Chapter 2

Inoperable Early Stage Non-Small Cell Lung Cancer: Comorbidity, Patterns of Care and Survival

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Abstract

Purpose

To evaluate comorbidities, patterns of care, and outcomes for patients with inoperable stage I and II non-small cell lung cancer (NSCLC)

Materials and Methods

Patients diagnosed with stage I or II NSCLC in British Columbia between 1996-2005 who did not undergo primary surgery and were referred for oncology assessment were identified in a retrospective analysis. Baseline comorbidity and pulmonary function data for patients treated with curative radiotherapy (CurRT; biologically effective dose [BED]>58 Gy_{10}) were abstracted by chart review. Kaplan-Meier and Cox regression were used to determine factors associated with overall survival (OS) and cause specific survival (CSS) based on treatment group [no radiotherapy (NoRT), palliative radiotherapy (PallRT), or CurRT].

Results

Of 1043 patients identified, approximately 1/3 received CurRT, and these patients had better performance status and lower stage disease than the other groups. There was a high prevalence of co-morbid conditions in the CurRT group; 90% of CurRT patients had an age-adjusted Charlson Comorbidity Index (CCI) score ≥5. CurRT patients had a median survival 1 year longer than patients treated with PallRT or NoRT ($p<0.0001$). In CurRT patients, CCI was predictive of OS (HR 1.1 per point CCI increase; $p=0.044$), but not CSS. Patients receiving PallRT with a BED >50 Gy_{10} had significantly longer OS than those receiving PallRT of ≤50 Gy_{10} ($p<0.0001$).

Conclusions

Treatment of medically inoperable early stage NSCLC patients with CurRT is associated with a significantly longer survival, and for these patients CCI is a significant predictor of OS. For patients treated with PallRT, higher doses of palliative thoracic RT is associated with improved OS.

Introduction

Although surgery has historically been the treatment of choice for patients with early stage non-small cell lung cancer, approximately 25% of patients do not undergo resection, usually because of patient refusal or comorbidities precluding surgery (1). For these patients, radiotherapy (RT) has been the primary treatment of choice (2,3). Long-term survival is uncommon even with curative-intent RT, in part due to high rates of intercurrent deaths from co-morbid disease, more than 30% in some series (4,5).

Although the benefit of immediate radiotherapy for inoperable early stage NSCLC has been questioned in the past (6,7), current guidelines recommend radical RT for inoperable patients with reasonable life expectancy and performance status (8,9). Several studies have reported outcomes after curative-intent RT for patients with early stage NSCLC (6), but few have also assessed patients treated palliatively and those not treated at all. Patients who are untreated are of particular importance, as they represent approximately one-third of inoperable early-stage patients, are more likely to be older and of racial minority status, and rarely survive more than a few years (1,10).

The goal of this study was to determine patterns of care and outcomes for patients with stage I and II NSCLC in the province of British Columbia (BC) who were not treated with primary surgical resection. The BC Cancer Agency (BCCA) is the sole provider of RT in BC (population ~4 million), and treatment guidelines for the province are developed by a multidisciplinary tumor group and published online (9). In particular, we sought to examine the influence of co-morbidity on survival for patients treated with curative intent, the influence of RT dose on survival for patients treated palliatively, and differences in survival between patients treated curatively, palliatively, or not at all.

Methods

Data Sources

The BCCA maintains a database which prospectively captures detailed information on all patients referred to the BCCA for management, including baseline characteristics, detailed RT information, surgical procedures, and Eastern Cooperative Oncology Group (ECOG) performance status. Information on date and cause of death is included by automatic linkage to the British Columbia Ministry of Health Vital Statistics agency, which is responsible for all

death certificates in British Columbia. Deaths occurring before January 1, 2008 were captured in the database for this study. Patients alive January 1, 2008 were censored at the time of last institutional contact. Institutional ethics review board approval was obtained prior to initiation of the study.

Patients were identified who were diagnosed with stage I or II NSCLC (based on the 1997 AJCC definition) between January 1, 1996 and December 31, 2005 who did not undergo primary surgical resection and had been referred to the BCCA for assessment by a surgical, medical or radiation oncologist. According to institutional guidelines, RT was to be considered for any patient who was medically inoperable or refused surgery (9). This time period was chosen since routine 3-dimensional conformal radiotherapy was available throughout the province after 1995.

Patients were classified into three treatment groups: no radiotherapy (NoRT, essentially untreated), palliative radiotherapy (PallRT), or curative radiotherapy (CurRT). PallRT included all courses with biologically effective doses (BED) less than 58 Gy_{10} (e.g. 8-10 Gy in 1 fraction, 20 Gy in 5 fractions, 30 Gy in 10 fractions, 40 Gy in 15 fractions). CurRT included all courses with BED≥58 Gy_{10} (e.g. 45 Gy in 15 fractions, 50Gy in 25 fractions, or higher doses). BED was calculated using the linear-quadratic formula, and correcting for actual total treatment time:

$$BED = nd[1+d/(\alpha/\beta)] - \ln 2\ (T-T_k) / [(T_p)(\alpha)], \quad (11,12)$$

with parameters as follows: n=number of fractions, d=dose per fraction, α/β ratio=10, T=total treatment time in days, T_k=start of accelerated repopulation (taken as 28 days); Tp=potential doubling time (taken as 3 days), α=0.3.

For patients treated with CurRT, a supplemental chart review was undertaken to abstract data on baseline comorbidities, pulmonary function, and local recurrence. Age-adjusted Charlson Comorbidity Index (CCI) scores were calculated, with points assigned depending on the presence and severity of various co-morbidites and for increasing age; higher scores denote more severe comorbidies and advanced age (13,14).

In general, CurRT patients were seen in follow-up at the BCCA in 3-6 monthly intervals after treatment. PallRT and NoRT patients were generally seen in follow-up by their physicians outside of the BCCA, but death outcomes were available for all patients through electronic linkage with the Vital Statistics Agency.

Statistical Analysis

Differences between treatment groups in baseline factors were compared using Pearson's chi-square test. Kaplan-Meier estimates of overall survival (OS) and cause specific survival (CSS) were generated and differences compared using the log-rank test. Cox regression analysis was used to determine factors associated with OS and CSS. Factors included in the multivariable analysis were age, sex, T- and N-stage, ECOG score, and treatment group. A separate model for CurRT patients included CCI, and a separate model for PallRT patients included BED. Age and CCI were examined as continuous variables, and all other variables were categorical. Patients who were coded as NX were assumed to be N0 for the multivariable model. Given the large number of missing ECOG scores, 'unknown' was coded separately and the variable was examined categorically. For PallRT patients, BED was assessed using a cutoff of 50 $Gy_{10,}$ based on an exploratory analysis from a previous meta-analysis that showed a survival advantage for patients receiving palliative doses 30 Gy in 10 fractions or higher (15), which corresponds to a BED cutoff of approximately 50 Gy_{10} based on formula above.

All statistical tests were two-sided with $p \leq 0.05$ indicative of statistical significance, and were done using the Statistical Package of Social Sciences (SPSS version 15.0, Chicago, Illinois).

Results

Demographics and Baseline Characteristics

Between January 1996 and December 2005, 1043 patients with stage I or II NSCLC were identified who did not undergo primary surgical resection and who were referred to the BCCA. Median age at diagnosis was 76 years (range 42-98 years), with 64 patients (6.1%) aged ≤ 60 years. Median follow-up was 7.2 years.

CurRT was delivered to 338 patients (32%), with hypofractionated regimens delivered in 94% of cases. Baseline clinical characteristics by treatment group are shown in Table 1. Major differences between the groups were found in stage (with PallRT patients having the highest stage disease), and performance status (with 49% of CurRT patients having ECOG 0-1, compared to 25% of others). Patients treated with CurRT were also slightly younger and more often male.

Table 1. Baseline clinical characteristics for 1043 patients with early stage inoperable NSCLC. CurRT: curative radiotherapy; PallRT: palliative radiotherapy; NoRT: no radiotherapy.

Variable	**All patients** n=1043 *No. (%)*		**CurRT** n=338 *No. (%)*		**PallRT** n=479 *No. (%)*		**NoRT** n=226 *No. (%)*		**p-value (χ^2)**
Age (median 75.8)									
≤70	289	(28)	98	(29)	147	(31)	44	(20)	0.033
71-75	243	(23)	77	(23)	104	(22)	62	(27)	
76-80	250	(24)	89	(26)	107	(22)	54	(24)	
>80	261	(25)	74	(22)	121	(25)	66	(29)	
Gender									
Male	587	(56)	207	(61)	265	(55)	115	(51)	0.044
Female	456	(44)	131	(39)	214	(45)	111	(49)	
Clinical T stage									
T1	260	(25)	126	(37)	47	(10)	87	(39)	<0.001
T2	530	(51)	155	(46)	266	(55)	109	(48)	
T3	253	(24)	57	(17)	166	(35)	30	(13)	
Clinical N stage									
N0	660	(63)	270	(80)	257	(54)	133	(59)	<0.001
N1	111	(11)	35	(10)	56	(11)	20	(9)	
NX	272	(26)	33	(10)	166	(35)	73	(32)	
Clinical Stage									
I	679	(65)	246	(73)	257	(54)	176	(78)	<0.001
II	364	(35)	92	(27)	222	(46)	50	(22)	
Performance Status									
0-1	341	(33)	167	(49)	125	(26)	49	(22)	<0.001
2-4	338	(33)	59	(18)	200	(42)	79	(35)	
Unknown	364	(35)	112	(33)	154	(32)	98	(43)	

Detailed pulmonary function and comorbidity data for patients treated with CurRT are shown in Table 2. There was a high prevalence of co-morbid conditions, with 90% of patients having an age-adjusted CCI score of 5 or more. Many patients had a history of heavy smoking, and this is reflected in low pulmonary function scores. Nearly all CurRT patients received hypofractionated radiotherapy regimens (12), with a dose of 50-55 Gy in 20 fractions most common (Table 3), with a mean BED of 66 Gy_{10} (range 58-73 Gy_{10}). Histological or pathological diagnosis was made in 296 CurRT patients (88%), usually by bronchoscopy (112 patients) or fine needle aspirate (179 patients).

Table 2. Baseline pulmonary, co-morbidity, and radiotherapy data for 338 patients with inoperable early stage NSCLC treated with curative intent. FEV1: forced expiratory volume in one second; FVC: forced vital capacity; DLCO/VA: diffusion capacity of carbon monoxide per liter of alveolar volume

Variable	Median (range) or No. (%)
Pulmonary Function	
FEV1	1.45 L (0.41 - 4.12 L)*
FVC	2.57 L (1.18 - 5.29 L)*
FEV1/FVC [%]	59% (26% - 100%)
DLCO/VA [ml/min/mmHg/L]	3.06 (0.95-5.45)
Smoking status	
Never smoked	8 (2)
Former smoker (>1 year cessation)	186 (55)
Current smoker	125 (37)
Unknown	19 (6)
Pack-years of smoking	55 (0-232)
Age-adjusted Charlson comorbidity score	
≤4	25 (6)
5-6	144 (44)
≥7	155 (46)
Unknown	14 (4)
Radiotherapy dose/fractionation	
50-55 Gy in 20 fractions	227 (67)
45-50 Gy in 15 fractions	26 (8)
60 Gy in 30 fractions	16 (5)
Other	69 (20)

*percent predicted not available

For patients treated with PallRT, median BED was 45.1 Gy_{10} (range 24.7-57.9 Gy_{10}). The most common fractionation schemes are shown in Table 3. Intra-bronchial brachytherapy was delivered to 17 patients: 15 in the Pall RT group (of which 5 also had external beam radiotherapy) and 2 in the CurRT group, who had brachytherapy as part of their initial treatment. Fifteen patients in the CurRT group also received chemotherapy as part of primary treatment, delivered concurrently in 12 and sequentially in 3 patients (8).

Table 3. Most common dose-fractionation schemes for patients treated with curative radiotherapy (CurRT) or palliative radiotherapy (PallRT). Biological Equivalent Dose (BED) values are given, corrected for treatment time

Fractionation	BED (Gy_{10})	No. (%)
CurRT patients		
50-55 Gy in 20 fractions	64-70	227 (67)
45-50 Gy in 15 fractions	65-72	26 (8)
60 Gy in 30 fractions	63	16 (5)
Other		69 (20)
PallRT patients		
20 Gy in 4-5 fractions	46-48	198 (41%)
30 Gy in 10 fractions	51	77 (16%)
8-10 Gy in 1 fraction	35-41	59 (13%)
40 Gy in 15 fractions	57	23 (5%)
Other		122 (25%)

Survival Outcomes

All Patients

There were 942 deaths (92% of patients) during the follow-up period. Median OS was 1.1 years. Patients undergoing CurRT had a significantly better OS than patients in the PallRT or NoRT groups (log rank $p<0.0001$). CurRT was associated with a prolongation in median OS of at least 1 year (median survival 2.0 years for CurRT patients, 0.8 years for PallRT patients, and 1.0 years for NoRT patients; Figure 1). OS at 2 years was 51% for CurRT patients, but only 18% for PallRT patients and 24% for NoRT patients. At 5-years, 17% of CurRT patients were alive, compared to only 3-4% of the PallRT or NoRT patients.

Most deaths (841/942, 89%) were attributed to lung cancer. CSS was significantly longer for patients treated with CurRT ($p<0.0001$), relative to the PallRT or NoRT groups. CSS for CurRT patients was 56% at 2 years and 26% at 5 years, compared to 20% and 6% respectively for PallRT patients, and 30% and 6% for NoRT patients (Figure 2).

Figure 1. Overall survival from date of diagnosis for 1043 patients with inoperable early stage lung cancer. Patients treated with curative radiotherapy had significantly better survival than the other groups (p<0.0001). CurRT: curative radiotherapy; PallRT: palliative radiotherapy; NoRT: no radiotherapy

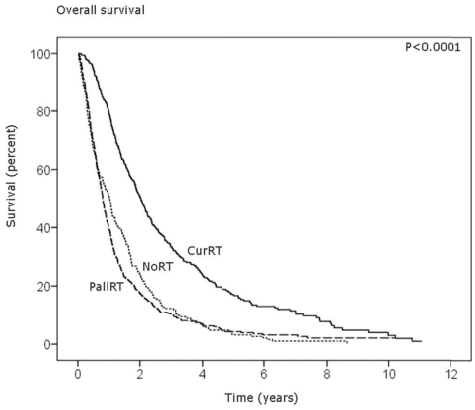
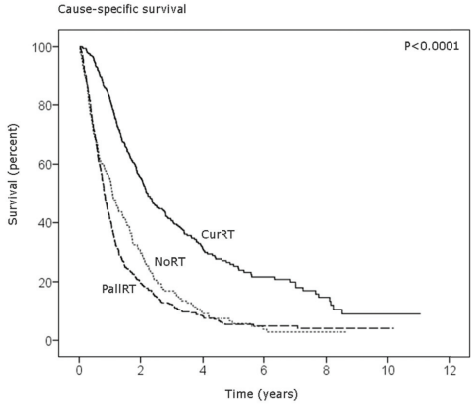


Figure 2. Cause-specific survival (CSS) from date of diagnosis for 1043 patients with inoperable early stage lung cancer. Patients treated with curative radiotherapy had significantly better CSS than others (p<0.0001). CurRT: curative radiotherapy; PallRT: palliative radiotherapy; NoRT: no radiotherapy



A multivariable model was constructed to examine factors predictive of OS and CSS (Table 4) for all patients. Compared to NoRT patients, CurRT patients had a significantly reduced hazard

ratio (HR) of death of 0.49 (95% CI 0.41-0.59), with a similar reduction in the HR for CSS (HR 0.47, 95% CI 0.38-0.57). There were no significant differences in OS or CSS between NoRT and PallRT groups. Other factors predicting OS and CSS were age, gender, T-stage, N-stage, and performance status.

Table 4. Factors predictive of overall survival and cause-specific survival for 1043 patients with non-operable early stage lung cancer. HR: hazard ratio; CI: confidence interval. CurRT: curative radiotherapy; PallRT: palliative radiotherapy; NoRT: no radiotherapy.

Overall Survival			
Factor	**HR**	**95% CI**	**p-value**
Age (continuous, per year)	1.015	1.007-1.023	<0.001
Sex			
Male	1 (ref)		
Female	0.84	0.74-0.96	0.009
T-stage			
T1	1 (ref)		
T2	1.40	1.18-1.66	<0.001
T3	1.97	1.61-2.41	<0.001
N-stage			
N0/X	1 (ref)		
N1	1.43	1.15-1.77	0.001
Performance Status			
0-1	1 (ref)		
2-4	1.58	1.34-1.86	<0.001
Treatment Category			
NoRT	1 (ref)		
CurRT	0.49	0.41-0.59	<0.001
PallRT	0.91	0.76-1.09	0.31

Cause-Specific Survival			
Factor	**HR**	**95% CI**	**p-value**
Age (continuous, per year)	1.016	1.007-1.024	<0.001
Sex			
Male	1 (ref)		
Female	0.86	0.74-0.98	0.027
T-stage			
T1	1 (ref)		
T2	1.60	1.33-1.93	<0.001
T3	2.37	1.90-2.95	<0.001
N-stage			
N0/X	1 (ref)		
N1	1.47	1.17-1.83	0.001
Performance Status			
0-1	1 (ref)		
2-4	1.58	1.33-1.88	<0.001
Treatment Category			
NoRT	1 (ref)		
CurRT	0.47	0.38-0.57	<0.001
PallRT	0.94	0.79-1.13	0.55

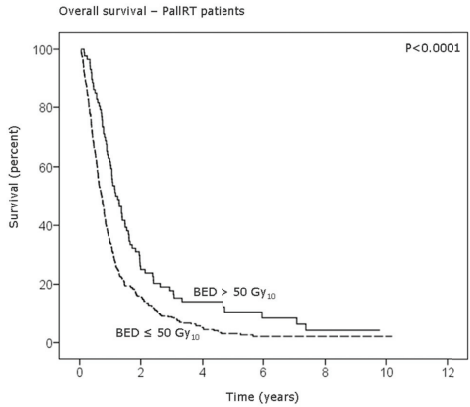
Patients Treated with CurRT

A separate model was constructed to determine factors associated with survival for patients treated with CurRT, to incorporate comorbidity data. CCI was a significant predictor of OS in these patients (HR 1.1 per one point increase in CCI; p=0.044), along with T-stage (p<0.001) and N-stage (p=0.007), but age (p=0.74), sex (p=0.24), and ECOG score (p=0.88) were not significant predictors.

For CSS in CurRT patients, only T-stage (p<0.001) was predictive of outcome. N-stage (p=0.075), CCI (p=0.22), sex (p=0.33), age (p=0.51), and ECOG score (p=0.94) did not significantly predict CSS.

There were 56 local recurrences in the CurRT group, corresponding to actuarial local recurrence rates of 17% at 2 years and 26% at 5 years.

Figure 3. Overall survival from date of diagnosis for 479 patients with inoperable early stage lung cancer treated with palliative radiotherapy (PallRT). Patients treated with biologically effective doses (BED) >50 Gy_{10} (e.g. 30 Gy/10 fractions) had improved survival, compared to those receiving ≤50 Gy



Patients Treated with PallRT

The relationship between BED and survival was assessed for patients receiving PallRT. Those receiving a dose with BED >50 Gy_{10} had significantly longer overall survival than those receiving ≤50 Gy_{10} (Figure 3; log rank p<0.0001), which remained highly significant on multivariable analysis (HR 0.56 95% CI 0.43-0.73; p<0.0001). Stratification of the model by ECOG group demonstrated this survival benefit of BED >50 Gy_{10} in patients with the best performance status (ECOG 0-1; HR 0.64 95% CI 0.41-0.995; p=0.048), and those with unknown performance status (HR 0.55 95% CI 0.37-0.83, p=0.004), but not in those with poor performance status (ECOG 2-4 HR 0.69 95% CI 0.43-1.11 p=0.13).

Discussion

To our knowledge, this is the largest study of patients with inoperable early stage NSCLC that has separately assessed outcomes for patients treated with RT with curative intent, palliative intent, or not at all (16). This study demonstrates that although CurRT patients have substantial co-morbid disease, treatment with CurRT is associated with significantly reduced HR of death compared to no RT, a 1 year improvement in survival, and a chance of long-term survival.

Patients treated with PallRT or no RT are even less fit (with worse performance status), have higher stage disease, and are older. The PallRT and NoRT patients have poor outcomes, with median survival of ≤1 year, and long-term survivors are rare.

The ability of RT to achieve long-term cures for early stage NSCLC has been questioned in the past. In a large study of patients from the Surveillance, Epidemiology and End Results (SEER) database, the use of RT for early-stage NSCLC was associated with only a small improvement in CSS compared to patients getting no treatment, with very few long-term survivors, suggesting that RT does not result in any long-term cures (1). However, this study did not distinguish between patients receiving palliative vs. curative RT. In contrast, by separating patients receiving CurRT from those receiving PallRT, we demonstrated that CurRT is associated with a 1-year improvement in median survival, a survival improvement that persisted at 5-years and beyond.

For patients receiving palliative radiotherapy, our study supports previous data suggesting that higher doses may result in improved survival in patients with good performance status. In patients with advanced NSCLC, a meta-analysis of 13 randomized trials showed that higher palliative doses were associated with improved survival. (15) In an exploratory analysis, this improvement in survival was found to be most associated with doses of 30 Gy in 10 fractions over 2 weeks, or higher, similar to the findings in our study. Higher doses of palliative RT were also associated with improved total symptom scores, at the cost of higher toxicity and a longer time investment. In patients with stage I disease treated with curative radiotherapy, higher RT dose has been associated with improved survival in several studies (2,6,17). Proposed mechanisms by which palliative RT improves OS include the avoidance of life-threatening intrathoracic complications (e.g post-obstructive pneumonia), or preventing a deterioration in performance status that could lead to complications associated with loss of ambulation (such as thrombosis) (15) .

In patients who receive curative-intent treatment (either surgery or RT), age is generally not a predictor of survival after treatment (6,17), indicating that elderly patients fit enough for radical treatment fare as well as their younger counterparts. However, the picture is different when patients treated with palliative RT or no RT are included, as age is associated with a higher risk of OS and CSS. This confirms that patients treated curatively reflect a highly selected

population, and outcomes and prognostic factors for curatively-treated patients do not necessarily extend to all patients with early stage NSCLC.

We did not find an improvement in survival for the PallRT patients as a whole group, compared to the NoRT group, as might be expected. This is likely due to negative selection, in that some of the patients in the PallRT group would have undergone treatment due to complications associated with a poor prognosis, such as hemoptysis or dyspnea. This is reflected in baseline characteristics: the PallRT group had the highest proportion of patients with ECOG 2-4, and the highest proportion of stage II patients. Although the Kaplan-Meier curves suggest that PallRT patients have shorter median survival than the NoRT patients, after controlling for baseline characteristics in the multivariable analysis, this pattern is reversed, and the PallRT patients have a HR of death <1 compared to the NoRT group (although neither of these differences are statistically significant).

Local recurrence rates vary highly between studies, ranging from 6% to 70% (2), likely reflecting differences between studies in radiation dose and fractionation, completeness of imaging follow-up, and death from competing causes (which renders patients no longer at risk of local recurrence). The local recurrence rates in the CurRT group compares favourably with that in the literature and points to the efficacy of the types of doses (mostly hypofractionated, with total doses less than 60 Gy) used during the study era.

The data presented here indicate that the majority of patients with inoperable early stage NSCLC do not undergo treatment with curative intent, and this likely reflects the poor performance status, advanced age, and poor general medical condition of this population of patients. The proportion of patients receiving curative treatment in this study is broadly in keeping with other studies (1,16,18,19), including SEER data, in which approximately 2/3 of patients with inoperable stage I/II NSCLC receive either palliative or curative RT (1,19).

Clearly, more treatment options are needed for this large subset of patients ineligible for curative treatment, and for patients treated today, more options are available than in the past (20). There has been a shift in the RT treatment paradigm, with a move towards even more dramatically hypofractionated, highly conformal radiotherapy. For stage I NSCLC, stereotactic body radiation therapy (SBRT) delivers large ablative doses, such as 60 Gy in 3 fractions in about 1 week, with local control rates reported as 90% or higher in most studies using sufficient doses (21-24), with a favorable toxicity profile. Oncologic outcomes after SBRT may be

superior to wedge resection (25), and implementation of SBRT has been associated with increased radiotherapy utilization and survival in elderly patients (26). Favorable outcomes have been demonstrated with other hypofractionated or otherwise dose-intensified regimens (6,27).

In addition, developments in surgical technology have expanded the eligibility for surgery. For patients who can tolerate anesthesia, minimally invasive video-assisted thoracic surgery (VATS) decreases operative morbidity, allowing for resection in some elderly patients who would otherwise be unfit for surgery (20,24). Elderly and frail patients benefit most from minimally invasive surgical techniques (28). A recent review of VATS outcomes reported local control rates ranging from 88-100% (24), and a meta-analysis suggests that 5-year OS is better with VATS than with open lobectomy (29). Surgical risk can be assessed pre-operatively using validated instruments (30,31).

The findings of this study must be considered in light of its strengths and limitations. Outcomes for patients treated with curative or palliative RT are population-based. Most data was captured prospectively, and outcomes were based on provincial death registries. However, the study has the limitations inherent to a retrospective analysis. As is common with large registries, not all data of interest was available, such as co-morbidity, staging and pulmonary function data for PallRT and NoRT patients, weight loss at presentation, treatment toxicity, and quality of life outcomes. Some data, such as ECOG scores, were not captured for all patients, limiting the power to detect relationships. Although cause of death was assessed prospectively at the time of death, usually by a physician in the community, determination of cause of death is difficult and may be subject to bias in some settings (32).

Patients selected for CurRT may have been better-staged or fitter than patients in the other two groups. Nonetheless, some patients herein may have been understaged by current standards (especially with the lack of PET scanning during most of this era). In light of this and the low rates of mediastinal staging, a proportion of patients in this study likely had occult disease of a higher stage. Not all patients had histological confirmation of diagnosis. Although histological confirmation should be obtained wherever possible, in some cases a decision was made to treat without confirmation (e.g. if the risk of trans-thoracic biopsy was thought to be too high, or repeated biopsy was non-diagnostic). Patients treated without histological confirmation may have inferior survival (26), likely a reflection of the risk of death from the underlying comorbidities that precluded biopsy.

Patients who went untreated and were never referred to the BC Cancer Agency were not captured in the database. It is possible that these non-referred, untreated patients reflect a negatively selected group with poor performance status and poor outcomes, in which case our study would overestimate the true survival of all untreated patients.

In conclusion, patients with curative radiotherapy had a median survival 1 year longer than patients treated with palliative or no RT. In patients treated curatively, co-morbidity was a predictor of OS, and despite the high level of baseline co-morbidities of this population, long-term survival was achieved in almost 20% of patients. Higher doses of palliative radiotherapy are associated with improved survival outcomes. Ongoing advances in surgical and radiotherapy treatment technology may result in higher proportions of treated patients and better outcomes in the future.

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