Analyzing the effect of physician assignment in the survival of patients with advanced non-small-cell lung cancer

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ABSTRACT

Background Non-small-cell lung cancer (NSCLC) is the most common cause of cancer deaths worldwide, with a 5-year survival of 17%. The low survival rate observed in patients with NSCLC is primarily attributable to advanced stage of disease at diagnosis, with more than 50% of cases being stage IV at presentation. For patients with advanced disease, palliative systemic therapy can improve overall survival (OS); however, a recent review at our institution of more than 500 consecutive cases of advanced NSCLC demonstrated that only 55% of the patients received palliative systemic therapy. What is unknown to date is whether that observed low rate of systemic therapy in our previous study is uniform across oncologists.

Methods With ethics approval, we performed a retrospective analysis of newly diagnosed patients with stage IV NSCLC seen as outpatients at our institution between 2009 and 2012 by 4 different oncologists. Demographics, treatment, and survival data were collected and compared for the 4 oncologists.

Results The 4 oncologists saw 528 patients overall, with D seeing 115; L, 158; R, 137; and M, 118. Significant variation was observed in the proportion receiving 1 line or more of chemotherapy: D, 60%; L, 65%; R, 43%; and M, 52%. Physician assignment was not associated with a difference in median OS, with D's cohort having a median OS of 6.8 months; L, 8.4 months; R, 7.0 months; and M, 7.0 months.

Conclusions Practice size and proportion of patients treated varied between oncologists, but those differences did not translate into significantly different survival outcomes for patients.

Key Words Physician effect, non-small-cell lung cancer, chemotherapy

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INTRODUCTION

Non-small-cell lung cancer (NSCLC) is the most common cause of cancer deaths in North America and worldwide. Lung cancer accounts for about 27% of all cancer deaths and has a 5-year survival of about 17%—a proportion that has seen only small improvements in recent decades¹. The low survival rate observed in patients with NSCLC is primarily attributable to the advanced stage of the disease that is typically already present at diagnosis. Approximately half of all cases are stage IV at presentation, and for the remaining 50% of cases, where patients present with earlier-stage disease, initial treatment might be given with curative in-

tent, but a significant proportion will subsequently relapse with incurable advanced disease. As an illustration, consider this review of NSCLC cases referred to our institution in 2007: Of 374 patients with NSCLC assessed by a medical oncologist, only 160 were initially treated with curative intent, and of those 160, 56% subsequently relapsed². For patients with advanced disease, palliative systemic therapy can improve overall survival (OS) and palliate symptoms of cancer, thereby improving or maintaining quality and quantity of life. However, many patients can have multiple co-existing comorbidities, potentially resulting in a performance status that might be too poor to allow for safe and efficacious delivery of therapy³.

Brule *et al.*⁴ recently published a detailed review of more than 500 consecutive patients with advanced NSCLC seen at our institution. Of those 500 patients, only 55% received palliative systemic therapy, with poor performance status and patient choice being the commonly stated reasons for the omission of palliative therapy. What is unknown to date is whether the low observed rate of systemic therapy in that earlier study is uniform. Are some oncologists more conservative, offering systemic therapy to fewer patients? And are others possibly more “aggressive” in their recommendations for chemotherapy? If there are differences, then do those differences result in different outcomes for patients? To try to address those questions, we analyzed the cohort described by Brule *et al.*⁴, which comprised the clinical practices of 4 medical oncologists.

METHODS

Study Design

We previously reported the results of a single-institution retrospective chart review of all cases of stage IV NSCLC seen in initial outpatient consultation at our institution between September 2009 and August 2012, and methods are therefore described in full in that publication⁴. In brief, all patients with newly diagnosed stage IV NSCLC seen in outpatient consultation by a thoracic medical oncologist were eligible. Patients previously followed with subsequent relapse were not included, and patients seen in initial consultation while hospitalized were also excluded. For the purposes of the analysis, the 4 oncologists were anonymized before analysis and interpretation of results.

Endpoints

The co-primary endpoints were the proportion of patients who received any palliative systemic therapy (comparing the 4 oncologists) and the OS from the time of first consultation with the medical oncologist until date of death or last follow-up. Secondary endpoints included the number of patients receiving 0–4 or more lines of therapy in each group, stated reasons for not treating patients who received no lines of therapy, and a descriptive analysis of the cohorts. Data collected included patient demographics, cancer characteristics, type of presentation, baseline functional and laboratory values, treatment administered, and survival outcomes.

Statistical Analysis

The statistical analysis plan included both descriptive and statistical analyses.

The 4 oncologists were anonymized to avoid bias in interpretation of the results. Median patient age is presented overall and for the 4 oncologist cohorts. The Kruskal–Wallis test was used to compare the 4 oncologist cohorts to look for significant differences in patient age. Other demographics, cancer presentation, cancer characteristics, and palliative systemic therapy are presented as numbers and percentages. The chi-square test or Fisher exact test was used, as appropriate, to analyze differences between the 4 oncologist cohorts. The Kaplan–Meier method was used to report median survival overall and in cohorts representing the number of lines of therapy, each oncologist, and each

oncologist by number of lines of therapy. The log-rank test was applied to determine whether differences in OS were evident between the latter cohorts. Univariable and multivariable Cox proportional hazards models were created to uncover any factors associated with OS.

RESULTS

The 4 anonymized oncologists saw 528 patients in total, with “Donatello” (D) seeing 115; “Leonardo” (L), 158; “Raphael” (R), 137; and “Michaelangelo” (M), 118. Median age in the overall cohort was 67 years (range: 34–89 years). In that cohort, 55% of the patients were men, 50% had an Eastern Cooperative Oncology Group performance status of 0–1, and 48% had experienced more than 5% weight loss. Statistically significant differences in the distribution of certain baseline patient characteristics were evident between the 4 oncologists (Table I): performance status ($p = 0.015$), anemia (hemoglobin <100 g/L vs. ≥ 100 g/L, $p = 0.013$), lactate dehydrogenase (<250 U/L, ≥ 250 U/L, unknown; $p = 0.091$), presenting symptoms ($p = 0.0011$), and interval between symptoms and diagnosis ($p = 0.027$).

With respect to the rate at which each oncologist prescribed chemotherapy, significant variation was observed in the proportion of patients receiving 1 or more lines of chemotherapy ($p = 0.0015$), with D treating 60% of patients; L, 65%; R, 43%; and M, 52% (Tables II and III). However, despite those differences in the baseline characteristics of the patients and in the proportion receiving chemotherapy, physician assignment was not associated with a difference in median OS ($p = 0.47$), with D’s cohort having a median OS of 6.8 months; L, 8.4 months; R, 7.0 months; and M, 7.0 months. Table I presents the median OS for treated and untreated patients in each physician’s cohort. Figure 1 presents the Kaplan–Meier curves for the OS of all patients by oncologist. As can be seen in Figure 1, patient OS was very similar for all 4 oncologists. Patients of the physician with the largest practice (L) had the longest median OS, but the difference was not statistically significant. Figure 2 shows the maximum lines of chemotherapy given by each physician.

In multivariate analysis, the factors that were associated with survival were performance status ($p < 0.01$), weight loss ($<5\%$, $\geq 5\%$; $p < 0.01$), white blood cells ($<11 \times 10^9/L$, $\geq 11 \times 10^9/L$; $p = 0.056$), and platelets ($<400 \times 10^9/L$, $\geq 400 \times 10^9/L$; $p = 0.037$), but not physician assignment.

Overall, although practice size and proportion of patients treated varied for the oncologists, those differences did not translate into significantly different survival outcomes for patients.

DISCUSSION

Many patients with advanced NSCLC do not receive systemic therapy, as is evidenced by the present dataset⁴, but also by other publications, including population-based studies⁵. Treatment rates in the cohort described here (55% overall) were higher than in the population study by Sacher *et al.*⁵, it should be remembered that our dataset was confined to patients well enough to be referred to and to see an oncologist in the outpatient setting. In Sacher *et al.*⁵, up to

TABLE I Patient characteristics overall and for each anonymized medical oncologist

Characteristic	Oncologist cohort					<i>p</i> Value
	Overall	Donatello	Leonardo	Raphael	Michaelangelo	
Patients (<i>n</i>)	528	115	158	137	118	
Sex (% men)	55	49	56	58	58	0.42
Median age (years)	67.5	66.8	67.0	70.0	67.5	0.23
Performance status 0–1 (%)	50	50	55	47	48	0.015
Weight loss > 5% (%)	48	46	49	49	48	0.87
Hemoglobin < 100 g/L (%)	6	4	4	11	3	0.013
Platelets < 400×10 ⁹ /L	71	78	70	64	75	0.12
WBCs < 11×10 ⁹ /L	62	68	60	56	68	0.12
LDH < 250 U/L	28	27	33	21	30	0.091
Symptoms at presentation (%)						0.0011
Constitutional	5.5	3.5	3.8	6.6	8.5	
Cough	18	17	16	20	21	
Dyspnea or SOB	18	15	23	16	14	
Hemoptysis	3.8	0	5.7	6.6	1.7	
None or incidental finding	9.9	4.4	15	12	5.9	
Other	16	19	15	17	13	
Pain	23	30	19	15	32	
Pneumonia	5.5	9.6	3.8	5.8	3.4	
Interval between symptoms and Dx (%)						0.027
<2 Weeks	5.3	10	4.4	2.9	4.3	
2–6 Weeks	13	18	9.5	12	12	
6 Weeks to 6 months	50	44	51	50	57	
>6 Months	21	14	22	27	20	
Unknown	11	14	14	8	6.8	

WBCs = white blood cells; LDH = lactate dehydrogenase; SOB = shortness of breath; Dx = diagnosis.

TABLE II Lines of therapy given by each anonymized medical oncologist

Therapy lines	Oncologist cohort [n (%)]				
	Overall (528 pts)	Donatello (115 pts)	Leonardo (158 pts)	Raphael (137 pts)	Michaelangelo (118 pts)
0	237 (44.9)	46 (40.0)	56 (35.4)	78 (56.9)	57 (48.3)
1	163 (30.9)	39 (33.9)	62 (39.2)	26 (19.0)	36 (30.5)
≥1	291 (55.1)	69 (60.0)	102 (64.6)	59 (43.1)	61 (51.7)
2	74 (14.0)	20 (17.4)	26 (16.5)	18 (13.1)	9 (7.6)
3	40 (7.6)	6 (5.2)	12 (7.6)	14 (10.2)	9 (7.6)
4	14 (2.7)	4 (3.5)	2 (1.3)	1 (0.7)	7 (5.9)

Pts = patients.

30% of patients were reported as not seeing an oncologist, and so naturally the overall treatment rates were lower. To determine whether the observed rates of systemic therapy were influenced by specific oncologists, we analyzed the practices of 4 oncologists at our institution to determine whether OS in NSCLC was affected by physician assignment.

Our results concluded that, although practice size and proportion of patients treated did vary between the oncologists, those differences did not translate into significantly different survival outcomes for patients. Statistically

significant differences in the distribution of baseline characteristics were evident between the 4 oncologists, which could potentially cause differences in the proportion of treated patients for each oncologist. Some evidence that physicians might be guided more by personal experiences was revealed in studies that assessed the effect of physician caseload on patient outcomes and OS. The results are, however, far from conclusive, with several studies reporting improved survival with higher caseload^{6–10}, and others reporting the opposite^{11–13}. Furthermore, the

TABLE III Median overall survival (OS) for untreated and treated patients, by anonymized oncologist

Oncologist	Pts receiving 1 or more lines of Ctx (%)	Median patient OS (months)	
		Untreated	Treated
All	55	3.9	7.5
Donatello	60	3.1	6.8
Leonardo	65	4.4	8.4
Raphael	43	4.0	7.0
Michaelangelo	52	4.2	7.0
		$p<0.01$	$p=0.47$

Ctx = chemotherapy.

FIGURE 1 Overall survival by the Kaplan–Meier method for all patients, by anonymized medical oncologist.

foregoing findings relate to caseload for surgeons and radiation oncologists; little to no data are available for medical oncologists. In our study, patients of the physician with the largest practice had the longest median OS; however, that was likely a chance finding, because all 4 oncologists have large lung cancer-specific practices. If there is such an effect for medical oncologists, it cannot be deduced from the present study. Interestingly, the physician whose patients had the longest median OS also had the largest percentage of patients with a performance status between 0 and 1. The statistical analysis was not strong enough to prove that link, however.

We hypothesized that as long as oncologists are adequately trained, display good practice, and make an effort to keep up with recent research, patient survival does not depend on the individual. Our results suggest support for that hypothesis. However, we did not, in the present study, measure other valuable characteristics such as rapport, experience, time spent with the patient, and traits such as compassion and empathy, which presumably vary between physicians. Still, it is encouraging to know that the treatment preferences of individual oncologists do not have a huge effect on patient outcome.

FIGURE 2 Lines of patient chemotherapy given, by anonymized medical oncologist.

A weakness of our study might be the obvious uniformity of the 4 clinicians. All worked at the same academic institution—and not as general oncologists, but rather as specialist thoracic oncologists, each with a large lung cancer practice. Further, all 4 are academically active, leading clinical trials and publishing in the field, and most had, in their career, undertaken specialist lung cancer fellowships at some of the most globally recognized cancer institutions. Therefore, either because of having more specific knowledge of lung cancer or because of shared practices at the same institution, similar outcomes for the patients of these oncologists might not be a surprising observation. The generalizability of the findings reported here might thus be questionable, but of merit nonetheless. It would be interesting to compare these data with data for physicians who are generalists or who treat lung cancer only occasionally to see if practices and outcomes vary. Other variables could include comparisons by country—raising the relevance of issues such as availability of therapy, cultural norms and expectations, and different training programs. For a better understanding of the role that oncologist assignment might play in patient outcomes and survival, such questions could be explored in future studies.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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