

# Treatment outcomes in stage IIIA non-small-cell lung cancer in a community cancer center

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**Background** Treatment outcomes for non-small-cell lung cancer (NSCLC) patients diagnosed at stage IIIA have been analyzed in many studies, which generally involve patients younger and healthier than the average patient with this disease.

**Objective** To analyze demographics and treatment outcomes in patients with stage IIIA NSCLC at a community cancer center.

**Methods** We reviewed charts of 226 patients diagnosed with stage IIIA NSCLC from January 2003 to December 2008 treated at our community cancer center.

**Results** Median overall survival for all patients and sequentially and concurrently treated chemoradiation patients were 18 months, and 18 months, and 20 months, respectively. Median overall survival for women and men was 24 months and 16 months, respectively.

**Limitations** Study design was retrospective and some medical records were not available. However, this population is likely representative of patients treated in similar settings.

**Conclusions** In our population, advanced age and male gender were associated with lower median survival. Responses to concurrent and sequential chemoradiation seemed to differ based on age group, which may be useful as a prognostic guideline for similar populations.

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In 2015, there will be an estimated 221,200 new cases of lung cancer in the United States, of which 83% will be non-small-cell lung cancer (NSCLC).<sup>1</sup> Generally, about one-third of patients present with stage III or locally advanced disease. This is defined as tumor that has spread significantly within the chest, but lacks distant metastasis.

The results from multiple trials have shown that there is a survival benefit in treating patients with stage III NSCLC by using the combined modality of chemotherapy with radiation. One of the more definitive phase 3 trials to date shows a survival benefit in using concurrent versus sequential chemoradiation (median survival, 17 vs 14.6 months, respectively).<sup>2</sup> The average age at the time of diagnosis of lung cancer in the United States is 70 years.<sup>3</sup> However, participants in clinical trials of lung cancer treatments are often younger. For instance, the median age in the aforementioned trial was 61 years.<sup>2</sup>

In the current study, we examined all patients with stage III lung cancer from January 2003 to December 2008 in a single-practice, community-based cancer

center. We compared our patient characteristics and survival outcomes with the results from the clinical trials done at larger academic centers.

## Methods

This was a retrospective review of the medical records of patients with stage IIIA non-small-cell lung cancer (NSCLC) at our institute in Newark, Delaware, using records of patients diagnosed from January 2003 to December 2008. Institutional Review Board approval was granted for data abstraction from the institute's tumor registry, as well as for medical record review of patients at the institute.

The primary outcome was overall survival for all patients. Secondary outcomes included survival in various treatment subgroups. Data for these outcomes was limited to patients for whom complete medical records were available, because we needed to verify relevant aspects of disease management. Available medical records underwent review by 3 of the authors (SH, KP, XQ).

A total of 226 patients were identified through

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the registry. Of those patients, 118 were seen by a single practice, for which records were available. Of those records, 88 were for patients who had been treated with chemoradiation and provided the basis for most of our analysis.

Within the limits of the above description, no patients were excluded from the study. All of the data was entered securely without patient identifiers and processed using Excel spreadsheet software. Processing of data included creating subject subsets, sorting by characteristics, determining counts, medians, and means, and assessing survival percentage at various intervals. Calculation of *P* values by *z* score was also performed using Excel as entered securely without patient identifiers and processed using Excel spreadsheet software.

## Results

A total of 226 patients (112 men, 114 women) were identified from the hospital tumor registry as patients with stage IIIA non-small-cell lung cancer (NSCLC). Overall, the median age was 68 years, (range, 34-88 years). The median age for men was 69 years (range, 42-87 years) and for women, 66 years (range, 34-88 years). The overall median survival was 17 months (range, 0-123 months); for men, it was 14 months (range, 0-114 months) and for women, 18 months (range, 1-123 months).

Of the 226 patients, 118 were seen in a practice with consistent chart availability and were evaluated in-depth (Table). There were 64 women and 54 men, with a median age of 66 years (range, 43-86 years). Treatment was grouped according to concurrent or sequential chemoradiation, which applied to 88 of the patients who received chemoradiation; or to other, which encompassed chemotherapy only, radiation therapy only, or supportive therapy only.

The population represented a diverse group of patients. The most common decade of life for diagnosis was the 7th decade (*n* = 47, 40%; Table). There were 107 patients (91%) who had a history of cigarette smoking. Positron-emission tomography (PET) scan was used in 105 patients (89%). Distant recurrence was present in a third of patients overall.

Patients were evaluated for 2- and 5-year survival based on gender and treatment modality, and by age of diagnosis alone (Figure

1). At 2 years, male survival for concurrent and sequential patients was 13.0% in each group (*P* = .5), and female survival for concurrent and sequential patients was 25% and 14.1%, respectively (*P* = .06). At 5 years, male survival for concurrent and sequential patients was 1.9% and 5.6%, respectively (*P* = .15), and female survival for concurrent and sequential patients was 10.9% and 6.3%, respectively (*P* = .18).

In the female group, the percentages of surviving patients at 2 years was higher with concurrent treatment compared with sequential treatment, and approached statistical significance. The sequential arm showed no major differences between genders for 2- or 5-year survival.

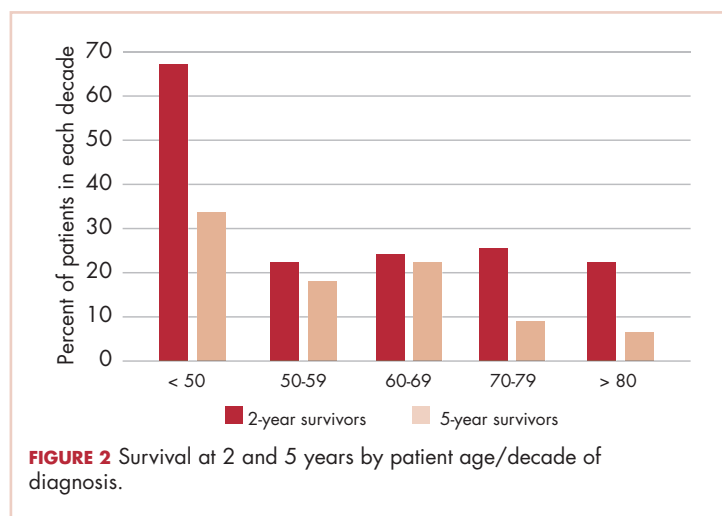
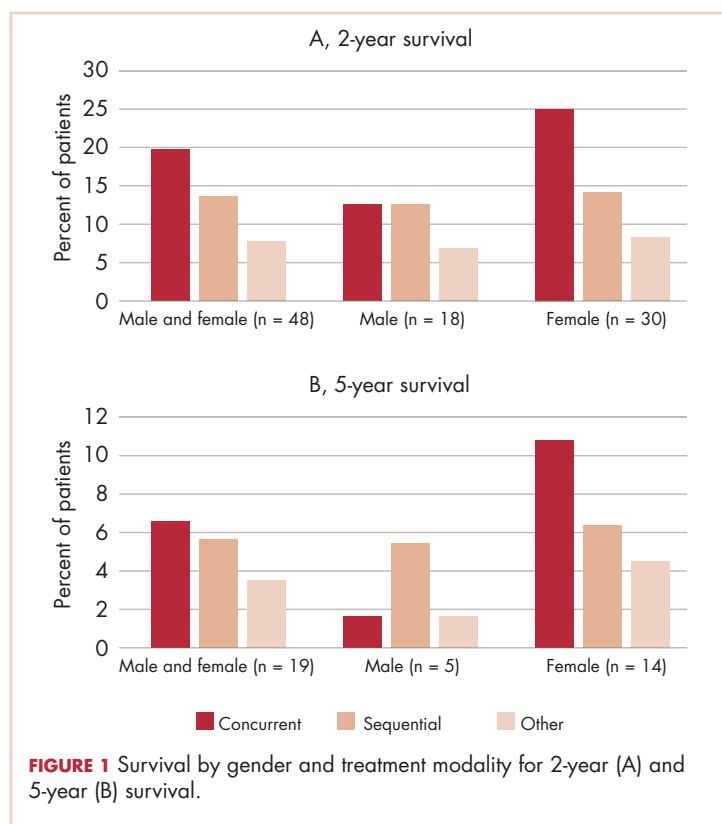
Survival based on age of diagnosis favored patients who were younger than 50 years (Figure 2). Patients' 2-year survival was notably uniform at about 20% for all age groups of more than 50 years. The 5-year survival for patients who were older than 70 years was significantly lower, at less than 10%.

In the present study, our population of chemoradiation-treated patients had a median age of 66 years. Median overall survival was 18 months. Just over half of our participants (54%) were women. In the female subgroup, the median age was 3 years younger than that in males, the ratio of adenocarcinoma to squamous-cell histopathology was greater, and overall median survival was higher than in the male subgroup (24 vs 16 months, respectively). This

**TABLE** Patient characteristics

Characteristic	No. of patients	Treatment modality, n		
		Concurrent	Sequential	Other
<b>Patients</b>				
Total	118	50	38	30
Men	54	24	17	13
Women	64	26	21	17
<b>Age, y</b>				
<50	3	1	2	0
50-59	22	13	5	4
60-69	47	21	16	10
70-79	33	13	11	9
>80	13	2	4	7
<b>PET scan</b>				
Yes	105	49	32	24
No	13	1	6	6
Distant recurrence	39	17	16	6
<b>History of smoking</b>				
History of smoking	107	48	33	26
Nonsmoker	11	2	5	4
<b>Surgical history (lobectomy and pneumonectomy)</b>				
Surgical history (lobectomy and pneumonectomy)	35	8	13	14

PET, positron-emission tomography



younger age at lung cancer diagnosis in women, as well as a greater incidence of adenocarcinoma histopathology, is consistent with prior observations<sup>4</sup> and may in part account for a greater median overall survival.

## Discussion

At present, treatment of locally advanced non-small-cell lung cancer remains a formidable challenge. New trends in screening techniques and guidelines may improve over-

all lung cancer mortality,<sup>5</sup> but many patients will continue to present beyond the window during which resection is a reasonable option. Managing their disease to limit toxicity in the face of a daunting mortality rate remains a challenge for researchers and community oncologists alike.

One tool in improving this process has been the ongoing characterization of treatment outcomes in patients receiving chemotherapy and radiation. A meta-analysis by Pritchard et al consolidated evidence that combining the 2 modalities of therapy resulted in improved outcomes, with a relative risk of death of 0.83 at 3 years for combined treatment compared with radiation alone. In that study, however, there was no significant difference in mortality between patients who received concurrent or sequential chemoradiation.<sup>6</sup> Since the publication of that study, many authors have weighed in to provide an increasingly clear picture of potential benefit for the concurrent approach, delivering radiation therapy during a chemotherapy course to fully harness the synergy of these modalities. Furuse et al demonstrated in a phase 3 trial a median overall survival of 16.5 months in 156 patients who received concurrent chemoradiation, compared with 13.3 months in 158 patients who were treated sequentially.<sup>7</sup> Curran et al had corroborative findings in a randomized controlled trial that had about 200 patients in each arm. Median overall survival for concurrent treatment was 17.0 months, compared with 14.6 months for sequential treatment, thus demonstrating a median survival benefit of 2.4 months with concurrent treatment compared with sequential treatment.<sup>2</sup> O'Rourke et al conducted a meta-analysis of 6 similar trials comparing concurrent with sequential therapy, which yielded a hazard ratio for death of 0.74 for patients randomized to concurrent treatment arms. However, the investigators did note a cost to concurrent treatment: the relative risk for severe esophagitis was 4.96.<sup>8</sup>

Each of the aforementioned studies noted the characteristics of its participants, and many aspects of those demographics are striking. Furuse excluded patients with hematological, hepatic, renal, pulmonary, or cardiac disease. Patients in their study had a median age of 63 years, and the majority had an ECOG performance status of 1.<sup>5</sup> Curran's patients were primarily in the Karnofsky Performance Status range of 90-100 (range, 1-100, KPS of 100 represents patients with no complaints or functional limitations) and had a median age of 61 years.<sup>2</sup> Given that these patients were enrolled in clinical trials, they may not be representative of the overall population. Many locally advanced non-small-cell lung cancer patients are older and have poorer functional status than the patients in these studies. The increase in toxicity that O'Rourke captured in the form of severe esophagitis may apply more saliently to patients who are older and have a poorer functional status at the outset of treatment, and mortality benefits depen-

dent on aggressive therapy may not apply to those who would not tolerate treatment well.

Among the limitations of our study are retrospective design, which introduces selection bias, some medical records not being available owing to paper chart storage issues, and some subgroups being too small to provide a useful amount of data (such as clinical trial participants). Our concurrently treated patients had a median overall survival of 20 months, and our sequentially treated patients had a median overall survival of 18 months. However, this data is drawn from a population that was not randomly selected, in which treatment decisions likely took into consideration the patient's predicted ability to tolerate aggressive therapy. However, outcomes in this population are likely representative of patients who are treated in similar settings, because selection of therapy would occur based on the same type of physician judgments.

Applying the findings of this study to a community setting, from which our data derives, may provide clinicians with a guideline as to what demographics their patients may demonstrate, and may support decisions regarding treatment of locally advanced non-small-cell lung cancer patients. These findings may be complementary to those derived in the context of clinical trials.

In conclusion, in our community-based single-cancer center retrospective study, we have found data complementary to the current literature that highlights outcomes based on demographic data as well as the management approach. Advanced age in our population was associated with a significant impact on prognosis. Differences in out-

comes based on gender seem similar to those found in the literature. Responses to concurrent and sequential chemoradiation among various age groups may be difficult to interpret in light of non-randomization, but may be useful as a prognostic guideline for similar populations.

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