first study to compare survival and pattern of failure following concurrent chemoradiation for locally advanced NSCLC with conventional and new chemotherapy agents. In a meta-analysis (29), third-generation chemotherapy agents (paclitaxel, docetaxel, gemcitabine, vinorelbine, and irinotecan) have been proven to increase survival in patients with locally advanced or metastatic NSCLC compared to conventional chemotherapy agents (cisplatin, etoposide, vindesine, mitomycin, and ifosfamide). Thus, it follows when combined with radiation therapy, further potential gains may be achieved in local control and survival for locally advanced NSCLC as these agents were excellent radiation sensitizers (14, 30-32). Except for one study (8),

Table I. *Outcome of conventional chemotherapy concurrently with radiation for locally advanced non-small cell lung cancer.*

Study	Patient no.	Stage dose (Gy)	Chemotherapy	Tumor	Survival
Furuse *et al*. (6)	158	49IIIA 109IIIB	Cisp 80 mg/m^2 d1, 29, vindesin 3 mg/m^2 d1, 29 and mitomycin 8 mg/m^2 d1, 29	56	5-y 17.9% *et al*. (3)
Schild *et al*. (7)	234	123IIIA 121IIB	Cisp 30 mg/m^2 d1-3, d28-30 etoposide 100 mg/m^2 d1-3, d28-30	60	2-y 37% *qd* 2-y 40% *bid*
Yuan *et al*. (8)	200	124IIIA 76IIIB	Cisp 25 mg/m^2 d1-3, etoposide 75 mg/m^2 d1-5 q 3 weeks	68-74 60-64	5-y 25% 5-y 18%
Ball *et al*. (9)	105	49IIIA 32IIIB	Carboplatin 70 mg/m^2 d1-5, d35-40 5-y 5% *bid*	60	5-y 8% *qd*
Bonner *et al*. (10)	32	17IIIA 15IIIB	Cisp 30 mg/m^2 d1-3, d28-30 etoposide 100 mg/m^2 d1-3, d28-30	60	3-y 10%
Fournel *et al*. (17)	100	33IIIA 67IIIB	Cisp 20mg/m^2 d1-5, d29-34 etoposide 50 mg/m^2 d1-5, d29-34	66	4-y 14.2%
Komaki *et al*. (18)	162	NS	Cisp 75 mg/m^2 d50, 71, 92 (induction+concurrent) Cisp 50 mg/m^2 d1,8, etoposide 75-100 mg/m^2 d1-10 (concurrent)	63 69.6	1-y 65% 1-y 58%
Jeremic *et al*. (19)	195	103IIIA 92IIIB	Carboplatin and etoposide 50 mg/m^2/5d/week Carboplatin and etoposide 30 mg/m^2/5d/week and carboplatin and etoposide 100 mg/m^2/d/weekend	69.6	5-y 20% 5-y 23%
Cakir and Egehan (20)	88	61IIIA 27IIIB	Cisp 20 mg/m^2 d1-5, week 2, 6	64	3-y 10%
Clamon *et al*. (21)	130	70IIIA 60IIIB	Carboplatin 100 mg/m^2/week, week 1-6	60	4-y 13%
Jeremic *et al*. (22)	108	53IIIA 55IIIB	Carboplatin 100 mg/m^2 d1-2/week, etoposide 100 mg d1-3/week Carboplatin 200 mg/m^2 d1-3, week 1, 3, 5, etoposide 100 mg/m^2 d1-5/week1, 3, 5	64.8	5-y 21% 5-y 16%
Jeremic *et al*. (23)	65	33IIIA 32IIIB	Carboplatin 50 mg/m^2/d, etoposide 50 mg/m^2/d	69.6	4-y 23%
Blanke et al (24)	104	7I+II 57IIIA 40IIIB	Cisp 70 mg/m^2 week 1, 3, 5	60-65	5-y 5%
Dasgupta *et al*. (25)	36	24IIIA 12IIIB	Cisp 20 mg/m^2 d1-5, d22-26, etoposide 120 mg/m^2 d1-5, d22-26	50	2-y 66%
Belderbos *et al*. (27)	80	45IIIA 47IIIB	Cisp 6 mg/m^2 *qd*	66	3-y 29%

Cisp: Cisplatinum; d: day; *qd*: once a day; *bid*: twice a day; y: year.

radiation therapy technique and dose was comparable among the studies with tumor dose and mediastinal dose ranging from 60-66 Gy and 40-45 Gy, 69.6 Gy and 50.4 Gy respectively for once a day fractionation and twice a day fractionation. Three-year survival remained poor for all chemotherapy regimens (less than 30%) despite severe grade 3-4 toxicity during concurrent chemoradiation and occasional death from pneumonitis. Locoregional recurrences remained the predominant failure pattern. Distant metastasis rates also remained unacceptably high despite induction chemotherapy

Table II. *Pattern of failure reported following concurrent chemoradiation for locally advanced non-small cell lung cancer with conventional chemotherapy agents.*

Study	Local recurrence	Regional recurrence	Locoregional Recurrence	Distant metastasis	Follow-up (months)
Furuse *et al.* (6)	NS	NS	32% (5-y)	47% (5-y)	NS
Schild *et al.* (7)	NS	NS	45% (*qd*) (2-y) 41% (*bid*)	33% (*qd*) (2-y) 34% (*bid*)	NS
Yuan *et al.* (8)	49% (68-74 Gy) 64% (60-64 Gy)	7% (68-74 Gy) 4% (60-64 Gy)	56% (68-74 Gy) 68% (60-64 Gy)	25% (5-y) 18%	27
Ball *et al.* (9)	NS	NS	NS	NS	NS
Bonner *et al.* (10)	NS	NS	70% (3-y)	78% (3-y)	30
Fournel *et al.* (17)	NS	NS	31% (4-y)	34% (4-y)	NS
Komaki *et al.* (18)	50% (*qd*) (1-y) 29% (*bid*)	37% (*qd*) (1-y) 27% (*bid*)	87% (*qd*) (1-y) 56% (*bid*)	34% (*qd*) (1-y) 33% (*bid*)	NS
Jeremic *et al.* (19)	NS	NS	72% (5 days) (5-y) 73% (7 days)	71% (5 days) (5-y) 66% (7 days)	NS
Cakir and Egehan *et al.* (20)	NS	NS	71% (3-y)	31% (3-y)	NS
Clamon *et al.* (21)	43% (4-y)	16% (4-y)	59% (4-y)	40% (4-y)	NS
Jeremic *et al.* (22)	NS	NS	66% (low dose CP) 80% (high dose CP)	51% (5-y) 48%	NS
Jeremic *et al.* (23)	73% (4-y)	56% (4-y)	100% (4-y)	60% (4-y)	NS
Blanke *et al.* (24)	NS	NS	48% (5-y)	48% (5-y)	52
Dasgupta *et al.* (25)	NS	NS	51% (2-y)	44% (2-y)	24
Belderbos *et al.* (27)	NS	NS	46% (3-y)	50% (3-y)	39

NS: Not specified; *qd*: once a day; *bid*: twice a day; CP: carboplatin; y: year.

with new chemotherapy agents which suggested that poor locoregional control leads to distant failures. The failure pattern of concurrent chemoradiation for locally advanced NSCL was also similar to sequential chemoradiation with high rates of locoregional failures and distant metastasis ranging from 64%-69% and 36%-46% respectively (17, 33). It is clear that conventional radiation dose is inadequate to reliably reproducibly establish local control. In a dosimetric study, Moreno-Jimenez *et al.* (34) demonstrated that most local recurrences were located in area of high radiation dose within the tumor in patients undergoing concurrent chemoradiation for locally advanced NSCLC. The effect of radiation on the

Table III. *Outcome of new chemotherapy agents concurrently with radiation for locally advanced non-small cell lung cancer.*

Study	Patient no.	Stage (Gy)	Chemotherapy	Tumor dose	Survival
Huber *et al*. (11)	99	10IIIA 88IIIB 1NS	Induction Paclitaxel 200 mg/m^2 followed by CP AUC6 d1-22 Concurrent Paclitaxel 60 mg/m^2 weekly	60-66	3-y 29% 5-y 25%-
Vokes *et al*. (12)	175	92IIIA 83IIIB	*1*: Induction Cisp 80 mg/m^2 d1,22, Gemc 1250 mg/m^2 d1, 8, 22, 29 followed by concurrent Gemc 600 mg/m^2 d43, 50, 64, 71 during RT *2*: Induction Cisp 80 mg/m^2 d1, 22, Paclitaxel 225 mg/m^2 d1, 22 followed by concurrent Paclitaxel 125 mg/m^2 d43, 64 during RT *3*: Induction Cisp 80mg/m^2 d1, 22, vinorelbine 25 mg/m^2 d1, 8, 15, 22, 29 followed by concurrent Vinorelbine 25 mg/m^2 d43, 50, 64, 71 during RT	66	3-y 28% 3-y 19% 3-y 23%
Gouda *et al*. (13)	40	9IIIA 21IIIB	*1*: Induction Paclitaxel 175 mg/m^2, CP AUC6 d1-28 followed by concurrent chemoradiation. *2*: Concurrent chemoradiation alone (Paclitaxel 45 mg/m^2 and CP AUC2 weekly during RT)	60	2-y 40% 2-y 45%
Scagliotti *et al*. (14)	43	11IIIA 32IIIB	Induction Docetaxel 85 mg/m^2 d1, Cisp 40 mg/m^2 d1-2 q 3 weeks for 2 cycles followed by concurrent Docetaxel 20 mg/m^2 weekly during RT	60	2-y 30%
Zatloukal *et al*. (26)	52	8IIIA 44IIIB	Cisp 80 mg/m^2 d1, Vinorelbine 25 mg/m^2 d1, 8, 15 every 4 weeks	60	3-y 18.6%

CP: Carboplatin; AUC: area under curve, Cisp: cisplatin; Gemc: gemcitabine; y: year.

Table IV. *Pattern of failure reported following concurrent chemoradiation for locally advanced non-small cell lung cancer with new chemotherapy agents*.

Study		LR	RR	Locoregional recurrence	Distant metastasis	Follow-up (months)
Huber *et al*. (11)		NS	NS	65.7% (3-y)	NS	37.4
Vokes *et al*. (12)	Gemc	46%	38%	84% (3-y)	41% (3-y)	NS
	Paclitaxel	46%	36%	82%	63%	
	VB	45%	40%	85%	49%	
Gouda *et al*. (13)		NS	NS	NS	NS	NS
Scagliotti *et al*. (14)		NS	NS	30% (2-y)	20% (2-y)	NS
Zatloukal *et al*. (26)		NS	NS	63% (3-y)	44% (3-y)	39

NS: Not specified; Gemc: gemcitabine; VB: vinorelbine; y: year.

tumor is assessed with the biologic equivalent dose (BED10) based on the linear-quadratic equation: BED10 = nd [1+d/(α/β)] where n and d represent the number of fractions and the dose per fraction, respectively. If one takes into consideration that for early stages NSCLC, a minimal BED dose of 100 Gy is required for tumor control of small lesions (T1) (35) , current radiotherapy dose of 60-66 Gy is clearly inadequate for locally advanced diseases (T2-T4). Thus,

Table V. *Acute grade 3-4 complications reported during concurrent chemoradiation for locally advanced non-small cell lung cancer.*

Study	Patient no.	Grade 3-4 complications
Furuse *et al*. (6)	158	98% Neutropenia, 58% thrombocytopenia, 10% anemia, 2% esophagitis, 1% pneumonitis.
Shild *et al*. (7)	234	*qd* RT: 78% Neutropenia, 29% thrombocytopenia, 20% esophagitis, 11%pneumonitis *bid* RT: 79% Neutropenia, 19% thrombocytopenia, 18% esophagitis, 15% pneumonitis
Yuan *et al*. (8)	200	68-74 Gy: 4% Esophagitis, 2% myelosuppression, 1% pneumonitis 60-64 Gy: 5% Esophagitis, 4% myelosuppression, 3% pneumonitis
Ball *et al*. (9)	105	*qd* RT: 21% Esophagitis, 13% pneumonitis, 6% thrombocytopenia *bid* RT: 48% Esophagitis, 4% thrombocytopenia, 2% neutropenia.
Bonner *et al*. (10)	32	69% Neutropenia, 21% thrombocytopenia, 13% esophagitis
Huber *et al*. (11)	99	12.8% Esophagitis
Vokes *et al*. (12)	175	Gemcitabine: 56% thrombocytopenia, 51% neutropenia, 32% anemia, 52% esophagitis, 14% pneumonitis Paclitaxel: 53% neutropenia, 6% thrombocytopenia, 4% anemia, 39% esophagitis, 20% pneumonitis. Vinorelbine: 65% neutropenia, 19% anemia, 2% thrombocytopenia, 25% esophagitis, 20% pneumonitis, 1 patient died from respiratory failure.
Gouda *et al*. (13)	40	Concurrent chemoradiation: 80% hematologic, 25% esophagitis induction chemotherapy followed by concurrent chemoradiation: 100% hematologic, 30% esophagitis.
Scagliotti *et al*. (14)	43	80% Lymphocytopenia, 17% esophagitis
Fournel *et al*. (17)	100	77% Neutropenia, 20% anemia, 16% thrombocytopenia, 32% esophagitis, 24% nausea and vomiting, 5% pneumonitis
Komaki *et al*. (18)	162	*qd*: 62% Hematologic, 6% esophagitis *bid*: 33% hematologic, 38% esophagitis
Jeremic *et al*. (19)	195	5-d Chemotherapy: 15% esophagitis, 12% hematologic, 12% pneumonitis 7-d Chemotherapy: 28% hematologic, 17% esophagitis, 13% pneumonitis
Cakir and Egehan (20)	88	24% Nausea and vomiting, 15% neutropenia, 10% esophagitis
Clamon *et al*. (21)	130	25% Neutropenia, 17% anemia, 14% thrombocytopenia, 12% esophagitis 2 patients died from pneumonitis
Jeremic *et al*. (22)	108	Low dose carboplatin: 16.8% (type of complications not specified) High dose carboplatin: 27% (type of complications not specified)
Blanke *et al*. (24)	104	5% Neutropenia, 3% esophagitis, 2 patients died (1 pneumonitis, 1 heart failure)
Dasgupta *et al*. (25)	36	28% Esophagitis, 19% anemia
Zatloukal *et al*. (26)	52	65% Neutropenia, 12% anemia, 6% thrombocytopenia, 18% esophagitis, 4% pneumonitis, 4% neurologic, 2% cardiac
Belderbos *et al*. (27)	80	17% Esophagitis, 4% neutropenia

qd: Once a day; *bid*: twice a day; RT: radiation therapy.

escalating radiation dose to the tumor may potentially improve survival by improving local control. Yuan *et al*. (8) demonstrated the feasibility of radiation dose escalation reducing local recurrence rate to 49% from 64%, using tumor dose of 68-74 Gy compared to 60-64 Gy respectively. The mediastinum was not radiated electively for patients in the high radiation dose group and may account for favorable toxicity rate. This innovative radiotherapy technique allowed sparing of the esophagus from radiation, thus preventing treatment breaks which may compromise local control because of tumor accelerated repopulation. In addition, pneumonitis rates decreased because of the reduced lung volume exposed to radiation. To illustrate our argument, dose escalation does carry the increased toxicity risk when the mediastinum was included in the radiation fields. Socinski *et al*. (32) reported preliminary results of a randomized study comparing carboplatin-paclitaxel and carboplatin-gemcitabine concurrently with radiation for locally advanced non-small cell lung cancer. The tumor dose was 74 Gy in both arms. Grade 3-4 pneumonitis rate was respectively 16% and 37% for paclitaxel- and gemcitabine-based chemotherapy regimen. There were two reported deaths from pneumonitis (7%) in the gemcitabine arm. Gemcitabine was discontinued prematurely because of the toxicity. Stinchcombe *et al*. (36) also confirmed the feasibility of dose escalation to 74 Gy with three-dimensional conformal thoracic radiation for NSCLC. Gefinitib was combined with paclitaxel and carboplatin for concurrent chemoradiation. A high rate of grade 3 esophagitis (19.5%) and cardiac arythmia (9.5%) was observed. However, grade 3 pneumonitis rate was low (4.8%) in this study.

Grade 3-4 pneumonitis and esophagitis remained limiting factors for patients undergoing concurrent chemoradiation for locally advanced NSCLC. Toxicity of combined modality was related to volume of normal tissue lung and esophagus irradiated (37-39). Thus, limiting radiation target volume to gross tumor and pathologically enlarged lymph nodes instead of elective whole mediastinal irradiation may substantially decrease treatment toxicity (8) and may be an adequate elective treatment volume in the environment of substantial chemotherapy. Incorporation of positron emission tomography (PET) in radiation treatment planning may improve treatment accuracy, avoid marginal miss, and decrease treatment toxicity (40). De Ruysscher *et al*. (41) demonstrated feasibility for such approach. In 44 patients with non-metastatic NSCLC, tumor bed and positive nodes seen on pretreatment PET were irradiated. Twenty-nine patients had radiation dose escalation to 64.8 Gy (1.8 Gy *bid*). Only one patient recur in the mediastinum outside of irradiated area. Treatment toxicity was minimal with only two patients developing severe pneumonitis (1) and esophagitis (1). A different alternative to reduce treatment toxicity was to repeat the PET/CT in weeks 5-6 of radiation and to boost the residual tumor to a higher dose (42).

Tumor shrinkage allow high tumor dose (78 Gy) delivery while sparing normal tissues from excess radiation. Such approach may have a predictive value for survival as post-chemotherapy gross tumor volume has been demonstrated to correlate with prognosis (43). The introduction of stereotactic body radiotherapy (SBRT) provided a feasible technique of radiation which effectively increased tumor dose while sparing normal tissues. In early stages NSCLC, local control and survival were comparable to surgery in patients with multiple co-mor*bid*ities precluding surgery (15). Stereotactic body radiotherapy technique may allow increased local control and survival for locally advanced NSCLC as well by targeting the PET positive tumor and grossly enlarged mediastinal lymph nodes to a high radiation dose. Pulmonary function test performed following SBRT for early stages NSCLC demonstrated the safety of this technique in patients with limited pulmonary function (44). There was minimal changes in forced expiratory volume at 1 second (FEV1) and diffusion capacity to carbon monoxide (DLCO) following SBRT as the amount of lung radiated to lung tolerance dose was reduced (55). Thus, SBRT to PET-positive tumor areas instead of mediastinal radiotherapy with conventional radiotherapy techniques may be an innovative mean to increase radiotherapy dose for locoregional control because of the high radio biologic equivalent dose achieved with this technique.

Conclusion

Concurrent chemoradiation for locally advanced NSCLC remains associated with poor survival and significant toxicity. Locoregional failures and distant metastasis rates remain high despite second- and third-generation systemic chemotherapy agents. Current radiation therapy dose with conventional radiotherapy techniques is inadequate to reliably reproducibly establish local control. Clinicians should investigate alternative techniques of radiation such as SBRT to permit tumor dose increase while minimizing normal tissue toxicity.

Conflict of Interest

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