Patterns of End-of-Life Oncologic Care for Stage IV Non-small Cell Lung Cancer in the United States

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Abstract. *Background/Aim:* Because aggressive oncological management just prior to death constitutes a substantial proportion of end-of-life (EOL) costs, we investigated patterns of EOL oncologic care for stage IV non-small cell lung cancer (NSCLC) in USA to better determine at which point in the patient's management new treatments were being initiated. *Materials and Methods:* The National Cancer Database was queried for stage IV NSCLC patients who received any cancer-directed therapy with known timing thereof. *Results:* A total of 281,990 stage IV NSCLC patients were analyzed. Of all patients, 10.8% commenced any first-course cancer therapy within four weeks of death, and 24.5% within eight weeks of death. *Conclusion:* 10-15% of stage IV NSCLC patients start cancer therapy within four weeks of death, and 25-30% within eight weeks. This represents a population for whom cancer therapy may not be required, which has implications on reducing EOL healthcare costs.

Costs of cancer care (roughly \$173 billion in the US by 2020) (1) are proportionally greatest in the last year of life; in that interval, they account for >25% of the entire Medicare budget (over half of which is spent in the final 60 days) (2).

The most common cause of cancer-related death worldwide, non-small cell lung cancer (NSCLC) is most commonly diagnosed as stage IV disease and carries a very poor prognosis. Because aggressive oncologic management just prior to death constitutes a substantial proportion of end-of-life (EOL) costs, we investigated patterns of EOL oncologic care for metastatic NSCLC in USA.

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Key Words: Non-small cell lung cancer, stage IV, end-of-life, healthcare costs, cost-effectiveness.

Materials and Methods

Details regarding the National Cancer Database (NCDB), which captures about 70% of the USA population, are provided elsewhere (3). The primary goal herein was to evaluate proportions of stage IV NSCLC patients initiating cancer therapy (radiation, chemotherapy, immunotherapy, or any therapy) within certain intervals of death. The NCDB does not give information on therapy cessation. Statistics included multivariable logistic regression to determine factors associated with death within 15 days of commencing cancer therapy.

Results

From 2004-2015, 1,393,073 NSCLC cases were recorded in the NCDB; 894,368 were stage I-III and 216,715 had no record/timing of death and/or therapy and were hence excluded. The overall population thus consisted of 281,990 stage IV NSCLC patients (Table I). There were several factors independently predictive of dying within 15 days of initiating cancer therapy: advancing age, male gender, higher comorbidities, Caucasian race, lower income, and advancing tumor/nodal disease ($p < 0.05$ for all).

Figure 1A illustrates the distribution of patients starting any cancer therapy as a function of the time to death. Overall, 10.8% commenced first-course therapy within four weeks of death, and 24.5% within eight weeks of death. Just 23.2% of patients survived >52 weeks from the day of starting therapy.

Figure 1B-D provides a sub-breakdown regarding radiotherapy, chemotherapy, and immunotherapy, respectively. Within four and eight weeks of death, 13.9% and 27.7% started a course of radiotherapy; corresponding figures for chemotherapy and immunotherapy were 10.9% & 25.2% and 4.9% & 11.5%.

Discussion

Although stage IV NSCLC is being more aggressively managed (4), only a proportion of well-selected patients achieve oncologic benefit; rather, many patients starting cancer therapy die soon after the initiation of treatment.

Figure 1. Proportion of patients receiving cancer therapy as a function of the time to death. A) Any cancer therapy, B) radiotherapy, C) chemotherapy, D) immunotherapy.

Oncological management is expensive, and because oncologic and EOL costs are rising worldwide, it is essential to perform audits regarding delivering “futile” cancer care just prior to death. This study of a large, contemporary national database shows that 10-15% of stage IV NSCLC patients start cancer therapy within four weeks of eventual death, and 25-30% within eight weeks. This represents a population for whom cancer therapy may not be required, which has implications on reducing EOL healthcare costs.

Herein, it is not insinuated that EOL oncologic interventions do not help patients. For instance, palliative

radiotherapy is effective to reduce symptomatic local tumor progression; in fact, studies have shown that effective palliative care actually reduces healthcare costs (5). We suggest that certain subpopulations herein received oncologic interventions as part of aggressive, unnecessary management towards the EOL. To this extent, several factors may be utilized by clinicians to carefully evaluate the risk of death a short time after intervention(s) are initiated (Table I).

The staggering rise of immunotherapy for metastatic NSCLC must also be contextualized with its immense costs (over \$100,000 for a single course). Because not all patients

Table I. Clinical characteristics for all patients, and multivariable logistic regression analysis for factors associated with death within 15 days of starting cancer therapy.

Characteristic	Multivariable logistic regression			
	All patients (n=281990)	Odds ratio	95% Confidence interval	p-Value
Age				
≤50	25015 (8.9%)	1 (reference)		
51-60	63737 (22.6%)	1.233	1.176-1.292	<0.001
61-70	91239 (32.4%)	1.363	1.300-1.430	<0.001
71-80	76012 (27.0%)	1.559	1.483-2.640	<0.001
81-90	25987 (9.2%)	1.900	1.800-2.010	<0.001
Gender				
Male	158212 (56.1%)	1 (reference)		
Female	123778 (43.9%)	0.820	0.803-0.837	<0.001
Race				
White	238787 (84.7%)	1 (reference)		
African American	33405 (11.9%)	0.900	0.871-0.930	<0.001
Other	9798 (3.5%)	0.882	0.831-0.935	<0.001
Insurance				
Medicaid	21539 (7.6%)	1 (reference)		
Medicare	148878 (52.8%)	0.978	0.934-1.023	0.333
Private	89620 (31.8%)	0.847	0.811-0.884	<0.001
Uninsured	12700 (4.5%)	1.319	1.244-1.400	<0.001
Other	9253 (3.3%)	1.119	1.047-1.197	0.001
Charlson/Deyo score				
0	183940 (65.2%)	1 (reference)		
1	69580 (24.7%)	1.375	1.343-1.408	<0.001
2	20921 (7.4%)	1.631	1.573-1.690	<0.001
≥3	7549 (2.7%)	1.895	1.794-2.002	<0.001
Income				
<\$46,000	173766 (61.6%)	1 (reference)		
≥\$46,000	97302 (34.5%)	0.947	0.927-0.969	<0.001
Not recorded	10922 (3.9%)	1.016	0.963-1.071	0.572
Facility				
Academic	86216 (30.6%)	1 (reference)		
Non academic	193399 (68.6%)	1.055	1.031-1.079	<0.001
Not recorded	2375 (0.8%)	0.880	0.763-1.015	0.080
Histology				
Adenocarcinoma	138996 (49.3%)	1 (reference)		
Squamous cell carcinoma	53118 (18.8%)	1.005	0.977-1.034	0.727
Other	89876 (31.9%)	1.169	1.142-1.197	<0.001
T classification				
T1	33159 (11.8%)	1 (reference)		
T2	70555 (25.0%)	1.274	1.223-1.328	<0.001
T3	38337 (13.6%)	1.534	1.467-1.604	<0.001
T4	87742 (31.1%)	1.786	1.717-1.858	<0.001
Not reported	52197 (18.5%)	1.681	1.609-1.757	<0.001
N classification				
N0	49961 (17.7%)	1 (reference)		
N1	25278 (9.0%)	1.077	1.030-1.126	0.001
N2	111007 (39.4%)	1.301	1.261-1.342	<0.001
N3	53342 (18.9%)	1.379	1.332-1.429	<0.001
Not reported	42402 (15.0%)	1.324	1.273-1.378	<0.001
Year				
2004-2006	64953 (23.0%)	1 (reference)		
2007-2009	75260 (26.7%)	0.941	0.914-0.969	<0.001
2010-2012	87103 (30.9%)	0.937	0.910-0.965	<0.001
2013-2014	54674 (19.4%)	1.092	1.058-1.128	<0.001

will benefit, careful patient selection is critical to ensure that immunotherapy is delivered to well-selected patients with adequate life expectancy to reap its benefits (6). To this end, an important finding herein was that substantially lower proportions of patients started immunotherapy immediately before death, indicating some degree of more judicious screening for these expensive agents.

Limitations of the NCDB include the lack of treatment indications, costs, cancer-specific survival, number/volume of metastases, or type/duration of chemotherapy/immunotherapy agents. This study was not designed to address the increasing number of stage IV NSCLC patients who experience long-term survival (4).

Conflicts of Interest

None. This study has never been presented/published before in any form. All Authors declare that conflicts of interest do not exist.

Authors' Contributions

WH, VV, EBB, and BST contributed to the conception of the project and drafting the manuscript.

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