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High lung cancer surgical procedure volume is associated with shorter length of stay and lower risks of readmission and death: national cohort analysis in England.

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## Abstract

It is debated whether treating cancer patients in high-volume surgical centres can lead to improvement in relevant outcomes, such as shorter length of hospital stay, decreased frequency and severity of postoperative complications, decreased re-admission, and decreased mortality.

The dataset for the analysis was based on cancer registration and hospital discharge data and comprised information on 15,738 non-small cell lung cancer patients diagnosed in England in 2006-2010 and treated by surgical resection as part of their initial care. The volume of lung cancer resections was computed for each hospital in each calendar year, and patients were assigned to a hospital volume quintile on the basis of the volume of their hospital.

Hospitals with large lung cancer surgical resection volumes were less conservative in their selection of patients for surgical management, and provided a higher resection rate to their geographical population. The large hospitals had shorter length of stay and the odds of re-admission were 15% lower in the highest hospital volume quintile compared with the lowest quintile. Mortality risks were 1% after 30 days and 3% after 90 days. Patients from hospitals in the highest volume quintile had about half the odds of death within 30 days than patients from the lowest quintile.

Variations in outcomes were all in the same direction, with consistent better outcomes in the larger hospitals. This gives support to the ongoing trend towards centralisation of clinical services, but service re-organisation needs to take account of not only the size of hospitals but also referral routes and patient access.

## Introduction

Lung cancer is one of the most frequent types of cancer and the leading cause of cancer death globally (1, 2). There has been notable progress in lung cancer prevention, as evidenced by declining incidence rates in males (3), and treatment for lung cancer has become more active and more effective (4-6). Despite this, the annual number of deaths due to lung cancer in the United Kingdom exceeds 35,000, which is the highest number of deaths from any type of cancer in the country (2). Surgical resection remains the preferred treatment option for medically fit patients with early-stage disease (7), and there is evidence that increasing resection rates (5), contributes to improvements in survival of lung cancer patients (8-10).

Lung cancer surgery is highly specialised and increasingly centralised (5). There is evidence that patient survival is better when surgical care is provided by a multi-disciplinary team in hospitals with high-volume practices, and analysis of surgical data from England in patients diagnosed in 2004-2008 showed lower death rates in patients operated in large-volume hospitals (11). It remains to be addressed whether treating patients in high-volume surgical centres can lead to improvement in other relevant outcomes, such as shorter length of hospital stay, decreased frequency and severity of postoperative complications, decreased re-admission to hospital, and improved patient experience and satisfaction. The present study extends the earlier work on patients undergoing lung cancer surgery in England to examine other outcomes, specifically length of stay in hospital after lung cancer resection, and risks of re-admission and death within 30 and 90 days of surgery. These outcomes are relevant both to the well-being of patients and to the organisation and costs of the health care system.

## Methods

### *Study population and main predictor variables*

The principles of data extraction and linkages were as described previously (9, 11). The dataset for the analysis was based on national cancer registration and hospital discharge

data and comprised information on 15,738 non-small cell lung cancer patients diagnosed in England in 2006-2010 and treated by surgical resection as part of their initial care. This is a complete and population-based ascertainment of surgically treated lung cancer in the country. The volume of lung cancer resections was computed for each hospital in each calendar year, and patients were assigned to a hospital volume quintile on the basis of the volume of their hospital in the year of diagnosis.

The geographical resection rate was computed as the proportion of all non-small cell lung cancer patients in each of 152 geographical primary care trust areas in the period 2006-2010 that underwent surgical resection (9).

### *Covariates*

Seven covariates were considered. Sex and age were analysed as categorical variables (age categorised in five-year groups). Socio-economic status was characterised by the quintile of the income domain of the indices of multiple deprivation 2010 on the basis of the residential postcode of each lung cancer patient. Co-morbidity was characterised by a modified Charlson co-morbidity index on the basis of in-patient hospital discharge diagnoses, ignoring the contribution to the co-morbidity index from cancer. Clinical tumour stage and histology were obtained from the National Cancer Registration Service and the National Lung Cancer Audit Dataset (LUCADA) (12). Ethnicity was derived from the electronic patient record at hospitals in England in the Hospital Episodes Statistics dataset.

### *Outcomes*

Outcome variables were the length of stay in hospital (in days) at the time of the surgical resection for lung cancer, re-admission to hospital as an in-patient within 30 and 90 days among the patients who were discharged home after the lung cancer resection, and death within 30 and 90 days from the date of surgery.

### *Statistical analysis*

Length of hospital stay distribution was described by the means, and the means of log-transformed values (called the 'log-average' length of stay). Length of stay was analysed in relation to hospital volume quintile and covariates by linear regression of log-transformed length of stay. A two-level linear regression model was fitted with the individual patient as the lower level and a random effect of hospital as the higher level. The risks of re-admission and death were analysed in relation to hospital volume quintile with a one degree-of-freedom Chi-square test and with univariate and multivariate logistic regression analysis. Two-level logistic regression models were fitted with hospital as a random effect. The covariates that were used in adjusted analyses were: geographical resection rate, age, co-morbidity, performance status, stage, histology and ethnicity using categorical variables as described in Table 1.

### Results

#### *Patients*

Table 1 gives an overview of the study cohort of 15,738 lung cancer patients diagnosed in the period 2006-2010 in England and treated with surgical resection.

#### *Hospital volume in relation to covariates*

Table 1 shows the marginal distributions of the variables in the analysis, and cross-tabulations between the quintile of lung cancer surgical procedure volume (the principal independent variable) and covariates. A high hospital volume was strongly associated with a high geographical resection rate ( $\chi^2=538.2$ ;  $p<0.0001$ ). There was no association between hospital volume and sex of the patient, but high-volume hospitals had a higher proportion of older patients ( $\chi^2=14.2$ ;  $p=0.0002$ ). There was no association with socio-economic status but there were slightly more co-morbid patients in high-volume hospitals ( $\chi^2=4.1$ ;  $p=0.04$ ). High-volume hospitals had more complete reporting of performance status and clinical

tumour stage than low-volume hospitals, and they used the unspecific histology code “Non-small cell lung cancer (NSCLC)” less frequently. Within the patients with non-missing performance status, the larger hospitals had a higher proportion of patients with poor performance status (2 or higher) ( $\chi^2=14.3$ ;  $p=0.0002$ ) (Appendix table).

#### *Hospital volume in relation to length of hospital stay*

Table 2 shows the length of stay in hospital during the hospitalisation where the lung cancer resection took place. The average length of stay was 9.82 days in the quintile with the lowest hospital volume and 9.35 days in the highest-volume quintile. The linear regression of log-transformed length of stay on hospital volume quintile suggested that the difference in length of stay was about 0.3 days between the extreme quintiles. This gradient was statistically significant with a negative slope ( $p=0.004$ ). Adjustment for the covariates that were associated with resection quintile (geographical resection rate, age, co-morbidity, performance status, stage, histology and ethnicity) made the regression slope marginally steeper, reflecting the more adverse case-mix of patients in high-volume hospitals. A two-level adjusted regression model with the individual hospital as a random effect reduced the statistical significance of the association between hospital volume and length of hospital stay (data not shown).

#### *Hospital volume in relation to re-admission and mortality*

Table 3 shows the associations between hospital volume quintile and the risks of re-admission to hospital and mortality, each within 30 days and within 90 days. Patients operated in high-volume hospitals had lower re-admission risks (19% in quintile 5 vs. 22% in quintile 1 for 30-day readmission,  $p$  for trend over the five quintiles:  $p=0.08$ ; and 44% vs. 47% for 90-day readmission,  $p<0.0001$ ). Similarly, mortality risk were lower in high-volume hospitals (0.5% vs. 1.0% within 30 days,  $p=0.01$ ; and 2.2% vs. 3.1% within 90 days,  $p=0.02$ ).

Table 4 shows the more detailed analyses of 30-day and 90-day readmission risks in relation to hospital volume quintile. Statistical adjustment for geographical resection rate, age, co-morbidity, performance status, stage, histology and ethnicity strengthened the associations

between hospital volume and 30-day and 90-day readmission risks. Further allowance for the two-level structure of the data by fitting a random effect of individual hospital further strengthened the association with 30-day re-admission risk, but the association with 90-day readmission was much attenuated in the two-level model.

Table 5 shows the detailed analyses of 30-day and 90-day mortality outcomes. For both endpoints, hospital volume was associated with low risks of death, and this did not change much with adjustment for covariates or with the allowance for variation between hospitals.

## Discussion

### *Interpretation of the results of adjusted analyses and two-level analyses*

The unadjusted analyses provide a first-line answer to the research question of variation in outcomes between groups of hospitals defined by their quintile of lung cancer resection procedure volume. In general, larger hospitals have better patient outcomes. It is clear, however, that there are case-mix differences between large and small hospitals, and that large hospitals are less conservative in their criteria for patient selection for surgery. They therefore have an adverse case-mix, compared to smaller hospitals, and the analyses that entail adjustment for case-mix characteristics tend to show associations in favour of large hospitals that are stronger than the unadjusted analyses. The adjusted analyses provide a fairer, more *like-with-like* comparison.

The crude and the adjusted analyses both ignore the multi-level structure of the data, and pretend naïvely that there are 15,738 individual and independent patient-level observations in the dataset. They ignore that the measurement of procedure volume (the principal predictor of outcomes) was not done 15,738 times, but only once for each hospital. The interpretation of the parameter values from the two-level model is akin to a sensitivity analysis: *“Does allowance for the clustering of patients and events in hospitals change the interpretation of results?”* This is an attempt to separate the effect of hospital size *per se* from the effect of particular hospitals. We consider that the adjusted, single-level analysis to



give a parameter estimate that corresponds to the natural research question, but when the parameter estimate changes in the two-level model, we appreciate that the association is partly due to clustering of outcomes in particular hospitals, and not entirely an effect of hospital size.

Applying these principles to the data at hand, the principal findings are:

1: Hospitals with large lung cancer surgical resection volumes are less conservative in their selection of patients for surgical management, and they provide a higher resection rate to their geographical population.

2: With adjustment for case-mix, the large hospitals have shorter length of stay, with approximately 0.3 days difference between the extreme quintiles of hospital volume. The error of this estimate is large, however, particularly when the two-level structure of the data is considered.

3: Re-admission risks are high after lung cancer resection (20% and 45% are readmitted as in-patients to hospital within 30 and 90 days, respectively). The odds of re-admission are about 15% lower in the highest hospital volume quintile compared with the lowest quintile. The estimated 30-day re-admission risk is not influenced by clustering of this outcome within individual hospitals, but the variation in 90-day readmission risk has a large contribution from the level of the individual hospital.

4: Mortality risks after lung cancer resection are 1% after 30 days and 3% after 90 days. Patients from hospitals in the highest volume quintile have about half the odds of death within 30 days than patients from the lowest quintile. For 90-day mortality the corresponding odds ratio is 0.7.

### *Comparison with other studies*

The analyses of 30-day and 90-day mortality risks in relation to hospital volume are consistent with previous analyses of hazard ratios for death, obtained from Cox proportional hazards regression (11). The analyses of mortality outcomes in lung cancer patients in England in relation to surgical procedure volume adds to growing body of evidence of favourable outcomes in high-volume hospital settings (11, 13-16). It is noteworthy that the 30-day mortality outcome is insufficient to capture the full mortality effect, and that 90-day mortality is more than three times the magnitude of 30-day mortality (2.8% vs. 0.9%). Similar findings were reported in a large study in the USA (17). This emphasises that mortality outcomes should be considered both in the short and the longer term (11).

The present study extends the previous analyses of mortality with other outcomes: length of stay and re-admission risk. The results for length of stay and re-admission emphasise that other relevant outcomes vary along the gradient from low hospital volume (and high mortality) to high volume (and lower mortality). A number of recent studies have explored associations within the wider set of outcomes: hospital volume, length of stay, complications, re-admission, mortality, and cost (17-30). None of these papers addresses all of the possible associations, but the emerging pattern is one of correlated and consistently favourable outcomes in high-volume hospitals. We are not aware of studies of patient-reported outcomes and patient experience in relation to hospital volume, and this is an area for further research.

### *Threshold of effects?*

It has been considered whether the associations with hospital volume would be characterised by a threshold above which increasing hospital volume would not provide any further increase in clinical benefit (31). The present analysis was not designed to establish a threshold value. Rather than merely letting the data suggest the threshold, we consider that such analysis should preferably pre-specify (on rational and practical grounds, reflecting national geography and travel times) the hypothetical threshold value, and then proceed similarly to a formal equivalence trial (32). Regardless, the present data suggests that there

may well be different thresholds (if any) for different outcomes. Length of stay and re-admission risks are numerically similar in quintiles 4 and 5 (i.e. above a possible threshold around 150 procedures per year), but in the analysis of mortality risks the data would suggest either continued increase in benefit above around 190 procedures per year (or no threshold at all).

The analysis based on within-study quintiles (or another similar grouping) is rational in that it allows for non-linear association, does not sacrifice statistical power, and provide results that are easily visualised, compared with an analysis based on smoothing of the relationship with hospital volume.

The structure of health care systems varies between countries, and it is not necessarily the case that associations with procedure volume would be similar between countries or that any thresholds would be the same. For example, the large study of lung cancer resection in the USA (17) considered 90 procedures per year as the cut-off point for their high-volume group of patients, but this falls within the second quintile in the present data and would be considered as a low volume in England.

### *Strengths and limitations*

The present analysis benefit from systematically collected data with uniform standards and classifications in a large national population. Data quality and completeness have improved in recent years and tumour stage is now available in the majority of cases, and indeed most completely collected in the largest hospitals. Ascertainment of outcomes is based on routinely collected data and unlikely to differ artifactually between hospitals with different practice volume. However, the use of routinely collected data is also the main limitation of the study, and information on co-morbidity, performance status and histology are subject to a higher degree of error than we would expect from a smaller study based on more fully quality-assured clinical data.

The 30 and 90-day re-admission rates are remarkably high regardless of which type of hospital treated the patients. The data does not define why the patients were re-admitted,

which may be for reasons other than for management of post-operative complications, e.g. co-morbidity, social network, and family situation may play a role.

Although the differences in the mean length of stay between hospitals are small, this outcome is fraught with difficulties as an accurate marker of quality of care. Many patients treated in NHS institutions in England have their discharge delayed due to lack of social support, which particularly applies to the elderly and those with other illnesses. These patients form a larger proportion of the cohort treated in large volume hospitals, so it is possible that this factor may have impacted on the length of stay outcome for large volume hospitals in a negative way, and have led to a reduced difference when comparing the different hospital groups.

We note that a high number of hospitals contribute to this data set. The record linkages identified the combination of lung cancer registration and a relevant surgical resection in patients with resection reported from 78 hospitals, but these resections should mainly or entirely take place in the 30 thoracic centres in England (6). The data set includes a number of hospitals that contributed only a single or a few records of to the data set and we have no means of quality assuring these records. These hospitals with very few resections are all in quintile 1 of the hospital procedure volume grouping, and make up a small proportion of the 3190 patients in this group. We can judge the magnitude and direction of possible bias from the inclusion of these records by looking at associations across quintiles 2-4. Such restriction strengthens the association with length of stay (Table 2) and with mortality (Table 5), and it has little or no impact on the analysis of readmission risks (Table 4).

#### *Are the observed differences clinically relevant?*

We have described differences in bed-days, readmissions and deaths in terms of a relative measure (the odds ratio), Chi-square measures of association, and associated p-values. These standard measures allow for testing of the *a priori* hypotheses of association, but tells us little about the clinical and practical relevance of the observed variations in outcomes. With a large study population as the present one, statistical significance may arise in situations where the magnitude of effect is small and of little practical consequence. In

order to address this we computed (from the data in Tables 2 and 3) the total counts of bed-days, readmissions and deaths, and the number and proportion of these that would have been avoided if the patients in hospital volume quintiles 1-4 had experienced the same (lower) bed-days and risks as the patients in quintile 5.

In absolute terms, the strongest signal in these data is found for 30-day post-operative mortality. Of the 145 deaths that were observed, 65 deaths (45%) would have been avoided if the 12,635 patients in quintiles 1-4 had experienced the low 0.5% mortality risk of the 3103 patients in quintile 5.

Similar calculations show that 24% of the 90-day post-operative deaths are attributable to the variation in 90-day mortality between the quintiles, but for bed-days and readmissions, the proportions so attributable are only a few percent and each of these variations are not of practical relevance in itself. It remains important that all the variations are in the same direction, with consistent better outcomes in the larger hospitals.

#### *Practical implications*

Taken together, all studied outcomes and other outcomes in previous research indicate that patients operated on at high volume hospitals do better. We may infer that further centralisation can potentially lead to further improvement in cancer outcomes for patients with lung cancer. However, there are other important factors relating to travel distance and to referral pathways that needs to be considered. Crawford et al (33) looked at the socio-economic status of patients and the distance they lived both from the diagnostic and the surgical centre. Patients who lived far from the surgical centre had lower rate of surgery than those who lived closer to the centre. Likewise, Khakwani et al (6) showed that surgical centres with large catchment areas resected a high proportion of patients referred directly to the centre, but a smaller proportion of the patients referred to them from other hospitals. So, service re-organisation needs to take account of not only the size of hospitals but also referral routes and patient access (34).

*Research ethics and information governance.*

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