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ORIGINAL REPORT

High Procedure Volume Is Strongly Associated With Improved Survival After Lung Cancer Surgery

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ABSTRACT

Purpose
Studies have reported an association between hospital volume and survival for non–small-cell lung cancer (NSCLC). We explored this association in England, accounting for case mix and propensity to resect.

Methods
We analyzed data on 134,293 patients with NSCLC diagnosed in England between 2004 and 2008, of whom 12,862 (9.6%) underwent surgical resection. Hospital volume was defined according to number of patients with resected lung cancer in each hospital in each year of diagnosis. We calculated hazard ratios (HRs) for death in three predefined periods according to hospital volume, sex, age, socioeconomic deprivation, comorbidity, and propensity to resect.

Results
There was increased survival in hospitals performing > 150 surgical resections compared with those carrying out < 70 (HR, 0.78; 95% CI, 0.67 to 0.90; P_{trend} < .01). The association between hospital volume and survival was present in all three periods of follow-up, but the magnitude of association was greatest in the early postoperative period.

Conclusion
High-volume hospitals have higher resection rates and perform surgery among patients who are older, have lower socioeconomic status, and have more comorbidities; despite this, they achieve better survival, most notably in the early postoperative period.

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INTRODUCTION

Non–small-cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancers. Surgical resection is the first-line treatment offered to patients with early-stage disease who are considered medically fit.[1]

Many studies have shown that patients undergoing surgery for lung cancer benefit from receiving treatment in hospitals where high numbers of lung cancer resections are carried out.[2-13] Almost all of these studies were carried out in the United States. In contrast, a number of studies, for the most part carried out in countries other than the United States, did not find an association between hospital volume and outcome after lung cancer resection.[14-20] Some of these were smaller studies.[14,16,19] A recent meta-analysis showed that increasing hospital volume was associated with improved mortality in the short term, but not with long-term survival.[21] To our knowledge, no study has been carried out to assess the effect of hospital volume on survival among patients with lung cancer in England.

Virtually all patients with lung cancer who reach hospital care in England are managed by a multidisciplinary team, with details of their cases discussed in a structured meeting. There are 154 lung cancer multidisciplinary teams in England, and almost all have a thoracic or cardiothoracic surgeon in attendance. The surgery itself is mostly carried out in a smaller number of specialist centers by specialist thoracic or cardiothoracic surgeons. Our report explores the association between hospital volume and survival among all patients with NSCLC diagnosed in England who underwent surgical resection and takes into account the differences in case selection and propensity to resect.

METHODS

Patients

We extracted data on 161,737 lung cancers (International Classification of Diseases [version 10] codes C33 to

C34) diagnosed in England between 2004 and 2008 from the National Cancer Data Repository (NCDR). The NCDR contains data collected and quality assured by the eight regional cancer registries in England. Death information is supplied by the National Health Service (NHS) Central Register via the Office for National Statistics. Information on surgical resections was obtained from inpatient and day-case episodes recorded in the Hospital Episode Statistics (HES) data set collated by the NHS Information Centre.

We excluded 7,547 lung cancers identified from death certificates only and 358 cases without recorded NHS numbers. Only the first lung cancer recorded for each patient was selected, which affected 573 patients with multiple primary lung cancers. Because they are rarely considered for surgical resection, 18,966 patients (12.4%) with small-cell lung cancer were also excluded from analysis. The final data set thus included 134,293 patients with NSCLC, of whom 12,862 (9.6%) underwent surgical resection in 58 NHS hospital trusts.

Patient Characteristics

Information on surgery was derived from linked Hospital Episode Statistics (HES) records. Types of surgical resections were included as previously defined[22]: lobectomy or bilobectomy (68%), partial lobectomy or wedge resection (16%), pneumonectomy (12%), sleeve resection (1%), and other less common procedures (other or unspecified excisions of [or lesions of] trachea, carina, lung, and chest wall, 4%). Data on surgery from 1 month before to 6 months after the date of diagnosis were included. If patients had > one record of a relevant surgical procedure, the first procedure was used in analysis.

Socioeconomic deprivation was measured by lower super output area of residence (each comprising a population of approximately 1,500) based on the income domain of the Index of Deprivation 2007[23] and grouped into quintiles. Each patient was thereby assigned to a socioeconomic quintile based on his or her postcode of residence.

For each patient, comorbidity information was obtained using diagnosis codes recorded in HES. All diagnoses from 2 years before to 3 months after the patient's date of diagnosis were classified according to scores from the weighted Charlson comorbidity index[24] and modified to exclude cancer as a comorbid condition. The resulting scores were aggregated into four categories of increasing severity of comorbidity.

Hospital Volume and Resection Quintile

The number of resections was available at the organization level of NHS hospital trusts. In England, an NHS hospital trust manages ≥ one local hospital. In this article, we refer to NHS hospital trusts simply as hospitals, and the annual number of resections in an NHS hospital trust is referred to as the hospital volume. Hospital volume was defined according to the number of patients with lung cancer undergoing surgical resection in each hospital in each year of diagnosis, which ranged from one to 194. Similar numbers of resected patients were allocated to five hospital volume groups, which were defined as follows: < 70, 70 to 99, 100 to 129, 130 to 149, and ≥ 150 procedures per year (Table 1).

We created resection quintiles based on the proportion of patients with lung cancer resident in each Primary Care Trust (PCT) geographic area who underwent surgery by year of diagnosis, with quintile one representing PCT areas where the lowest proportion of patients received surgery (5.5%) and quintile five the highest (14.3%). Each patient with lung cancer was assigned to a resection quintile, depending on his or her PCT area of residence.

Data Analysis

The number and proportions of patients who underwent surgical resection were calculated according to resection quintile and patient characteristics (sex, age, socioeconomic deprivation, comorbidity, morphology, surgical procedure, and year of diagnosis). We also explored associations between hospital volume and patient characteristics.

Cox proportional hazards regression analyses were used to assess the association between hospital volume and survival among resected patients (n = 12,862). Survival time was calculated from date of surgery until date of death resulting from any cause or end of study on December 31, 2009. We calculated multivariable hazard ratios (HRs) according to hospital volume, with appropriate adjustment for a priori identified potential confounders (sex, age, socioeconomic deprivation, comorbidity, and resection quintile). In addition, to account for the risk of death potentially varying between groups of patients treated within a given hospital, a shared frailty Cox model was used, with hospital as a random effect. We estimated χ^2 and *P* values for trend or heterogeneity, as appropriate, excluding the not-known categories. To assess the association between hospital volume and survival in different time intervals after surgery, the follow-up period was divided into three predefined periods: perisurgical (0 to 30 days postsurgery), intermediate (31 to 365 days postsurgery), and long term (> 365 days postsurgery).

Fit of the regression model was assessed with χ^2 tests and Harrell's c concordance statistic. We considered the assumption of proportional hazards and explored the joint effects of independent variables by fitting first-order interaction terms. All analyses were carried out using STATA (version 11.2; STATA, College Station, TX).

RESULTS

An overview of the patients and proportions of patients undergoing surgical resection included in the analysis is presented in Table 1. A greater proportion of female patients underwent surgical resection compared with male patients (9.9% *v* 9.4%; $P = .001$). The proportion of patients undergoing surgical resection decreased with advancing age ($P < .001$). Increasing level of socioeconomic deprivation was associated with a decreasing proportion of patients undergoing surgical resection ($P < .001$). Patients with more severe comorbidity were less likely to undergo surgery ($P < .001$). We also assessed the associations between hospital volume and case-mix variables. There was a positive association between hospital volume and resection quintile ($P < .001$). Sex was not associated with hospital volume ($P = .55$). Increasing hospital volume was associated with a higher proportion of older patients undergoing surgery ($P = .01$). Higher-volume hospitals included relatively greater numbers of patients from more-deprived areas ($P = .002$) as well as relatively higher numbers of patients with comorbidity ($P < .001$).

Table 2 lists the HRs as estimated by the sex- and age-adjusted (model one), multivariable (model two), and multivariable shared-frailty regression models (model three). After adjustment for age and sex (model one), increasing hospital volume was associated with lower mortality ($\chi^2 = 7.08$; $P_{trend} < .01$). Compared with hospitals performing < 70 surgical procedures per year, hospitals carrying out more were all associated with decreased mortality, but the magnitude of the association was similar in the range of hospital volume, from 70 to 149 procedures per year. Among hospitals carrying out > 150 procedures compared with those carrying out < 70 per year, this association was strongest (HR, 0.87; 95% CI, 0.80 to 0.95).

Further adjustment for socioeconomic deprivation, comorbidity, and resection quintile (model two) strengthened the association ($\chi^2 = 12.77$; $P_{trend} < .001$), particularly in hospitals performing > 150 surgical resections (HR, 0.83; 95% CI, 0.76 to 0.91). Using the shared-frailty model to account for hospital-level variability in mortality (model three) diminished the statistical significance of the association ($\chi^2 = 8.08$; $P_{trend} < .01$) but increased the absolute magnitude of the association. For hospitals performing > 150 surgical resections, HR was 0.78 (95% CI, 0.67 to 0.90).

Table 3 lists fully adjusted (age, sex, socioeconomic deprivation, comorbidity, and resection quintile) HRs estimated by the shared-frailty model in the different time periods after surgery. Each of the three periods of follow-up contributed to the overall association between hospital volume and survival (Table 2; model three), but the linear trend in HRs did not reach statistical significance in all three

Table 1. Characteristics of Patients With NSCLC in England: 2004 to 2008

Characteristic	Total No. of Patients	Resected Patients		Resection Volume (No. of procedures per year)*				
		No.	%	< 70 (%)	70 to 99 (%)	100 to 129 (%)	130 to 149 (%)	≥ 150 (%)
Total	134,293	12,862	9.6	2,582	2,662	2,378	2,651	2,589
No. of hospitals contributing to category				44	13	11	9	6
Resection quintile								
1	26,970	1,483	5.5	14	12	14	12	6
2	26,800	2,041	7.6	16	22	15	16	11
3	26,824	2,517	9.4	21	19	18	24	16
4	26,990	3,011	11.2	25	20	29	26	18
5	26,709	3,810	14.3	26	27	25	22	48
χ^2†		1,344.04				211.26		
P_{trend}		< .001				< .001		
Sex								
Male	78,221	7,317	9.4	57	56	58	57	56
Female	56,072	5,545	9.9	43	44	42	43	44
χ^2†		10.78				0.36		
P		.001				.55		
Age group, years								
0-54	8,878	1,395	15.7	12	11	11	10	10
55-59	9,595	1,417	14.8	12	11	11	11	10
60-64	14,721	2,138	14.5	16	16	16	17	17
65-69	18,654	2,502	13.4	19	18	20	21	19
70-74	22,389	2,605	11.6	20	21	19	21	20
75-79	25,382	2,006	7.9	15	16	16	16	16
80-84	20,652	697	3.4	5	6	6	4	7
≥ 85	14,022	102	0.7	1	1	1	1	1
χ^2†		3,212.91				7.54		
P_{trend}		< .001				.01		
Socioeconomic deprivation								
1 (most affluent)	18,702	1,931	10.3	13	14	18	14	16
2	23,816	2,325	9.8	17	21	20	16	16
3	27,167	2,603	9.6	22	22	22	19	17
4	30,669	2,829	9.2	24	21	21	24	20
5 (most deprived)	33,939	3,174	9.4	24	23	19	27	31
χ^2†		15.51				9.26		
P_{trend}		< .001				.002		
Charlson comorbidity score								
0	64,013	6,840	10.7	53	57	59	50	49
1	36,618	4,250	11.6	34	32	28	36	35
2	13,129	1,175	8.9	9	8	9	9	11
≥ 3	8,671	597	6.9	5	4	5	5	5
Not known	11,862	—	—	—	—	—	—	—
χ^2†		92.77				24.06		
P_{trend}		< .001				< .001		

Abbreviation: NSCLC, non–small-cell lung cancer.
*Results given as %, except first two rows (ie, Total, No. of Hospitals Contributing to Category), which are presented as numbers.
†1 *df*.

periods. The extreme contrast between the lowest- and highest-volume groups was statistically significant in all three periods of follow-up. The magnitude of association was greatest in the period 0 to 30 days from surgery (HR for ≥ 150 hospital volume group compared with < 70, 0.58; 95% CI, 0.38 to 0.89) and smallest in the period 365 days after surgery (HR, 0.84; 95% CI, 0.71 to 0.99).

All variables in model three were statistically significant, and the overall model had a χ^2 (23 *df*) of 476.5 ($P < .001$). Harrell's c concordance statistic was 0.59. First-order interaction terms added to model three were not statistically significant.

DISCUSSION

In this study, we found that increasing hospital volume of lung cancer surgical resection is associated with increased survival, particularly in the early postoperative period. The association diminished but persisted throughout follow-up.

We have previously shown that there is substantial geographic variation in the proportion of patients with NSCLC who undergo surgical resection and that increasing resection rates are associated

Table 2. HRs and 95% CIs According to Hospital Volume Among Patients With NSCLC

	Model One*		Model Two†		Model Three‡	
Hospital Volume (No. of procedures per year)	HR	95% CI	HR	95% CI	HR	95% CI
< 70	1.00	—	1.00	—	1.00	—
70 to 99	0.89	0.82 to 0.97	0.90	0.83 to 0.98	0.86	0.77 to 0.97
100 to 129	0.92	0.84 to 1.00	0.93	0.85 to 1.01	0.90	0.79 to 1.02
130 to 149	0.91	0.84 to 0.99	0.91	0.83 to 0.98	0.89	0.78 to 1.02
≥ 150	0.87	0.80 to 0.95	0.83	0.76 to 0.91	0.78	0.67 to 0.90
χ^2§	7.08		12.77		8.08	
P	< .01		< .001		< .01	

Abbreviations: HR, hazard ratio; NSCLC, non–small-cell lung cancer.
*Adjusted for age and sex.
†Adjusted for age, sex, socioeconomic deprivation, Charlson comorbidity score, and resection quintile.
‡Shared-frailty model adjusted for age, sex, socioeconomic deprivation, Charlson comorbidity score, resection quintile, and hospital (random effect).
§1 *df*.

with increased survival.[25] Adjustment for the propensity to operate in the area of residence of the patient and for age, sex, socioeconomic deprivation, and comorbidity strengthened the association between hospital volume and survival. This indicates that hospital volume has an independent effect on survival, irrespective of other factors that affect the risk of dying. Interestingly, further adjustment for hospital-level variation in mortality increased the magnitude of the association, whereas statistical significance was attenuated because of the loss of statistical power.

The significant trend in association between hospital volume and survival is arguably a result of high mortality in the lowest hospital volume group and low mortality in the highest volume group only. In the three middle categories, representing hospital volumes ranging from 70 to 149, there was little variation in survival (HRs were 0.86, 0.90, and 0.89, respectively). A fair narrative summary, therefore, may be that low-volume hospitals have low survival, and high-volume hospitals have high survival. We conducted a post hoc analysis combining the three middle categories as the reference category and obtained the following HRs: < 70: HR, 1.14 (95% CI, 1.03 to 1.26); 70 to 149: HR, 1.00 (reference category); and ≥ 150: HR, 0.88 (95% CI, 0.79 to 0.97).

Hospital volume is a proxy measure, and it does not identify what aspects of the practice of high-volume hospitals drive the observed association with survival. Two potential explanations have been put forward that could explain our results.[26]

Higher-volume hospitals may have more specialized infrastructures, are more likely to have dedicated thoracic surgery on site, and could be expected to have advanced skills in the management of all patients with lung cancer in all staff groups, which intuitively could lead to higher survival.[26] Higher hospital volumes may increase the relevant experience and maintain the skills of surgeons in performing complex lung cancer resections. They could also improve the skills of the wider surgical team, including anesthetists, in managing postoperative complications in intensive care and high-dependency units, which could lead to a reduction in early postoperative mortality. This study found the biggest impact on survival in the early postoperative period, suggesting in-hospital management as an important contributor to better outcomes. One study found a strong association between individual surgeon volume and in-hospital deaths.[16] Other research, however, has suggested that the association with hospital volume may not be limited to surgeon experience alone, as illustrated by a study that found that surgeon volume accounted for just 24% of the observed association between lung cancer operative mortality and hospital volume, whereas 34% of the association with surgeon volume was explained by hospital volume.[27] In addition, a UK study suggested that individual surgeon volume per se was not associated with in-hospital mortality.[28]

The observed associations may also be the result of referral patterns (ie, larger surgical volumes are result of better outcomes) rather than the cause.[26] Some hospitals have more skillful surgeons and

Table 3. HRs and 95% CIs According to Hospital Volume Among Patients With NSCLC by Period of Follow-Up

	0 to 30 Days		31 to 365 Days		> 365 Days	
Hospital Volume (No. of procedures per year)	HR	95% CI	HR	95% CI	HR	95% CI
< 70	1.00	—	1.00	—	1.00	—
70 to 99	0.81	0.58 to 1.13	0.82	0.70 to 0.96	0.95	0.83 to 1.09
100 to 129	0.75	0.52 to 1.08	0.92	0.78 to 1.09	0.94	0.81 to 1.08
130 to 149	0.91	0.64 to 1.31	0.78	0.66 to 0.93	0.97	0.84 to 1.13
≥ 150	0.58	0.38 to 0.89	0.80	0.67 to 0.95	0.84	0.71 to 0.99
χ^2*	3.24		5.93		2.67	
P	.07		.01		.10	

NOTE. Based on shared-frailty model adjusted for age, sex, socioeconomic deprivation, Charlson comorbidity score, resection quintile, and hospital (random effect).
Abbreviations: HR, hazard ratio; NSCLC, non–small-cell lung cancer.
*1 *df*.

multidisciplinary teams and better equipment and, as a result, may attract a larger number of patients with NSCLC who would undergo surgical resection. Moreover, high-volume hospitals may employ better methods for accurate staging and select patients with better fitness and stage distribution. However, the data presented here show that higher-volume hospitals achieve better outcomes despite performing surgery among older patients with greater comorbidity and from lower socioeconomic backgrounds. This argues against selective referral of a more favorable patient population.

The findings in this study are in agreement with a number of studies that also observed better survival among patients with resected lung cancer with increasing hospital volume.[2-11] Moreover, we and others have shown similar effects in other types of cancer.[3,4,7-9,11-13,29] Postoperative mortality HRs were found to be of the same order of magnitude as previously published fatality odds ratios.[2,10] The magnitude of association between hospital volume and survival in this study was similar to those observed in three studies reporting similar measures.[2,4,6]

This study benefits from nationwide data on patients undergoing surgical resection in England. The NCDR case ascertainment for lung cancer is estimated to be high, at approximately 99%.[30] HES holds detailed records of admitted patient care delivered in England by NHS hospitals or delivered in the independent sector but commissioned by the NHS. A systematic review found acceptable accuracy for procedure codes from NHS administrative data.[31] We adjusted the survival analysis for potential confounding by age, sex, socioeconomic deprivation, comorbidity, and propensity to operate in the area where the patient was diagnosed, which strengthened the observed associations. However, a major limitation of the present study is the absence of data on staging procedures, pre- and postoperative stages, and treatments other than surgery. Although one explanation for the results is that lower-volume hospitals are performing surgery among patients with more-advanced tumors (perhaps as a result of less detailed preoperative staging [eg, because of poor access to positron emission tomography–computed tomography scanning and endoscopic ultrasound]), leading to poorer long-term survival, this concern is mitigated by higher-volume hospitals having a higher surgical resection rate. It is thus more likely that the higher-volume hospitals are extending rather than reducing the boundaries of resectability among the patients they manage.

In conclusion, our results indicate that hospitals in England with high volumes of surgical resection of lung cancer perform surgery among patients who are older, are more socioeconomically deprived, and have more comorbidity. Despite this, they achieve better survival, especially in the early postoperative period.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Manuscript writing: All authors
Final approval of manuscript: All authors

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Appendix

Research in Context

We reviewed evidence on the association between hospital surgical volume and lung cancer survival and mortality. We searched peer-reviewed publications using PubMed. We used different combinations of the terms lung cancer, surgery, resection, lobectomy, pneumonectomy, hospital volume, surgical volume, survival, and mortality. After initial identification of relevant articles, the referenced reports listed in those were also searched, as were articles indicated as related by PubMed.

Interpretation

Numerous studies, predominantly carried out in the United States, have shown that patients undergoing surgery for lung cancer benefit from receiving treatment in hospitals where high numbers of lung cancer resections are carried out.[2-13] However, a number of studies, for the most part carried out in countries other than the United States, and some based on smaller numbers of patients, did not find an association between hospital volume and outcome after lung cancer resection.[14-20] A recent meta-analysis showed that higher hospital volume was associated with improved mortality in the short term, but not with long-term survival.[21]

This study is the first to our knowledge to assess the relationship between hospital surgical volume and lung cancer survival in England. Moreover, this large national study over a 5-year period allowed for the investigation of both short- and long-term survival outcomes among patients with non–small-cell lung cancer across a wide range of hospital volumes. The results presented in our report indicate that hospitals in England with high volumes of surgical resection of lung cancer perform surgery among patients who are older, are more socioeconomically deprived, and have more comorbidity and, despite this, achieve better survival, especially in the early postoperative period. These findings would encourage centralization of lung cancer surgery.