Brain Metastases Recurrence Rate post-Whole Brain Radiation Therapy in Lung Cancer Smokers vs. Nonsmokers

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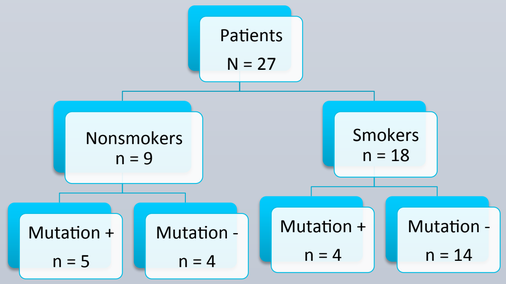
Introduction

It is estimated that as of 2016, there are approximately 526,510 Americans who have a diagnosis of lung cancer, with as many as 224, 390 new cases that will be diagnosed in the next year (1). Lung cancer is still known to have an extremely high death rate with a 5-year survival rate of 55% when localized to the lungs and 4% once it has metastasized to other organs (2). Unfortunately, once lung cancer spreads beyond its primary site of origin in the lungs to regions such as the adrenal glands, brain, or liver, it is deemed incurable and current standard of care focuses on stifling disease progression, promoting symptom palliation, and maintaining patient quality of life. Current standard of care for treating brain metastases secondary to lung cancer can involve surgical resection, chemotherapy, and either whole-brain radiation therapy or gamma-knife radiosurgery depending on the extensiveness and pattern of intracranial disease. According to the CDC, current risk factors for lung cancer include smoking, exposure to workplace substances such as radon, silica, asbestos, and family/genetic history (3). Our study aims to assess the effects of smoking on the recurrence rates of metastatic brain lesions in patients with primary lung cancer who have completed whole-brain radiation therapy (WBRT). We hypothesize that smokers with primary lung cancer will have a higher rate of recurrence in the brain post-WBRT when compared to nonsmokers.

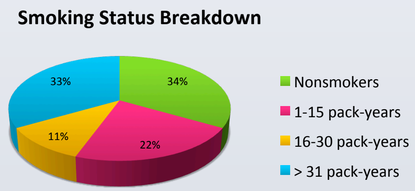
Methods

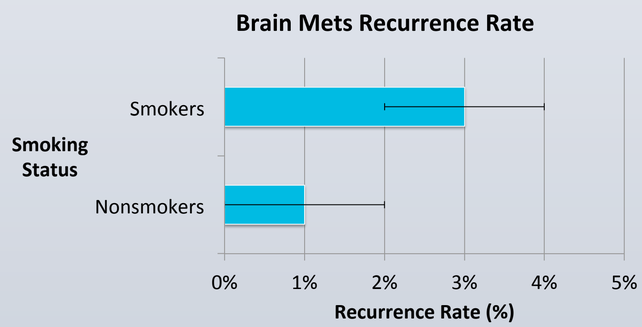
This is a preliminary retrospective review of 32 patients with lung cancer and concurrent brain metastases who were treated at the UC Davis Comprehensive Cancer Center or an outside institution. MRI records for 5 patients were not found in our electronic medical record system, so we did not include them in our final analysis (n = 27). All patients received whole-brain radiation therapy (WBRT) for their brain metastases. Patients were divided into nonsmokers and smokers, and smokers were further stratified into 1-15 pack-years, 16-30 pack-years, and > 31 pack-years. For our analysis purposes, we chose to classify patients as smokers or nonsmokers only and did not stratify further by pack-years. We also classified patients as mutation (+) for EGFR, ALK, or KRAS or mutation (-). Follow-up interval ranged from the date of WBRT initiation to the date of their last MRI. We determined recurrence rate by counting the number of lesions on the MRI pre-WBRT and the number of lesions on the MRI post-WBRT and calculating the percentage of lesions that recurred. We also counted the number of new metastatic lesions per patient.



Results

33.3% (9/27) patients were nonsmokers, 22.2% (6/27) had 1-15 pack-years, 11.1% (3/27) had 16-30 pack-years, and 33.3% (9/27) had > 31 pack-years. 33.3% (9/27) patients were mutation (+) for EGFR, ALK, or KRAS and 66.7% (18/27) patients were mutation (-) for these oncogenes. The mean follow-up interval was 0.69 years for nonsmokers and 0.56 years for smokers. Brain recurrence rates for mutation (+) nonsmokers and smokers were identical at 3%. Recurrence rate for mutation (-) nonsmokers was 0% and recurrence rate for mutation (-) smokers was 4%. Overall, regardless of mutation status, nonsmokers and smokers had brain recurrence rates of 1% and 3% respectively. Finally, there were 58 new metastatic brain lesions post-WBRT in nonsmokers and 10 in smokers.





Status	Pre-WBRT Lesions	Recurrences	New Mets	Recurrence Rate	Mean Follow-Up Interval (years)
Nonsmokers					0.69
Mut +	35	1	58	0.03	
Mut -	60	0	0	0.00	
Totals	95	1	58	0.01	
Smokers					0.56
Mut +	68	2	0	0.03	
Mut -	112	4	10	0.04	
Totals	180	6	10	0.03	

Discussion

The preliminary data indicates that smoking status may play a role in predicting brain metastases prognosis post whole-brain radiation therapy in lung cancer patients. Post-WBRT, nonsmokers and smokers had a 1% and 3% recurrence rates respectively. This is an observation that we did expect. Current literature suggests that lung cancer associated with smoking does tend to be more aggressive in its invasiveness and more resistant in its response to treatment. As a result, it is reasonable that smokers retain this phenotype in metastases such that recurrence rates post-treatment tend to be higher. Both groups had mean follow-up intervals of 0.69 years (nonsmokers) and 0.56 years (smokers). We are hoping to continue monitoring these patients such that we can potentially gather more data on recurrences that happen later in time. Our sample size of 27 patients has more smokers than nonsmokers which has the potential to skew our data. In the next months, we aim to acquire a new database of patients that meet our current research conditions such that we can increase our sample size of lesions and complete a more robust data analysis. In addition, we noted 58 new metastatic lesions in nonsmokers and 10 new ones in smokers. This was a surprising finding as we would expect more new metastatic lesions in the more aggressive cancer group, mainly the smokers. However, this was not the case and may be due to unique tumor mutations or pathogenic features that we do not know at this time. Increasing our sample size of both nonsmoker and smoker groups will allow us to ascertain if this pattern remains consistent, and if it does, this can be a new question we can pursue. Overall, the preliminary data shows that a history of smoking is associated with increased recurrence rates of brain metastases in lung cancer patients post-WBRT. We believe further work on this project may help us create another prognostic marker for this subset of patients such that we can further improve patient care, management, and survival.

References

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3. *CDC. "What are the risk factors for lung cancer?" CDC. CDC, 20 July 2016. Web. 14 Feb. 2017.*

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