ORIGINAL ARTICLE

Early mortality after surgical resection for lung cancer: an analysis of the English National Lung cancer audit

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ABSTRACT

Introduction For appropriately staged non-small cell lung cancer (NSCLC) surgical resection can dramatically improve survival, but some may not be offered this treatment because of concerns about perioperative mortality.

Methods We used data from the National Lung Cancer Audit (NLCA) to determine the proportions of English patients who died within 30 and 90 days after surgery for NSCLC. We quantified the predictors of early postoperative death and using these results devised a score to predict risk of death within 90 days of surgery.

Results We analysed data on 10 991 patients operated on between 2004 and 2010. Three per cent (334) of patients died within 30 days of their procedure and 5.9% (647) within 90 days. Age was strongly associated with early postoperative death (adjusted OR within 90 days for 80–84 years vs 70–74 years: 1.46, 95% CI 1.07 to 1.98); significant associations were also observed with performance status (PS) (adjusted OR within 90 days for PS 2 vs PS 0: 2.40, 95% CI 1.68 to 3.41), as well as lung function, stage and procedure type.

Conclusions Our results show that age is the most important predictor of death within both of these early postoperative periods. We used the data in the NLCA to develop a predictive score, based on an English population and specific to lung cancer surgery, which estimates risk of death within 90 days; this score should be tested in future cohorts.

Key messages

What is the key question?
► What are the mortality rates 30 and 90 days after lung cancer surgery in England, and can we use the data in the National Lung Cancer Audit (NLCA) to develop a predictive score to assist with the estimation of mortality risk within the early postoperative period?

What is the bottom line?
► Three per cent of patients in England died within 30 days of potentially curative surgery for non-small cell lung cancer between 2004 and 2010, and a further 2.9% (a total of 5.9%) died within 90 days. There were sufficient data in the NLCA to derive a predictive score based on 90-day mortality after lung cancer surgery.

Why read on?
► We present early mortality figures according to patient features and procedure type, demonstrate the importance of looking beyond 30-day mortality and compare our score with the commonly used Thoracoscore.

INTRODUCTION

For appropriately staged non-small cell lung cancer (NSCLC) surgery is generally accepted as the most effective treatment, but some people may not be offered surgery because of concerns about perioperative mortality. Hospitals with higher resection rates have better overall lung cancer survival, and it has been suggested that if all National Health Service (NHS) Trusts increased their resection rates the proportion of people surviving lung cancer would improve.[1]

Several predictive models for early postoperative mortality have been developed,[2–4] and the British Thoracic Society recommend the use of 'a global risk score such as Thoracoscore to estimate the risk of death' when assessing patients' eligibility for lung cancer surgery.[5] In developing Thoracoscore, Falcoz et al[6] included 10 122 patients (57% of whom had cancer) who underwent any thoracic surgical procedure between 2002 and 2005. The score predicts risk of in-hospital mortality and has recognised limitations, particularly with regard to lung cancer surgery.[7]

Like Thoracoscore, almost all previous studies of early mortality in lung cancer surgery[2–4 8–10] are based on 30-day or in-hospital mortality. These end points were used because they were felt to measure mortality directly attributable to the surgical procedure. For patients and their relatives, however, we believe an estimate of mortality within 90 days, which includes postoperative recovery time, may be more appropriate.

The National Lung Cancer Audit (NLCA) has collected demographic, tumour and treatment data from English NHS Trusts since 2004, and has been shown to be representative of people with lung cancer in England.[11] We used these data to estimate the proportion of patients who died within 30 and 90 days of potentially curative surgery for NSCLC and performed a multivariate analysis to quantify risk factors for death within 30 days and within 90 days. Our final aim was to see whether we could

use the data in the NLCA to produce a predictive score for early death after thoracic surgery which was specifically for people with lung cancer, and looked beyond 30-day mortality.

METHODS

Study population

Our initial dataset consisted of patients in the NLCA database first seen in an NHS Trust between 1 January 2004 and 31 March 2010 who had their record linked with their Hospital Episode Statistics (HES) data from 1 April 1997 to 31 March 2010.

Definition of surgery

Within this dataset we identified patients who had an Office of Population Censuses and Surveys Classification of Interventions (OPCS-4) code for a thoracic surgical procedure likely to have been performed with curative intent for NSCLC; these codes are recorded in the HES database (code list in online supplementary appendix A). We included procedures which took place between 1 January 2004 and 31 March 2010. We excluded patients with stage IIIB or IV disease and those with International Classification of Diseases—revision 10 (ICD-10) codes for metastases recorded prior to the procedure date.

We categorised procedures as pneumonectomy, bi-lobectomy, lobectomy, segmentectomy/wedge resection or other. When more than one relevant procedure code was identified for an individual, the most extensive procedure was used; for the few patients who had codes for more than one procedure of the same type, we used the date of the most recent procedure. If recorded procedure dates differed between HES and the NLCA we calculated the difference between the dates: if this was more than 10 days the patient was excluded from further analysis. We also excluded patients with a procedure date more than 3 months before or 6 months after their lung cancer diagnosis so that patient features, which are usually recorded at the time of diagnosis, might still be representative of the state of the patient at the time of surgery.

Definition of outcome

All records in the NLCA are linked to Office of National Statistics data to obtain dates of death. For patients in this study death records were last updated in August 2011 (16 months after the last procedure date). We used these dates, and HES procedure dates, to calculate the proportion of patients who died within 30 and 90 days of their operation.

Covariate definitions

Data from HES provided information on comorbidity and ethnicity; all other covariate data fields were from the NLCA. Socioeconomic status was measured by postcode-derived Townsend index of material deprivation, in quintiles.[12] We used our established method to calculate a Charlson comorbidity index using diagnoses recorded in patients' HES episodes any time before the procedure date.[13] [14] Charlson index was grouped into four categories for analysis (0, 1, 2–3 and ≥4), as were percentage predicted forced expiratory volume in 1 second (FEV_1: >80%, 60–80%, 40–59% and <40%) and WHO performance status (PS: 0, 1, 2 and 3–4). Stage and histological subtype were obtained from pretreatment records; if these data were missing we used post-treatment records.

Statistical methods

All statistical analyses were performed using Stata MP V.12 (StataCorp, Texas, USA). We calculated the percentages of patients who died within 30 and 90 days of surgery. To determine whether there were marked differences in the features of patients who died within the first 30 days after surgery and those who died between 31 and 90 days, we compared demographic, comorbid, tumour and procedure related features of patients who died in these two time periods.

We used logistic regression to estimate ORs associated with demographic, comorbid, tumour and procedure related factors for death within 30 days and within 90 days. We built a multivariate model including all factors that were significantly associated (defined as p<0.1) with death in univariate analysis and then assessed the significance of each variable in the multivariate model using a likelihood ratio test.

Predictive score

To calculate our predictive score we re-ran our model restricted to records with complete data on PS, stage and lung function. Because of the reduced power with this smaller sample we recoded Charlson index as a binary variable (0–1, ≥2) and age as <55, 55–65, 66–75 and >75 years. Our predictive score comprises the coefficients and constant from this model.

To demonstrate the function of this score, and to allow comparison with Thoracoscore, we applied both scores to hypothetical low, moderate and high risk cases.

RESULTS

There were 113 261 patients with NSCLC in the NLCA database first seen between January 2004 and March 2010; 46 013 with stage recorded as IIIB or IV and a further 102 who were aged less than 30 years at diagnosis were excluded. Of the remaining patients, 12 269 had an OPCS-4 code for a potentially curative procedure in HES between 1 January 2004 and 31 March 2010. We excluded 292 patients for whom the difference between the procedure date recorded in the NLCA and that recorded in HES was >10 days, 437 who had an ICD-10 code for metastatic cancer recorded prior to the procedure date, and a further 549 for whom the procedure date was >3 months before or >6 months after the NLCA date of diagnosis, leaving 10 991 patients for analysis.

The majority (56%) of these patients were men, 20% were aged 70–74 years and 31% had a PS of 0 (table 1). The most commonly performed procedure was lobectomy (64%), with only 10% of patients having had a pneumonectomy. Twenty-eight per cent of patients had stage IB NSCLC, although 26% did not have a preoperative or postoperative stage recorded. The most common preoperative histological subtype was adenocarcinoma (31%) followed by squamous cell (28%). Twenty-one per cent did not have a record of preoperative or postoperative histology; in most cases this is likely to reflect missing data rather than the absence of histological confirmation of lung cancer.

Mortality

Three per cent of patients (334) died within 30 days of their procedure and a further 2.9% (313) between 31 and 90 days (therefore a total of 5.9% (647) died within 90 days). There were no statistically significant differences in patient, comorbidity or tumour factors between patients who died within 30 days of their procedure and those who died between 31 and 90 days (table 1). A higher proportion of those who died within 30 days had a pneumonectomy or bi-lobectomy compared with those who died between 31 and 90 days. Given these findings, we elected to report results for 90-day mortality for the remainder

Table 1 Features of patients who died within 30 days and between 31 and 90 days after surgery

	Overall N=10991		Died within 30 days (n=334)		Died between 31 and 90 days (n=313)		χ^2
	n	%	n	%*	n	%†	
Sex							
Women	4824	43.9	107	2.2	103	2.1	
Men	6167	56.1	227	3.7	210	3.4	p=0.813
Age group							
<55	1008	9.2	12	1.2	23	2.3	
55–59	1090	9.9	21	1.9	24	2.2	
60–64	1847	16.8	31	1.7	32	1.7	
65–69	2128	19.4	56	2.6	49	2.3	
70–74	2226	20.3	84	3.8	78	3.5	
75–79	1828	16.6	88	4.8	62	3.4	
80–84	730	6.6	34	4.7	35	4.8	
85+	134	1.2	12	9.0	10	7.5	p=0.331
Ethnicity							
White	8983	81.7	254	2.8	256	2.8	
Black	82	0.7	1	1.2	0	0.0	
Asian	112	1.0	2	1.8	1	0.9	
Other	77	0.7	1	1.3	2	2.6	p=0.643‡
Missing	1737	15.8	76	4.4	54	3.1	p=0.317
Townsend quintile							
1	1343	12.2	36	2.7	30	2.2	
2	1602	14.6	45	2.8	41	2.6	
3	1609	14.6	52	3.2	46	2.9	
4	1723	14.6	64	4.0	55	3.4	
(most deprived) 5	2074	15.7	74	4.3	58	3.4	p=0.985‡
Missing	2640	18.9	63	3.0	83	4.0	p=0.328
Performance status							
0	3422	31.1	72	2.1	60	1.8	
1	2815	25.6	84	3.0	93	3.3	
2	465	4.2	23	4.9	28	6.0	
3–4	108	1.0	11	10.2	9	8.3	p=0.524‡
Missing	4181	38.0	144	3.4	123	2.9	p=0.523
Predicted FEV$_1$							
>80%	1891	17.2	34	1.8	39	2.1	
60–79%	1499	13.6	42	2.8	45	3.0	
40–59%	726	6.6	23	3.2	27	3.7	
<40%	141	1.3	5	3.5	7	5.0	p=0.975‡
Missing	6734	61.3	230	3.4	195	2.9	p=0.508
Charlson index							
0	5456	49.6	128	2.3	130	2.4	
1	2791	25.4	87	3.1	84	3.0	
2–3	2233	20.3	95	4.3	81	3.6	
≥4	511	4.6	24	4.7	18	3.5	p=0.715
Stage							
IA	2249	20.5	37	1.6	41	1.8	
IB	3064	27.9	87	2.8	82	2.7	
IIA	334	3.0	6	1.8	3	0.9	
IIB	1494	13.6	55	3.7	47	3.1	
IIIA	933	8.5	41	4.4	39	4.2	p=0.812‡
Missing	2857	26.0	108	3.8	101	3.5	p=0.903
Side							
Right	5067	46.1	157	3.1	161	3.2	
Left	3930	35.8	105	2.7	114	2.9	
Other	85	0.8	5	5.9	4	4.7	p=0.875‡
Missing	1909	17.4	67	3.5	34	1.8	p=0.014
							Continued

Table 1 Continued

	Overall N=10991		Died within 30 days (n=334)		Died between 31 and 90 days (n=313)		
	n	%	n	%*	n	%†	χ²
Histology							
Adenocarcinoma	3406	31.0	60	1.8	75	2.2	
Squamous cell	3106	28.3	125	4.0	107	3.4	
NSCLC NOS	1833	16.7	62	3.4	62	3.4	
Other	368	3.3	10	2.7	12	3.3	p=0.356‡
Missing	2278	20.7	77	3.4	57	2.5	p=0.235
Procedure							
Segmentectomy/wedge	1671	15.2	35	2.1	35	2.1	
Lobectomy	7051	64.2	160	2.3	165	2.3	
Bi-lobectomy	431	3.9	25	5.8	13	3.0	
Pneumonectomy	1121	10.2	78	7.0	51	4.5	
Other	717	6.5	36	5.0	49	6.8	p=0.028

*% of patients in each subgroup who died within 30 days.
†% of patients in each subgroup who died between 31 and 90 days.
‡Excluding missing.
FEV_1, forced expiratory volume in 1 s; NSCLC, non-small cell lung cancer; NOS, not otherwise specified.

of this paper; the results for death within 30 days of surgery are similar and can be found in online supplementary table A.

Within 90 days of surgery, men were more likely to die than women (7.1% vs 4.4%) and the proportion of patients who died after pneumonectomy was higher than for lobectomy (11.5% vs 4.6%) (table 2). Sixteen per cent of patients over 85 years and 18.5% of those with PS 3–4 died within this postoperative period. Age was strongly associated with postoperative mortality: Compared with a patient aged 70–74 years, the odds of death within 90 days of surgery for a patient aged >85 years

were markedly increased, even after accounting for other demographic, tumour and comorbidity factors (adjusted OR 2.84, 95% CI 1.71 to 4.71) (table 2). The next most strongly associated factors were procedure type and PS. Significant associations were also observed with percentage predicted forced expiratory volume in 1 s (FEV_1), stage, Charlson index, Townsend score, ethnicity, histological subtype and sex.

There were 3319 patients with complete data on PS, stage and lung function. The proportions of these patients who died within 30 and 90 days of surgery were slightly lower (2.5% and

Table 2 Factors associated with death within 90 days of surgery

	Overall N=10991		Died within 90 days of surgery (n=647)					
	n	%	n	%	OR	95% CI	Adjusted OR*	95% CI
Sex								
Women	4824	43.9	210	4.4	1.00		1.00	
Men	6167	56.1	437	7.1	1.68	1.42 to 1.98	1.37	1.15 to 1.63
						p<0.0001		p=0.0004
Age group								
<55	1008	9.2	35	3.5	0.46	0.32 to 0.67	0.46	0.32 to 0.68
55–59	1090	9.9	45	4.1	0.55	0.39 to 0.77	0.53	0.37 to 0.75
60–64	1847	16.8	63	3.4	0.45	0.33 to 0.61	0.44	0.32 to 0.59
65–69	2128	19.4	105	4.9	0.63	0.49 to 0.82	0.61	0.47 to 0.79
70–74	2226	20.3	162	7.3	1.00		1.00	
75–79	1828	16.6	150	8.2	1.14	0.90 to 1.44	1.19	0.94 to 1.51
80–84	730	6.6	69	9.5	1.33	0.99 to 1.79	1.46	1.07 to 1.98
85+	134	1.2	22	16.4	2.50	1.54 to 4.06	2.84	1.71 to 4.71
						p<0.0001**		p<0.0001**
Ethnicity								
White	8983	81.7	510	5.7	1.00		1.00	
Black	82	0.7	1	1.2	0.21	0.03 to 1.48	0.21	0.03 to 1.51
Asian	112	1.0	3	2.7	0.46	0.14 to 1.44	0.45	0.14 to 1.46
Other	77	0.7	3	3.9	0.67	0.21 to 2.14	0.71	0.22 to 2.31
Missing	1737	15.8	130	7.5	1.34	1.10 to 1.64	1.46	1.19 to 1.80
						p=0.0030		p=0.0005

Table 2 Continued

	Overall N=10991		Died within 90 days of surgery (n=647)					
	n	%	n	%	OR	95% CI	Adjusted OR*	95% CI
Townsend quintile								
1	1343	12.2	66	4.9	1.00		1.00	
2	1602	14.6	86	5.4	1.10	0.79 to 1.53	1.12	0.80 to 1.57
3	1609	14.6	98	6.1	1.25	0.91 to 1.73	1.35	0.97 to 1.88
4	1723	14.6	119	6.9	1.44	1.05 to 1.96	1.59	1.16 to 2.19
(most deprived) 5	2074	15.7	132	6.4	1.32	0.97 to 1.78	1.45	1.06 to 1.99
Missing	2640	18.9	146	5.5	1.13	0.84 to 1.53	1.13	0.83 to 1.55
						p=0.0221**		p=0.0028**
Performance status								
0	3422	31.1	132	3.9	1.00		1.00	
1	2815	25.6	177	6.3	1.67	1.33 to 2.11	1.38	1.09 to 1.75
2	465	4.2	51	11.0	3.07	2.19 to 4.31	2.40	1.68 to 3.41
3–4	108	1.0	20	18.5	5.66	3.38 to 9.49	4.08	2.37 to 7.02
Missing	4181	38.0	267	6.4	1.70	1.37 to 2.11	1.35	1.06 to 1.73
						p<0.0001**		p<0.0001**
Predicted FEV_1								
>80%	1891	17.2	73	3.9	1.00		1.00	
60–79%	1499	13.6	87	5.8	1.53	1.12 to 2.11	1.37	0.99 to 1.90
40–59%	726	6.6	50	6.9	1.84	1.27 to 2.67	1.64	1.12 to 2.41
<40%	141	1.3	12	8.5	2.32	1.23 to 4.38	2.07	1.06 to 4.04
Missing	6734	61.3	425	6.3	1.68	1.30 to 2.16	1.48	1.13 to 1.95
						p=0.0002**		p=0.0020**
Charlson index								
0	5456	49.6	258	4.7	1.00		1.00	
1	2791	25.4	171	6.1	1.31	1.08 to 1.60	1.20	0.98 to 1.48
2–3	2233	20.3	176	7.9	1.72	1.41 to 2.10	1.54	1.25 to 1.90
≥4	511	4.6	42	8.2	1.80	1.28 to 2.53	1.53	1.07 to 2.18
						p<0.0001**		p<0.0001**
Stage								
IA	2249	20.5	78	3.5	1.00		1.00	
IB	3064	27.9	169	5.5	1.62	1.24 to 2.14	1.39	1.05 to 1.84
IIA	334	3.0	9	2.7	0.77	0.38 to 1.55	0.67	0.33 to 1.37
IIB	1494	13.6	102	6.8	2.04	1.51 to 2.76	1.59	1.16 to 2.19
IIIA	933	8.5	80	8.6	2.44	1.77 to 3.36	1.85	1.32 to 2.60
Missing	2857	26.0	209	7.3	2.20	1.68 to 2.87	1.78	1.32 to 2.41
						p<0.0001**		p=0.0004**
Side								
Right	5067	46.1	318	6.3	1.00			
Left	3930	35.8	219	5.6	0.88	0.74 to 1.05		
Other	85	0.8	9	10.6	1.77	0.88 to 3.56		
Missing	1909	17.4	101	5.3	0.83	0.66 to 1.05		
						p=0.1063		
Histology								
Adenocarcinoma	3406	31.0	135	4.0	1.00		1.00	
Squamous cell	3106	28.3	232	7.5	1.96	1.57 to 2.43	1.38	1.10 to 1.73
NSCLC NOS	1833	16.7	124	6.8	1.76	1.37 to 2.26	1.36	1.05 to 1.76
Other	368	3.3	22	6.0	1.54	0.97 to 2.45	1.14	0.70 to 1.84
Missing	2278	20.7	134	5.9	1.51	1.19 to 1.94	1.08	0.82 to 1.42
						p<0.0001		p=0.0420
Procedure								
Segmentectomy/wedge	1671	15.2	70	4.2	0.90	0.69 to 1.16	0.80	0.61 to 1.05
Lobectomy	7051	64.2	325	4.6	1.00		1.00	
Bi-lobectomy	431	3.9	38	8.8	2.00	1.41 to 2.84	1.94	1.35 to 2.78
Pneumonectomy	1121	10.2	129	11.5	2.69	2.17 to 3.33	2.81	2.22 to 3.56
Other	717	6.5	85	11.9	2.78	2.16 to 3.57	2.12	1.62 to 2.77
						p<0.0001		p<0.0001

*ORs are adjusted for all other factors for which adjusted ORs are given. All p values calculated using likelihood ratio test.
**Likelihood ratio test p for trend.
FEV_1, forced expiratory volume in 1 s; NSCLC, non-small cell lung cancer; NOS, not otherwise specified.

5.1%) than in the overall population of 10 991, however in multivariate analysis age, procedure type, PS, stage, Charlson index and FEV_1 were again found to be significantly associated with early postoperative death, with similar ORs to the initial analysis (table 3 and online supplementary table B). Sex, ethnicity, Townsend quintile and histological subtype were not independently associated with 90-day mortality in this analysis but given the ease of accurately recording sex we retained this variable in our final model.

The coefficients and constant from our multivariate model are presented in table 4, and these are the values we have used in our predictive score. For comparison we also present similar information for Thoracoscore. Table 5 shows the predicted outcomes using our score and Thoracoscore for three hypothetical cases. Predicted mortality using our score was very similar to that of Thoracoscore for the low-risk patient, slightly higher for medium risk and almost double for the high-risk patient.

DISCUSSION
For people undergoing surgical resection with curative intent for NSCLC, we found postoperative mortality to be 3.0% within 30 days and 5.9% within 90 days. Patient demographic, comorbidity and tumour-related features were similar whether we considered those who died within 30 days or 31–90 days after surgery; we suggest that 90-day mortality risk should be considered by patients and doctors prior to surgery. Increasing

age, PS and procedure type were strongly associated with an increased risk of early postoperative death.

We were able to use data from the NLCA to develop a predictive score which provides an estimate of the risk of 90-day mortality after thoracic surgery specifically for lung cancer. This score requires assessment in other cohorts, but has potential to greatly improve the information available to patients and clinicians prior to surgery.

Strengths and weaknesses
The main strengths of our study are the large sample size and the representative nature of the cases included. As far as we are aware this is the largest study of postoperative mortality in lung cancer based on a UK population. There are few previous reports of 90-day mortality after lung cancer surgery and, to our knowledge, no predictive scores based on this outcome.

Whilst case ascertainment has improved and the number of records with missing data has declined since the NLCA was established in 2004,[15] the main weakness of this study remains the missing data. The variable with the greatest proportion of missing data was lung function (percentage predicted FEV_1 was missing in 61% of cases). It is unlikely that these patients underwent thoracic surgery without prior measurement of their lung function, and the data are probably missing because they were not available to administrative staff at the time of data entry. We analysed all variables using a separate category for missing data

Table 3 Factors associated with death within 90 days of surgery for patients with records of performance status, stage and lung function

	Overall N=3319		Died within 90 days of surgery (n=169)					
	n	%	n	%	OR	95% CI	Adjusted OR*	95% CI
Sex								
Women	1482	44.7	57	3.8	1.00		1.00	
Men	1837	55.3	112	6.1	1.62	1.17 to 2.25	1.24	0.88 to 1.75
						p=0.0030		p=0.2196
Age group								
<55	268	8.1	5	1.9	0.27	0.11 to 0.68	0.32	0.12 to 0.83
55–59	272	8.2	8	2.9	0.43	0.20 to 0.92	0.40	0.18 to 0.88
60–64	583	17.6	18	3.1	0.45	0.26 to 0.78	0.45	0.25 to 0.80
65–69	665	20.0	29	4.4	0.64	0.40 to 1.04	0.61	0.37 to 1.00
70–74	694	20.9	46	6.6	1.00		1.00	
75–79	566	17.1	40	7.1	1.07	0.69 to 1.66	1.15	0.73 to 1.82
80–84	236	7.1	18	7.6	1.16	0.66 to 2.05	1.43	0.80 to 2.58
85+	35	1.1	5	14.3	2.35	0.87 to 6.34	3.17	1.12 to 9.01
						p<0.0001**		p<0.0001**
Ethnicity								
White	2769	83.4	146	5.3	1.00			
Black	21	0.6	–	–				
Asian	28	0.8	–	–				
Other	24	0.7	–	–				
Missing	477	14.4	23	4.8	0.91	0.58 to 1.43		
Townsend quintile								
1	448	13.5	14	3.1	1.00			
2	512	15.4	23	4.5	1.46	0.74 to 2.87		
3	531	16.0	39	7.3	2.46	1.32 to 4.59		
4	615	18.5	28	4.6	1.48	0.77 to 2.84		
(most deprived) 5	772	23.3	38	4.9	1.60	0.86 to 3.00		
Missing	441	13.3	27	6.1	2.02	1.05 to 3.91		
						p=0.3325**		

<div align="right">Continued</div>

Table 3 Continued

	Overall N=3319		Died within 90 days of surgery (n=169)					
	n	%	n	%	OR	95% CI	Adjusted OR*	95% CI
Performance status								
0	1674	50.4	51	3.0	1.00		1.00	
1	1390	41.9	97	7.0	2.39	1.69 to 3.38	1.89	1.31 to 2.72
2	215	6.5	19	8.8	3.08	1.78 to 5.33	2.39	1.34 to 4.28
3–4	40	1.2	2	5.0	1.67	0.39 to 7.13	1.67	0.27 to 5.11
						p<0.0001**		p=0.0055**
Predicted FEV_1								
>80%	1508	45.4	58	3.8	1.00		1.00	
60–79%	1145	34.5	58	5.1	1.33	0.92 to 1.94	1.25	0.85 to 1.84
40–59%	557	16.8	43	7.7	2.09	1.39 to 3.14	2.01	1.30 to 3.10
<40%	109	3.3	10	9.2	2.53	1.25 to 5.09	2.78	1.31 to 5.88
						p=0.0001**		p=0.0004**
Charlson index								
0–1	2508	75.6	115	4.6	1.00		1.00	
≥2	811	24.4	54	6.7	1.22	1.03 to 1.44	1.19	1.00 to 1.42
						p=0.0233**		p=0.0514
Stage								
IA	949	28.6	30	3.2	1.00		1.00	
IB	1237	37.3	63	5.1	1.64	1.06 to 2.56	1.42	0.90 to 2.25
IIA	131	3.9	4	3.1	0.96	0.33 to 2.78	0.77	0.26 to 2.27
IIB	614	18.5	41	6.7	2.19	1.35 to 3.55	1.70	1.01 to 2.87
IIIA	388	11.7	31	8.0	2.66	1.59 to 4.46	2.18	1.25 to 3.81
						p=0.0001**		p=0.0085**
Side								
Right	1841	55.5	96	5.2	1.00			
Left	1365	41.1	64	4.7	0.89	0.65 to 1.24		
Other	18	0.5	1	5.6	1.07	0.14 to 8.12		
Missing	95	2.9	8	8.4	1.67	0.79 to 3.55		
						p=0.4988		
Histology (preoperative)								
Adenocarcinoma	1155	34.8	43	3.7	1.00		1.00	
Squamous cell	1151	34.7	74	6.4	1.78	1.21 to 2.61	1.08	0.72 to 1.63
NSCLC NOS	662	19.9	35	5.3	1.44	0.91 to 2.28	1.03	0.64 to 1.66
Other	82	2.5	3	3.7	0.98	0.30 to 3.24	0.83	0.25 to 2.82
Missing	269	8.1	14	5.2	1.42	0.77 to 2.63	1.37	0.73 to 2.60
						p=0.0538		p=0.8873
Procedure								
Segmentectomy/wedge	441	13.3	16	3.6	0.88	0.51 to 1.52	0.76	0.44 to 1.33
Lobectomy	2275	68.5	93	4.1	1.00		1.00	
Bi-lobectomy	131	3.9	12	9.2	2.37	1.26 to 4.44	2.37	1.23 to 4.60
Pneumonectomy	335	10.1	40	11.9	3.18	2.15 to 4.70	3.36	2.17 to 5.20
Other	137	4.1	8	5.8	1.46	0.69 to 3.06	1.10	0.51 to 2.36
						p<0.0001		p<0.0001

*ORs are adjusted for all other factors for which adjusted ORs are given. All p values calculated using likelihood ratio test.
**Likelihood ratio test p for trend.
FEV_1, forced expiratory volume in 1 s; NSCLC, non-small cell lung cancer; NOS, not otherwise specified; PS, performance status.

to ensure that the results were a true representation of the available data and, given the size of our study, we were still able to analyse data on lung function for over 4000 individuals. The UK lung cancer population is predominantly white and therefore we did not have sufficient power to detect any associations between ethnicity and outcome in this study.

We identified surgical procedures using HES coding, the accuracy of which is audited annually.[16] When calculating Charlson index we assigned a score of zero to any individual who either had no records of hospital admission in the HES database, or had no record of an ICD-10 code relating to any of the diagnoses in the Charlson index.[14] This method may have missed diagnoses which were only recorded in primary care; however 95% of patients had at least one inpatient episode prior to their procedure date and all relevant or major comorbidities should be recorded in each episode.

Comparison with previous studies
90-day mortality
There are few previous reports of 90-day mortality following surgery for lung cancer. One Dutch group reported 3.9% 30-day and 6.8% 90-day mortality after lobectomy,

Table 4 Coefficients from multivariate model using NLCA data and from Thoracoscore

	Coefficient	
	Thoracoscore[6]	NLCA data
Definition of early mortality	30 days or in hospital	90 days
Number of deaths	218	169
Age (years)		
<55	–	–
55–65	0.77	0.31
>65	1.01	
66–75		0.97
>75		1.40
Sex		
Women	–	–
Men	0.45	0.23
ASA score		
≤2	–	
≥3	0.61	
Performance status		
0		–
≤2	–	
1–2		0.68
≥3	0.69	0.21*
MRC dyspnoea score		
≤2	–	
≥3	0.91	
% predicted FEV₁		
>80%		–
61–80%		0.20
40–60%		0.69
<40%		0.95
Priority		
Elective	–	
Urgent/emergency	0.84	
Procedure class		
Other†	–	
(Bi-)lobectomy, wedge or segmentectomy		–
Other‡		0.07
Pneumonectomy	1.22	1.16
Diagnosis group		
Benign	–	
Malignant	1.24	
Comorbidity score§		
0	–	
1–2	0.74	
≥3	0.91	
Charlson index		
0–1		–
≥2		0.33
Stage		
IA		–
IB		0.42
IIA or IIB		0.51
IIIA		0.84
Constant	−7.37	−5.28

*Only 40 patients and two deaths in this group.
†Other includes mediastinoscopy or other mediastinal surgery, wedge resection, lobectomy or bi-lobectomy.
‡Other includes procedures listed in online supplementary appendix A. Odds=exp (total of coefficients+constant); probability of death=odds/(1+odds).
§Number of significant comorbid conditions, including smoking, history of cancer, chronic obstructive pulmonary disease, diabetes mellitus, arterial hypertension, peripheral vascular disease, obesity and alcoholism.
ASA, American Society of Anaesthesiologists; FEV₁, forced expiratory volume in 1 s; MRC, Medical Research Council; NLCA, National Lung Cancer Audit; –, indicates baseline group.

bi-lobectomy or pneumonectomy between 2000 and 2008.[17] These figures are comparable to ours.

Almost as many people died between 31 and 90 days as in the first 30 days after lung cancer resection in our study. Many previous studies included death prior to hospital discharge in their definition of 30-day mortality to account for people who were alive longer than 30 days due to improvements in perioperative management and intensive care. Discharge practices, however, vary between hospitals, and there remain a substantial proportion of patients who die after discharge but before 90 days.[18] One of the important findings from our study is that the features of patients who die within the first 30 days of surgery are no different to those of patients who die between 31 and 90 days postoperatively. Since postoperative recovery takes several months, we suggest that patients should be provided with an estimate of their risk of death within 3 months, instead or as well as within 1 month.

Comparison with Thoracoscore
The discrepancies between mortality risk estimates using our score and Thoracoscore (table 5) are likely to be due to the longer time period in our study (deaths within 90 days compared with deaths in hospital) and the differences in populations studied. The overall in-hospital mortality using the data on which Thoracoscore was based was 2.2% (218 deaths) compared with 5.1% 90-day mortality (169 deaths in the non-missing dataset) in our study.

The Epithor database, which was used for Thoracoscore, includes data on American Society of Anaesthesiologists (ASA) score and Medical Research Council (MRC) dyspnoea score, both of which are components of Thoracoscore but are not recorded in the NLCA. Our score includes stage and lung function but while these data were available to the authors of Thoracoscore they did not find them to be significantly associated with in-hospital mortality, perhaps due to the better overall health of their cohort of patients. In addition, Thoracoscore uses age categories <55, 55–64 and >64 years, and was developed using a dataset in which the mean age at operation was 54.7 years. In the UK, 75% of people diagnosed with lung cancer are over 65 years of age,[19] and the number of older patients undergoing surgical resection for lung cancer is increasing.[20] The mean age of patients in our dataset was 67 years.

A small study of lung cancer resections in England adds to concerns that Thoracoscore may not have good predictive ability for people with lung cancer.[7] Neither score has been validated in a large study of patients with lung cancer, and prospective evaluation needs to be undertaken as a matter of priority. If our score proves to be a useful clinical tool, care must be taken when applying it to people of non-white ethnicity given that they contributed such a small proportion of our study data (of note, this is also likely to be the case for Thoracoscore, although ethnicity is not reported in the publication by Falcoz et al[6]).

Other predictive models
We compared our predictive score with Thoracoscore because it is recommended in national guidelines,[5] however risk factors have also been assessed in other studies, including the European Thoracic Surgery Database Project, from which the European Societies Subjective Score (ESSS) was developed.[2] This study included 3426 patients of whom 66 died in hospital, and the ESSS comprises age, MRC dyspnoea score, ASA score and procedure type. Two of the four components of the ESSS model are subjectively assessed; we only included one such measure (PS) and Thoracoscore includes all three. The authors of the ESSS were concerned that their tool included predominantly subjective measures and so used a subgroup of 1753 patients to develop a score based on age and predicted postoperative FEV₁.

Table 5 Patient features and predicted outcomes

Description of patient	Estimated risk of death (%)	
Low risk: 56-year-old woman, MRC 1, ASA 2, PS 0, FEV$_1$ 81%, hypertension, ex-smoker, NSCLC stage IB, elective lobectomy	90-day mortality (NLCA score)	1.0
	In-hospital mortality (Thoracoscore)	1.1
Moderate risk: 70-year-old man, MRC 2, ASA 3, PS 1, FEV$_1$ 65%, COPD, hypertension, smoker, NSCLC stage IIB, elective lobectomy	90-day mortality (NLCA score)	6.4
	In-hospital mortality (Thoracoscore)	4.1
High risk: 81-year-old man, MRC 4, ASA 3, PS 2, FEV$_1$ 50%, COPD, ischaemic heart disease, hypertension, ex-smoker, diabetes, NSCLC stage IIB, elective pneumonectomy	90-day mortality (NLCA score)	43.0
	In-hospital mortality (Thoracoscore)	26.2

ASA, American Society of Anaesthesiologists grade; COPD, chronic obstructive pulmonary disease; FEV$_1$, forced expiratory volume in 1 s; MRC, Medical Research Council dyspnoea score; NLCA, National Lung Cancer Audit; NSCLC, non-small cell lung cancer; PS, performance status.

Clinical relevance

The proportions of patients who die after potentially curative surgery for NSCLC are 3.0% within 30 days and 5.9% within 90 days. Given that alternative treatments, particularly for stage II–IIIA disease, do not offer the same chance of long-term survival, we would suggest that these figures are low. The risks must be viewed in the context of prognosis without an operation and whilst clinicians must understand the factors associated with increased risk, it is not just the clinician's but also the patient's perception of risk which is important. A review of the currently accepted standards for surgical mortality in the context of open discussions with patients may be called for to ensure that all eligible patients are allowed to consider this potentially curative treatment.

The use of early deaths after lung cancer surgery as a measure of performance of individual thoracic surgeons, which may be introduced for revalidation, has raised concerns over risk-averse patient selection by surgeons. It is clearly important that if mortality figures are to be used in this way they are adjusted for the factors which we have shown to be strongly associated with early postoperative death (most importantly age and PS) and ideally fully adjusted using a risk prediction model, so that surgeons are not any less inclined to offer surgery to a patient of borderline fitness.

CONCLUSION

We were able to use the NLCA data to develop a score which estimates 90-day mortality risk for patients with NSCLC, based on an English population. Whilst this needs assessment in other cohorts, it has potential to increase the accuracy with which we can predict outcomes in lung cancer surgery. In the meantime, it is important that clinicians are aware of the limitations of risk estimates using Thoracoscore and 30-day mortality figures when applied to patients with lung cancer.

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