Radiotherapeutic Care of Patients With Stage IV Lung Cancer with Thoracic Symptoms in the Veterans Health Administration

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Background: Radiotherapy plays an important role in the palliation of lung cancer, which is the second most common cancer diagnosed in the Veterans Health Administration (VHA). The American Society for Radiation Oncology (ASTRO) developed evidenced-based treatment guidelines for the management of patients with metastatic lung cancer.

Methods: In May 2016, an electronic survey of 88 VHA radiation oncologists (ROs) was conducted to assess metastatic lung cancer management. Demographic information was obtained and 2 clinical scenarios were presented to glean opinions on dose/fractionation schemes preferred, preferences for/against concurrent chemotherapy, and use of endobronchial brachytherapy (EBB) and/or yttrium aluminum garnet (YAG) laser technology. Survey results were assessed for concordance with published ASTRO guidelines.

Results: The survey response rate was 61%, with 93% of the 40 VHA radiation departments represented. Among respondents, 96% were board certified, and 90% held academic appointments. 88% were familiar with ASTRO guidelines. Preferred fractionation schemes were 20 Gy in 5 fractions (69%) and 30 Gy in 10 fractions (22%). The vast majority (98%) did not recommend concurrent chemotherapy for palliation. In the setting of bronchial obstruction with lung collapse, about half (49%) recommended EBB or YAG lung reexpansion before external beam radiotherapy. A minority of respondents use stereotactic body radiotherapy or EBB for palliation.

Conclusion: Most respondents demonstrated up-to-date knowledge of current evidence-based treatment guidelines. We found no distinction in clinical decisions based on demographic profiles.

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Lung cancer is the leading cause of cancer mortality both in the US and worldwide.[1] Many patients diagnosed with lung cancer present with advanced disease with thoracic symptoms such as cough, hemoptysis, dyspnea, and chest pain.[2-4] Palliative radiotherapy is routinely used in patients with locally advanced and metastatic lung cancer with the goal of relieving these symptoms and improving quality of life. Guidelines published by the American Society for Radiation Oncology (ASTRO) in 2011, and updated in 2018, provide recommendations on palliation of lung cancer with external beam radiotherapy (EBRT) and clarify the roles of concurrent chemotherapy and endobronchial brachytherapy (EBB) for palliation.[5,6]

After prostate cancer, lung cancer is the second most frequently diagnosed cancer in the Veterans Health Administration (VHA).[7] The VHA consists of 172 medical centers and is the largest integrated health care system in the US. At the time of this study, 40 of these centers had onsite radiation facilities. The VHA Palliative Radiation Taskforce has conducted a series of surveys to evaluate use of palliative radiotherapy in the VHA, determine VHA practice concordance with ASTRO and American College of Radiology (ACR) guidelines, and direct educational efforts towards addressing gaps in knowledge. These efforts are directed at ensuring best practices throughout this large and heterogeneous healthcare system. In 2016 a survey was conducted to evaluate concordance of VHA radiation oncologist (RO) practice with the 2011 ASTRO guidelines on palliative thoracic radiotherapy for non-small cell lung cancer (NSCLC).

METHODS

A survey instrument was generated by VHA National Palliative Radiotherapy Taskforce members. It was reviewed and approved for use by the VHA Patient Care Services office. In May of 2016, the online survey was sent to the 88 VHA ROs practicing at the 40 sites with onsite radiation facilities. The survey aimed to determine patterns of practice for palliation of thoracic symptoms secondary to lung cancer.

Demographic information obtained included years in practice, employment status, academic appointment, board certification, and familiarity with ASTRO lung cancer guidelines. Two clinical scenarios were presented to glean opinions on dose/fractionation schemes preferred, use of concurrent chemotherapy, and use of EBB and/or yttrium aluminum garnet (YAG) laser technology. Survey questions also assessed use of EBRT for palliation of hemoptysis, chest wall pain, and/or stridor as well as use of stereotactic body radiotherapy (SBRT) for palliation.

Survey results were assessed for concordance with published ASTRO guidelines.

χ^2 tests were run to test for associations between demographic factors such as academic appointment, years of practice, full time vs part time employment, and familiarity with ASTRO palliative lung cancer guidelines, with use of EBRT for palliation, dose and fractionation preference, use of concurrent chemotherapy, and strategy for management of endobronchial lesions.

RESULTS

Of the 88 physicians surveyed, 54 responded for a response rate of 61%. Respondents represented 37 of the 40 (93%) VHA radiation oncology departments (Table 1). Among respondents, most were board certified (96%), held academic appointments (91%), and were full-time employees (85%). Forty-four percent of respondents were in practice for > 20 years, 19% for 11 to 20 years, 20% for 6 to 10 years, and 17% for < 6 years. A majority reported familiarity with the ASTRO guidelines (64%), while just 11% reported no familiarity with the guidelines.

When asked about use of SBRT for palliation of hemoptysis, stridor, and/or chest pain, the majority (87%) preferred conventional EBRT. Of the 13% who reported use of SBRT, most (11%) performed it onsite, with 2% of respondents referring offsite to non-VHA centers for the service. When asked about use of EBB for palliation, only 2% reported use of that procedure at their facilities, while 26% reported referral to non-VHA facilities for EBB. The remaining 72% of respondents favor use of conventional EBRT.

Respondents were presented with a case of a male patient aged 70 years who smoked and had widely metastatic NSCLC, a life expectancy of about 3 months, and 10/10 chest wall pain from direct tumor invasion. All respondents recommended palliative radiotherapy. The preferred fractionation was 20 Gray (Gy) in 5 fractions, which was recommended by 69% of respondents. The remainder recommended 30 Gy in 10 fractions (22%) or a single fraction of 10 Gy (9%). No respondent recommended the longer fractionation options of 60 Gy in 30 fractions, 45 Gy in 15 fractions, or 40 Gy in 20 fractions. The majority (98%) did not recommend concurrent chemotherapy.

When the above case was modified for an endobronchial lesion requiring palliation with associated lung collapse, rather than chest wall invasion, 20 respondents (38%) reported they would refer for EBB, and 20 respondents reported they would refer for YAG laser.

TABLE 1 Survey Responses

Questions	No. (%)
Years in practice, y	
< 6	9 (16.7)
6 to 10	11 (20.4)
11 to 20	10 (18.5)
> 20	24 (44.4)
Current or past academic appointment	49 (90.7)
ABR certified	52 (96.3)
Employment status	
Full-time	46 (85.2)
Part-time	6 (11.1)
Contractor	2 (3.7)
Familiar with ASTRO palliative lung cancer guidelines	
Yes	34 (64.2)
No	6 (11.3)
Limited	13 (24.5)
Do you offer SBRT for palliation of hemoptysis, stridor and/or chest pain?	
Yes, on site	6 (11.3)
Yes, we refer off-site to a VA center	0
Yes, we refer off-site to Non-VA	1 (1.9)
No, we use conventional EBRT	46 (86.8)
Do you offer EBB?	
Yes	1 (1.9)
No, we use conventional external beam photon therapy	38 (71.7)
No, I refer off-site to a VA center for EBB	0
No, I refer off-site to a non-VA center for EBB	14 (26.4)
Would use EBRT for chest pain palliation for a male aged 70 y with NSCLC, documented liver and bone metastases, and a life expectancy of 3 mo. has 10/10 chest wall pain from direct tumor invasion. His pain medications are no longer effective.	54 (100)
What fractionation scheme would you use to treat this patient?	
30 Gy in 10 fractions	12 (22.2)
20 Gy in 5 fractions	37 (68.5)
10 Gy in 1 fraction	5 (9.3)
Would you recommend concurrent chemotherapy with palliative radiotherapy?	
Yes	1 (1.9)
No	53 (8.1)
If the lesion were endobronchial (with a collapsed lower lung, rather than direct chest invasion), what would you recommend? (Mark all that apply)	
EBB	20 (37.7)
YAG laser	20 (37.7)
Neither	13 (24.5)
Other	21 (39.6)
Would you recommend EBB or YAG laser for lung reexpansion before definitive radiotherapy?	
Yes	25 (49)
No	26 (51)

Abbreviations: ABR, American Board of Radiology ASTRO, American Society for Radiation Oncology; EBB, endobronchial brachytherapy; EBRT, external beam radiotherapy; NSCLC, non-small cell lung cancer; SBRT, stereotactic body radiotherapy; VA, US Department of Veterans Affairs; YAG, yttrium aluminum garnet.

TABLE 2 Associations between Demographic Background and Treatment Preferences[a]

Item	Familiarity with Guidelines (Yes)	Offer SBRT for palliation of hemoptysis, stridor and/or chest pain (No, use EBRT)	EBRT scheme offered for palliation of chest pain (direct chest wall invasion) (20 Gy in 5 fractions)	Offer concurrent chemotherapy and palliative radiotherapy (for direct chest wall invasion (No)	Offer EBB or YAG laser for lung reexpansion before definitive radiotherapy (Yes)
Years in practice, y, No. (%)					
≤ 5	6 (11.3)	8 (15.1)	6 (11.1)	9 (16.7)	5 (9.8)
6 - 10	6 (11.3)	10 (18.9)	7 (13.0)	11 (20.4)	2 (3.9)
11 - 20	7 (13.2)	7 (13.2)	10 (18.5)	9 (16.7)	5 (9.8)
> 20	15 (28.3)	21 (39.6)	14 (25.9)	24 (44.4)	13 (25.5)
$\chi 2$ (*P*)	2.12 (.91)	5.58 (.47)	7.97 (.24)	4.48 (.24)	5.66 (.13)
Academic appointment, No. (%)					
Yes	30 (56.6)	41 (77.4)	34 (63)	48 (88.9)	23 (45.1)
No	4 (7.5)	5 (9.4)	3 (5.6)	5 (9.3)	2 (3.9)
$\chi 2$ (*P*)	0.89 (.64)	0.84 (.65)	1.35 (.51)	0.10 (.75)	0.18 (.67)
Employment status, No. (%)					
Full time	29 (54.7)	38 (71.7)	32 (59.3)	45 (83.3)	21 (41.2)
Part time	4 (7.5)	6 (11.3)	3 (5.6)	6 (11.1)	3 (5.9)
Contractor	1 (1.9)	2 (3.8)	2 (3.7)	2 (3.7)	1 (2.0)
$\chi 2$ (*P*)	1.13 (.89)	1.43 (.84)	1.94 (.75)	0.18 (.91)	0.27 (.87)
Familiar with ASTRO palliative lung cancer guidelines, No. (%)					
Yes	--	29 (55.8)	25 (47.2)	34 (64.2)	16 (32.0)
No	--	5 (9.6)	2 (3.8)	6 (11.3)	1 (2)
Limited	--	11 (21.2)	9 (17)	12 (22.6)	8 (16)
$\chi 2$ (*P*)	--	1.07 (.89)	0.84 (.30)	3.14 (.21)	3.16 (.21)

Abbreviations: ASTRO, American Society for Radiation Oncology; EBB, endobronchial brachytherapy; EBRT, external beam radiotherapy; SBRT, stereotactic body radiotherapy; YAG, yttrium aluminum garnet.
[a]The results are expressed as percentage of total responses for the item.

As > 1 answer could be selected for this question, there were 12 respondents who selected both EBB and YAG laser; 8 selected only EBB, and 8 selected only YAG laser. Many respondents added comments about treating with EBRT, which had not been presented as an answer choice. Nearly half of respondents (49%) were amenable to referral for the use of EBB or YAG laser for lung reexpansion prior to radiotherapy. Three respondents mentioned referral for an endobronchial stent prior to palliative radiotherapy to address this question.

χ^2 tests were used to evaluate for significant associations between demographic factors, such as number of years in practice, academic appointment, full-time vs part-time status, and familiarity with ASTRO guidelines with clinical management choices (Table 2). The χ^2 analysis revealed that these demographic factors were not significantly associated with familiarity with ASTRO guidelines, offering SBRT for palliation, EBRT fractionation scheme preferred, use of concurrent chemotherapy, or use of EBB or YAG laser.

DISCUSSION

This survey was conducted to evaluate concordance of management of metastatic lung cancer in the VHA with ASTRO guidelines. The relationship between respondents' familiarity with the guidelines and responses also was evaluated to determine the impact such guidelines have on decision-making. The ASTRO guidelines for palliative thoracic radiation make recommendations regarding 3 issues: (1) radiation doses and fractionations for palliation; (2) the role of EBB; and (3) the use of concurrent chemotherapy.[5,6]

Radiation Dose and Fractionation for Palliation

A variety of dose/fractionation schemes are considered appropriate in the ASTRO guideline statement, including more prolonged courses

such as 30 Gy/10 fractions as well as more hypofractionated regimens (ie, 20 Gy/5 fractions, 17 Gy/2 fractions, and a single fraction of 10 Gy). Higher dose regimens, such as 30 Gy/10 fractions, have been associated with prolonged survival, as well as increased toxicities such as radiation esophagitis.[8] Therefore, the guidelines support use of 30 Gy/10 fractions for patients with good performance status while encouraging use of more hypofractionated regimens for patients with poor performance status. In considering more hypofractionated regimens, one must consider the possibility of adverse effects that can be associated with higher dose per fraction. For instance, 17 Gy/2 fractions has been associated with myelopathy; therefore it should be used with caution and careful treatment planning.[9]

For the survey case example (a male aged 70 years with a 3-month life expectancy who required palliation for chest wall pain), all respondents selected hypofractionated regimens; with no respondent selected the more prolonged fractionations of 60 Gy/30 fractions, 45 Gy/15 fractions, or 40 Gy/20 fractions. These more prolonged fractionations are not endorsed by the guidelines in general, and particularly not for a patient with poor life expectancy. All responses for this case selected by survey respondents are considered appropriate per the consensus guideline statement.

Role of Concurrent Chemotherapy

The ASTRO guidelines do not support use of concurrent chemotherapy for palliation of stage IV NSCLC.[5,6] The 2018 updated guidelines established a role for concurrent chemotherapy for patients with stage III NSCLC with good performance status and life expectancy of > 3 months. This updated recommendation is based on data from 2 randomized trials demonstrating improvement in overall survival with the addition of chemotherapy for patients with stage III NSCLC undergoing palliative radiotherapy.[10-12]

These newer studies are in contrast to an older randomized study by Ball and colleagues that demonstrated greater toxicity from concurrent chemotherapy, with no improvement in outcomes such as palliation of symptoms, overall survival, or progression free survival.[13] In contrast to the newer studies that included only patients with stage III NSCLC, about half of the patients in the Ball and colleagues study had known metastatic disease.[10-13] Of note, staging for metastatic disease was not carried out routinely, so it is possible that a greater proportion of patients had metastatic disease that would have been seen on imaging. In concordance with the guidelines, 98% of the survey respondents did not recommend concurrent chemotherapy for palliation of intrathoracic symptom; only 1 respondent recommended use of chemotherapy for palliation.

Role of Endobronchial Brachytherapy

EBB involves implantation of radioactive sources for treatment of endobronchial lesions causing obstructive symptoms.[14] Given the lack of randomized data that demonstrate a benefit of EBB over EBRT, the ASTRO guidelines do not endorse routine use of EBB for initial palliative management.[15,16] The ASTRO guidelines reference a Cochrane Review of 13 trials that concluded that EBRT alone is superior to EBB alone for initial palliation of symptoms from endobronchial NSCLC.[17]

Of respondents surveyed, only 1 facility offered onsite EBB. The majority of respondents (72%) preferred the use of conventional EBRT techniques, while 26% refer to non-VHA centers for EBB. Lack of incorporation of EBB into routine VHA practice likely is a reflection of the unclear role of this technology based on the available literature and ASTRO guidelines. In the setting of a right lower lung collapse, more respondents (49%) would consider use of EBB or YAG laser technology for lung reexpansion prior to EBRT.

The ASTRO guidelines recommend that initial EBB in conjunction with EBRT be considered based on randomized data demonstrating significant improvement in lung reexpansion and in patient reported dyspnea with addition of EBB to EBRT over EBRT alone.[18] However, the guidelines do not mandate the use of EBB in this situation. It is possible that targeted education regarding the role of EBB would improve knowledge of the potential benefit in the setting of lung collapse and increase the percentage of VHA ROs who would recommend this procedure.

Limitations

The study is limited by lack of generalizability of these findings to all ROs in the country. It is also possible that physician responses do not represent practice patterns with complete accuracy. The use of EBB varied among practitioners. Further study of this technology is

necessary to clarify its role in the management of endobronchial obstructive symptoms and to determine whether efforts should be made to increase access to EBB within the VHA.

CONCLUSIONS

Most of the ROs who responded to our survey were cognizant and compliant with current ASTRO guidelines on management of lung cancer. Furthermore, familiarity with ASTRO guidelines and management choices were not associated with the respondents' years in practice, academic appointment, full-time vs part-time status, or familiarity with ASTRO guidelines. This study is a nationwide survey of ROs in the VHA system that reflects the radiation-related care received by veterans with metastatic lung cancer. Responses were obtained from 93% of the 40 radiation oncology centers, so it is likely that the survey accurately represents the decision-making process at the majority of centers. It is possible that those who did not respond to the survey do not treat thoracic cases.

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Author disclosures

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References

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015 65(2):87-108.
2. Kocher F, Hilbe W, Seeber A, et al. Longitudinal analysis of 2293 NSCLC patients: a comprehensive study from the TYROL registry. *Lung Cancer.* 2015;87(2):193-200.
3. Chute CG, Greenberg ER, Baron J, Korson R, Baker J, Yates J. Presenting conditions of 1539 population-based lung cancer patients by cell type and stage in New Hampshire and Vermont. *Cancer.* 1985;56(8):2107-2111.
4. Hyde L, Hyde CI. Clinical manifestations of lung cancer. *Chest.* 1974;65(3):299-306.
5. Rodrigues G, Videtic GM, Sur R, et al. Palliative thoracic radiotherapy in lung cancer: An American Society for Radiation Oncology evidence-based clinical practice guideline. *Pract Radiat Oncol.* 2011;1(2):60-71.
6. Moeller B, Balagamwala EH, Chen A, et al. Palliative thoracic radiation therapy for non-small cell lung cancer: 2018 Update of an American Society for Radiation Oncology (ASTRO) Evidence-Based Guideline. *Pract Radiat Oncol.* 2018;8(4):245-250.
7. Zullig LL, Jackson GL, Dorn RA, et al. Cancer incidence among patients of the United States Veterans Affairs (VA) healthcare system. *Mil Med.* 2012;177(6):693-701.
8. Fairchild A, Harris K, Barnes E, et al. Palliative thoracic radiotherapy for lung cancer: a systematic review. *J Clin Oncol.* 2008;26(24):4001-4011.
9. A Medical Research Council (MRC) randomised trial of palliative radiotherapy with two fractions or a single fraction in patients with inoperable non-small-cell lung cancer (NSCLC) and poor performance status. Medical Research Council Lung Cancer Working Party. *Br J Cancer.* 1992;65(6):934-941.
10. Nawrocki S, Krzakowski M, Wasilewska-Tesluk E, et al. Concurrent chemotherapy and short course radiotherapy in patients with stage IIIA to IIIB non-small cell lung cancer not eligible for radical treatment: results of a randomized phase II study. *J Thorac Oncol.* 2010;5(8):1255-1262.
11. Strøm HH, Bremnes RM, Sundstrøm SH, Helbekkmo N, Fløtten O, Aasebø U. Concurrent palliative chemoradiation leads to survival and quality of life benefits in poor prognosis stage III non-small-cell lung cancer: a randomised trial by the Norwegian Lung Cancer Study Group. *Br J Cancer.* 2013;109(6):1467-1475.
12. Strøm HH, Bremnes RM, Sundstrøm SH, Helbekkmo N, Aasebø U. Poor prognosis patients with inoperable locally advanced NSCLC and large tumors benefit from palliative chemoradiotherapy: a subset analysis from a randomized clinical phase III trial. *J Thorac Oncol.* 2014;9(6):825-833.
13. Ball D, Smith J, Bishop J, et al. A phase III study of radiotherapy with and without continuous-infusion fluorouracil as palliation for non-small-cell lung cancer. *Br J Cancer.* 1997;75(5):690-697.
14. Stewart A, Parashar B, Patel M, et al. American Brachytherapy Society consensus guidelines for thoracic brachytherapy for lung cancer. *Brachytherapy.* 2016;15(1):1-11.
15. Sur R, Ahmed SN, Donde B, Morar R, Mohamed G, Sur M, Pacella JA, Van der Merwe E, Feldman C. Brachytherapy boost vs teletherapy boost in palliation of symptomatic, locally advanced non-small cell lung cancer: preliminary analysis of a randomized prospective study. *J Brachytherapy Int.* 2001;17(4):309-315.
16. Sur R, Donde B, Mohuiddin M, et al. Randomized prospective study on the role of high dose rate intraluminal brachytherapy (HDRILBT) in palliation of symptoms in advanced non-small cell lung cancer (NSCLC) treated with radiation alone. *Int J Radiat Oncol Biol Phys.* 2004;60(1):S205.
17. Ung YC, Yu E, Falkson C, et al. The role of high-dose-rate brachytherapy in the palliation of symptoms in patients with non-small cell lung cancer: a systematic review. *Brachytherapy.* 2006;5:189-202.
18. Langendijk H, de Jong J, Tjwa M, et al. External irradiation versus external irradiation plus endobronchial brachytherapy in inoperable non-small cell lung cancer: a prospective randomized study. *Radiother Oncol.* 2001;58(3):257-268.