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Association between surgical volume and post-operative mortality and survival after surgical resection in lung cancer in Belgium: A population-based study

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ABSTRACT

Objectives: The existence of a relationship between hospital surgical volume and outcome after lung cancer surgery remains an ongoing debate. We aimed to evaluate the association between volume and 60-day mortality, 1- and 3-year observed survival (OS) in non-small cell lung cancer (NSCLC) patients in Belgium.

Methods: Patients diagnosed with NSCLC in 2010–2011 were identified in the database of the Belgian Cancer Registry, excluding patients with multiple tumours. Regression models were applied to assess the relationship between hospital surgical volume, 60-day mortality and 1- and 3-year OS, adjusting for different patient and tumour characteristics. Surgical volume was taken into account as a continuous variable in the models.

Results: In 2010-2011 a total of 9,817 patients with NSCLC were diagnosed in Belgium and 2,084 of them underwent surgery. After adjusting for patient and tumour characteristics, a relationship between hospital surgical volume and patients' outcome was found. Postoperative mortality and survival improved with increasing annual surgical volume up to 10 interventions. However, no further gain in outcome has been observed above 10. While the 60-day postoperative mortality is 3.5% for hospitals with an annual volume larger than 10, the predicted mortality rate for a hospital with an annual volume of only 5 interventions is 6.5%. Similar results were observed for 1- and 3-year OS.

Conclusion: In Belgium, a higher hospital surgical volume is associated with improved outcome in NSCLC patients after surgical resection. Minimally 10 surgical interventions per year seem to be required to achieve an optimal performance.

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Introduction

Based on scientific evidence, the Belgian guideline on the treatment of non-small cell lung cancer (NSCLC) recommends to surgically treat fit patients with clinical stage I-II and selected clinical stage III (T3N1) [1]. Moreover, it states that lung cancer surgery should be performed in high-volume hospitals specialised in thoracic surgery, but does not provide any cut-off criteria for

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volume [2].

The relationship between the number of surgical procedures performed within a hospital, or by an individual surgeon, and short- or long-term mortality, was frequently studied for different medical specialties, including oncology [3–5]. Although a volume-outcome effect is often observed, the proof of a positive association between volume and outcome is less clear in lung cancer. Regarding post-operative mortality, some studies demonstrated that the more surgical procedures performed in a hospital (or by an individual surgeon), the lower the postoperative mortality of the patient [6,7], while others did not confirm such relationship [8,9]. A meta-analysis, including 19 studies found a significant positive association between high hospital volume and post-operative mortality after lung cancer resection [10], without succeeding to determine a minimal required annual number of surgeries. Also for longer-term survival, some studies concluded to a positive association of a higher volume [11,12] while another did not [13]. The above-mentioned meta-analysis [10] concluded that long-term survival was not significantly higher in high-volume hospitals. However, the association was significant after adjustment for comorbidities. Studies included in this meta-analysis were heterogeneous in defining volume categories; cut-off values of both the highest and lowest volume strata varied widely.

The current study aims to evaluate the association between hospital surgical volume and 60-day mortality and 1- and 3-year survival in lung cancer patients in Belgium at a population level, adjusting for patient and tumour characteristics. In contrast to most studies e.g. [2,4,5,7] in which volume is categorized in two or more volume groups, we have opted to study volume as a continuous variable, as categorising continuous predictors can lead to loss of information, loss of power and residual confounding [14].

Methods

Databases

In Belgium reporting all newly diagnosed cancers to the population-based Belgian Cancer Registry (BCR) is obligatory since 2004. The BCR is authorised by law to link cancer diagnoses to claims data of health insurance companies obtained via the Intermutualistic Agency (IMA) to provide details on reimbursed diagnostic and therapeutic procedures. Linkage is done via the patients' unique Social Security Identification Number (SSIN). Since health insurance is compulsory in Belgium, linkage is almost complete (98.6%). The BCR is authorised by law and received approval of the Belgian Privacy Commission to conduct research on the linked databases of the BCR and the IMA. Information on patient's vital status is retrieved via the Crossroads Bank for Social Security.

Patient selection and follow-up

We extracted data on 12,135 NSCLC tumours (ICD-10: C34) from the BCR database, diagnosed in 2010–2011, from patients with an official residence in Belgium and with a SSIN available. The following patients were excluded from the analyses (Fig. 1): not linked with IMA data or deceased or lost to follow up at incidence date. Additionally, because medical procedures cannot unambiguously be linked to a diagnosis based on claims data, patients with more than one invasive tumour until the end of the study period (irrespective of the topography of the other tumour) were excluded from analyses. Following the applied TNM classification rules, multiple nodules in the same lobe are considered as one tumour and therefore these patients were not excluded from this study. Hence, the final dataset included a total of 9,817 patients of whom 2,084 underwent a major lung surgery (21.2%). No information on the reason of the surgery is available. Therefore, surgeries in an emergency situation cannot be excluded. Lymphadenectomies are not taken into account. In order to handle administrative errors in the database, surgery performed within a timeframe of 1 month before until 9 months after the incidence date was considered as primary treatment, to allow some time for diagnostic work ups and neo-adjuvant treatment. Although multiple procedures for one patient are very rare, the first procedure was always selected. Follow-up of the patients was complete up to December 31st 2014.

Patient and tumour characteristics

The following patient characteristics were available: sex, age (categorised in groups: <60, 60-69, 70-79 and 80 + years), comorbidities (derived from reimbursed pharmaceuticals) [15]: chronic respiratory disease, cardiovascular disease and diabetes mellitus, number of hospitalisation days during the year preceding the diagnosis of cancer [16] and WHO performance status at time of diagnosis. The following tumour characteristics were available: histological subtype, tumour sublocalisation, clinical and pathological stage (TNM 7th edition). Because very few patients with a tumour in the 'Main bronchus' (ICD-10: C34.0) were surgically treated, and very few patients with a tumour in the 'Overlapping lesion of bronchus and lung' (ICD-10: C34.8) were diagnosed, both were added to the category 'Bronchus or lung, unspecified' (ICD-10: C34.9) for the analyses. These patient and tumour characteristics were used as case-mix covariates in the regression models.

Surgical volume

Because defining the hospitals' lung cancer surgical volume requires to capture the whole volume of surgical procedures performed for lung cancer patients, irrespective of their cancer status (one or more tumours) or type of lung cancer (non-small cell, other types, …), the volume of hospitals was calculated on the basis of all lung cancer patients treated for the main tumour, by major lung surgery (defined as procedures for which a lung was partially or completely removed) during the period 2010-2011 and within the timeframe of 1 month before until 9 months after the incidence date. Since multiple procedures for one patient were very rare, only one surgical procedure per patient was counted. No analyses at the level of the individual surgeon were performed.

Outcome

The association between surgical volume of the hospital and outcome was assessed at three time points: 60-day postoperative mortality, 1-year and 3-year observed survival (OS). The post-operative mortality was defined as the proportion of patients who died within 60 days after the first major lung surgery, irrespective of whether they died in the hospital or after being discharged, over all surgically treated patients. OS was calculated at 1- and 3-years after incidence date, using the Kaplan-Meier method [17]. All patients had a theoretical follow-up of at least 3 years. Patients lost to follow-up after the incidence date were censored at the time of the last known contact alive (0.4% censored patients).

Statistical analysis

Regression models were applied to assess the relationship between surgical volume and, respectively 60-day mortality and 1- and 3-year OS, adjusted for the different patient and tumour characteristics. The stage of the tumour was used as one covariate in the models in which the pathological stage prevailed over the clinical stage, except when there was clinical proof of distant

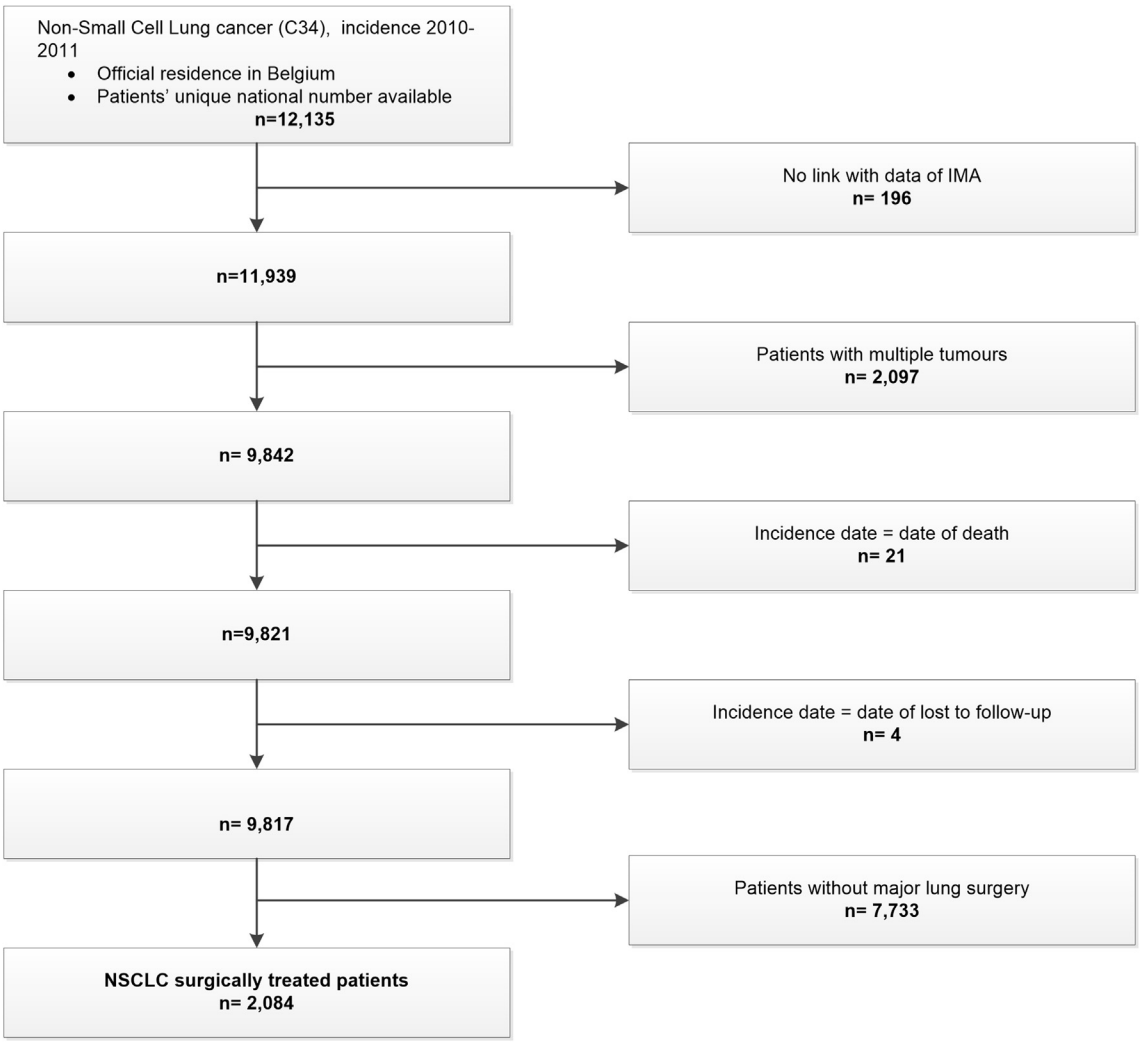

Fig. 1. Selection of patients included in the study.

metastases. A logistic regression model was applied for the 60-day postoperative mortality. Cox proportional hazards' regression models were applied to the 1- and 3-year OS outcomes, censoring observed event times above 1 and 3 years, respectively. The regression models consider the odds or hazard for all-cause death as event. The significance level used was 5% and 95% confidence intervals (CI) were reported.

Hospital volume as a continuous variable

We opted for including the hospitals' surgical volume as a continuous variable in the regression models instead of categorizing. To study the functional form of surgical volume, plots of the residuals versus surgical volume were constructed for the three outcome measures (Supporting information - Fig. 1), using models that contain all case mix covariates but not surgical volume. These plots may reveal the functional form for a volume. All three plots suggest a decreasing trend up to an annual surgical volume of about 10 surgeries, for larger volumes a more or less constant relationship is observed. A piecewise linear model is therefore selected, with a knot at an annual surgical volume of 10 procedures. This model requires 2 parameters for surgical volume, the first representing the slope in the interval 0-10 procedures and the second giving the slope above 10 procedures.

Intra-hospital correlations

To study the possible influence of intra-hospital correlations on the volume-outcome effect, additional regression models that take these correlations into account were performed, resulting in a generalised linear mixed effects model for the 60-day mortality [18] and frailty models for observed survival [19]. Intra-hospital correlations were found to be non-significant and the parameter estimates were very similar between the models with and without intra-hospital correlations. Because the estimates were similar, we have chosen for the less complex models without intra-hospital correlations.

All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

During the years 2010–2011, surgery for lung cancer was performed in 89 hospitals (86% of Belgian acute hospitals). The mean annual number of lung cancer surgical procedures (thus also including lung cancer surgeries for patients with multiple tumours or other types of lung cancer) per hospital was 15.8 - with a minimum, median and maximum of 0.5, 9, 149.5, respectively. The annual surgical volume for the different hospitals is given in Fig. 2.

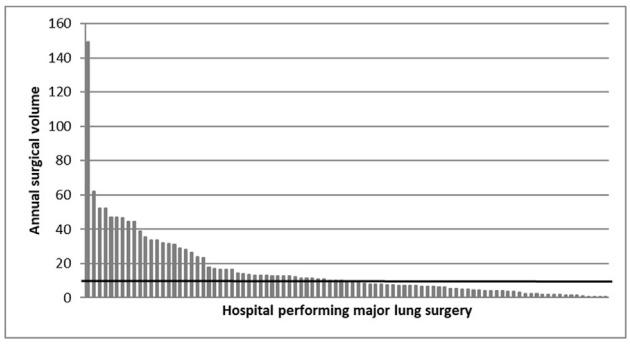

Fig. 2. Annual surgical volume of Belgian hospitals performing lung cancer surgery during 2010–2011 (N = 89 hospitals).

This figure shows that many Belgian hospitals surgically treat a small number of patients with lung cancer; 50% of Belgian hospitals have an annual volume smaller than 10.

Patients diagnosed in hospitals with a higher diagnostic volume (i.e. the number of patients who were diagnosed in this hospital with lung cancer) were more often surgically treated than patients diagnosed in hospitals with a lower diagnostic volume, $\chi^2(3) = 28.9$, $p < 0.001$. Hospitals with a diagnostic volume <50 per year had a resection rate of 17.9%, while hospitals with a diagnostic volume between 50 and 100 per year had a resection rate of 21.7%, between 100 and 150 per year a rate of 23.4% and the group with a diagnostic volume ≥150 per year had a resection rate of 24.0% (data not shown).

The proportion of surgically treated patients by patient and tumour characteristics is shown in Table 1.

Overall unadjusted 30-, 60- and 90-day postoperative mortality were 2.0%, 3.9% and 4.8%, respectively. Volume-outcome analyses were performed for 60-day postoperative mortality. 1-year observed survival was 88.3% and 3-year observed survival 68.8% (results stratified by patient and tumour characteristics, can be found in Table 2).

A piecewise linear model was selected, with a knot at an annual surgical volume of 10 procedures. For 60-day postoperative mortality, the odds ratio (OR) within the 0-10 volume interval was 0.877 (95%CI = [0.785,0.981], $p = 0.03$). So below a volume of 10 surgeries, the odds of death within 2 months is decreased by 13% per additional surgery. Above a surgical volume of 10, the OR was 0.998 (95%CI = [0.991–1.004], $p = 0.45$). So above a volume of 10 surgeries, no significant association was found between surgical volume and 60-day mortality. The dashed line in Fig. 3 visualises the relation of the predicted OR for 60-day postoperative mortality with surgical volume, in which the OR for volumes higher than 10 was set to 1 as a reference. To translate OR into a postoperative mortality probability, a probability has to be assigned to the reference group. The 60-day mortality for patients treated in hospitals with a volume above 10 surgical interventions was 3.5% (see Table 3). This value was used as reference and the predicted 60-day postoperative mortality is plotted in Fig. 3 by the solid grey line. The predicted postoperative mortality for smaller hospitals increased to 6.5% for a surgical volume of 5, and further increased to 10.5% for a surgical volume of only 1.

Very similar results were obtained for OS at 1 and 3 years since diagnosis. On average survival improved with increasing surgical volume up to a volume of 10 with no further gain for larger hospital volumes. For OS in the 0–1-year interval, the hazard ratio (HR) within the 0-10 volume interval was 0.907 (95%CI = [0.847,0.971], $p = 0.005$). And above a volume of 10 surgical interventions the HR was 0.997 (95%CI = [0.993,1.001], $p = 0.10$). So below a volume of 10 surgeries, the hazard of all-cause death up to one year is decreased by 9% per additional surgical intervention. Above a volume of 10, no association was found. For observed survival in the 0–3-year interval, the HR within the 0-10 volume interval was 0.948 (95% CI = [0.903,0.995], $p = 0.03$). And above a volume of 10 surgeries the HR was 0.999 (95%CI = [0.997,1.001], $p = 0.47$). So below a volume of 10 surgeries, the hazard of all-cause death up to three years is decreased by 5% per additional surgical intervention. Above a volume of 10, no association was found. Likewise, Fig. 3 shows the association of the hazard ratios and the corresponding predicted OS probabilities for the average patient by the dashed lines. The 1-year OS for the average patient was 89% for a large volume (>10) and the predicted survival decreased to 83% for a volume of 5 and further to 76% for a volume of only 1. The 3-year OS for the average patient was 69% for a large volume (>10) and the predicted survival decreased to 62% for a volume of 5 and further to 55% for a volume of only 1.

Discussion

The current study on nation-wide data in Belgium investigated the relationship between surgical volume of the hospital on the one hand and postoperative mortality and 1- and 3-year observed survival for NSCLC patients on the other hand, taking into account a range of patient and tumour characteristics. Because of the possibility to use the Belgian cancer registration database linked with administrative claims data of the obligatory health insurance, no additional data collection was needed and any kind of selection bias could be eliminated. Instead of using arbitrarily chosen volume categories, we opted in this study for a model in which volume is treated continuously [14]. As such, no information is lost by creating categories.

This study showed a 60-day mortality rate of 3.9%, which is well below the target of 5% set by the NHS Scotland [20] and the result of 8% reported by Rostad et al. [21]. The 30-day mortality rate was 2.0%. In the literature 30-day mortality rates vary between countries, but are often higher (e.g. 2.1% in USA [22], 4.4% in Norway [23], and 2.7% in the Netherlands [9]). A possible reason for this lower mortality rate is the exclusion of patients with multiple tumours. One year after incidence, still 88.3% of the patients is alive (this lowers to 68.8% after three years). In a Danish study, surgically treated patients diagnosed in 2010–2012 had a similar 1-year observed survival (90%) [24].

Results of this study reveal that after adjustment for patient and tumour characteristics, a higher surgical volume of the hospital is related to improved 60-day postoperative mortality as well as higher 1-year and 3-year survival for operated patients until an annual volume of about 10 surgeries. A further increase of the volume does not seem to present an additional beneficial effect in this population. It should be noted that (as presented in Fig. 2) surgery for lung cancer is dispersed in Belgium with a large number of very small hospital volumes and only few large centres. Compared with international standards, very few hospitals have a volume that can be considered as “medium” or “large”.

A previous Belgian study on the volume effect of lung cancer surgery already demonstrated an effect of the surgical volume of the hospital on outcome after 2 years [25]. In this study, the smallest volume category was based on the 25th percentile (4 interventions/year). The four other volume categories were chosen arbitrary by increasing the volume with 5, 10 and 20 interventions. Hospitals in the highest volume category (>40 interventions/year), had the lowest 2-year mortality (21.4%) compared to hospitals in smaller volume categories (26–29%). Differences in the study design may explain why the number of minimal surgical interventions differed. The previous study has taken all lung cancer

Table 1
Proportion of surgically treated NSCLC patients by patient and tumour characteristics (2010-2011).

Characteristics	All patients	Patients treated with major lung surgery	
		N	%
Overall			
Overall	9,817	2,084	21.2
Sex			
Female	2,913	680	23.3
Male	6,904	1,404	20.3
Age group			
0-59 years	2,478	624	25.2
60-69 years	3,058	783	25.6
70-79 years	2,981	596	20.0
80 years and more	1,300	81	6.2
Histological subtype			
Adenocarcinoma	5,152	1,095	21.2
Large Cell Carcinoma	550	60	10.9
Squamous cell carcinoma	3,144	730	23.2
Other subtypes	971	199	20.5
Sublocalisation			
C34.1 Upper lobe, bronchus or lung	3,669	994	27.1
C34.2 Middle lobe, bronchus or lung	344	89	25.9
C34.3 Lower lobe, bronchus or lung	1,930	557	28.9
C34.0, .8, .9 Main bronchus, Overlapping lesions of bronchus or lung, Bronchus or lung, unspecified	3,874	444	11.5
Stage[a]			
I	1,415	1,039	73.4
II	826	524	63.4
III	2,073	303	14.6
IIIA	1,313	290	22.1
IIIB	760	13	1.7
IV	3,987	114	2.9
X	1,516	104	6.9
Chronic respiratory disease			
No	7,048	1,483	21.0
Yes	2,769	601	21.7
Cardiovascular disease			
No	4,317	943	21.8
Yes	5,500	1,141	20.8
Diabetes mellitus			
No	8,497	1,827	21.5
Yes	1,320	257	19.5
Days of hospitalisation during the year preceding lung cancer			
None	7,222	1,428	19.8
1-5 days	1,484	421	28.4
6-15 days	640	147	23.0
More than 15 days	471	88	18.7
WHO - Performance Status at diagnosis			
0 – Asymptomatic	1,163	519	44.6
1 – Symptomatic but completely ambulatory	5,232	1,080	20.6
2 – Symptomatic, <50% in bed during the day	986	47	4.8
3 – Symptomatic, >50% in bed, but not bedbound	359	6	1.7
4 – Bedbound	113	5	4.4
Missing	1,964	427	21.7

[a] The stage of the tumour is used as one covariate in the models in which pathological stage prevails over clinical stage, except when there is clinical prove of metastases.

patients into account (NSCLC [88.6%], SCLC [2.2%] and others [9.2%]). Additionally, the study period might have an influence (2004 versus 2010-2011). The number of hospitals that performed surgeries lowered from 97 to 89 and the median number of surgically treated patients slightly augmented from 7 to 9.

Compared to the results of other countries, a minimal number of 10 surgeries a year appears rather low. For example, the minimal annual number of surgical procedures that hospitals need to perform is set at 20 in the Netherlands [26] and 30 in France [27]. However, the minimal number of required patients in different countries may also depend on other factors such as the incidence of this cancer in this country, the available infrastructure and personnel to manage patients, the selection of patients fit to undergo a surgical intervention. Consequently, the absence of a uniform threshold regarding the minimal number of such a complex surgery in guidelines is not really surprising. A threshold of 10 annual lung cancer surgeries should be interpreted as the minimum number of interventions to guarantee an attainable outcome level within the Belgian health care setting. Indeed, as shown in Fig. 2, surgical treatment of lung cancer patients is dispersed. A total of 44 hospitals had an annual surgical volume below 10. This means that patients in 50% of the Belgian hospitals could theoretically benefit of being transferred to a higher volume hospital to increase their chances of higher survival. Expressed in number of patients, these are about 243 patients annually. It is important to note, that the results of our study give an average view on the association with volume and do not imply a worse prognosis for all smaller hospitals or a better prognosis for all larger hospitals. Other factors besides volume of the hospital may play a role.

This study deals with some limitations: First, billing codes (which were used to capture surgeries) do not allow to make a distinction between different types of surgeries (e.g. wedge

Table 2
Unadjusted 60-day mortality and 1- and 3-year unadjusted observed survival (OS) by patient and tumour characteristics.

	Patients treated with major lung surgery	60 d mortality[a]		1-year OS		3-year OS	
	N	%	CI	estimate	CI	estimate	CI
Overall							
Overall	2,084	3.9	[3.1;4.8]	88.3	[86.9;89.6]	68.8	[66.8;70.8]
Sex							
Female	680	1.5	[0.6;2.5]	93.3	[91.2;95.0]	78.7	[75.5;81.7]
Male	1,404	5.1	[3.9;6.3]	85.8	[84.0;87.6]	64.0	[61.5;66.5]
Age group							
0-59 years	624	1.6	[0.6;2.7]	90.2	[87.6;92.3]	72.5	[68.9;75.9]
60-69 years	783	3.2	[2.0;4.5]	90.1	[87.8;92.0]	69.9	[66.6;73.0]
70-79 years	596	6.5	[4.7;8.6]	84.7	[81.6;87.4]	65.4	[61.5;69.1]
80 years and more	81	8.6	[3.7;14.8]	82.7	[72.6;89.4]	55.5	[44.1;65.6]
Histological subtype							
Adenocarcinoma	1,095	2.5	[1.6;3.4]	89.8	[87.9;91.5]	71.1	[68.4;73.8]
Squamous cell carcinoma	730	5.5	[3.8;7.1]	86.5	[83.9;88.8]	65.3	[61.8;68.7]
Large cell carcinoma	60	10.0	[3.3;18.3]	73.3	[60.2;82.7]	56.6	[43.2;68.1]
Other	199	4.0	[1.5;7.0]	90.9	[86.0;94.2]	72.8	[66.1;78.5]
Sublocalisation							
C34.1 Upper lobe, bronchus or lung	994	3.8	[2.7;5.0]	88.7	[86.6;90.5]	69.5	[66.6;72.3]
C34.2 Middle lobe, bronchus or lung	89	3.4	[0.0;7.9]	88.7	[80.1;93.8]	70.7	[60.1;79.1]
C34.3 Lower lobe, bronchus or lung	557	3.8	[2.3;5.4]	87.2	[84.2;89.8]	70.3	[66.4;74.0]
C34.0, .8, .9 Main bronchus, Overlapping lesions of bronchus or lung, Bronchus or lung, unspecified	444	4.3	[2.5;6.3]	88.7	[85.4;91.3]	65.2	[60.6;69.5]
Stage[b]							
I	1,039	2.6	[1.6;3.6]	93.6	[92.0;95.0]	78.6	[76.0;81.0]
II	524	4.0	[2.5;5.7]	87.0	[83.8;89.6]	65.0	[60.8;69.0]
III	303	7.3	[4.6;10.2]	80.1	[75.3;84.3]	51.7	[46.0;57.2]
IV	114	6.1	[1.8;10.5]	67.5	[58.1;75.3]	40.3	[31.3;49.2]
X	104	3.8	[1.0;7.7]	88.4	[80.6;93.3]	72.1	[62.4;79.7]
Chronic respiratory disease							
No	1,483	4.0	[3.0;5.0]	88.5	[86.9;90.1]	70.5	[68.1;72.8]
Yes	601	3.7	[2.2;5.2]	87.6	[84.8;90.1]	64.8	[60.9;68.6]
Cardiovascular disease							
No	943	3.2	[2.1;4.3]	88.6	[86.5;90.5]	70.4	[67.4;73.2]
Yes	1,141	4.5	[3.3;5.7]	88.0	[86.0;89.8]	67.6	[64.8;70.3]
Diabetes mellitus							
No	1,827	3.8	[2.9;4.7]	88.5	[87.0;89.9]	70.1	[68.0;72.2]
Yes	257	4.7	[2.3;7.4]	86.7	[82.0;90.4]	59.9	[53.7;65.6]
Days of hospitalisation during the year preceding lung cancer							
None	1,428	4.5	[1.1;9.1]	81.8	[72.0;88.4]	60.2	[49.2;69.6]
1-5 days	421	3.7	[2.7;4.7]	89.2	[87.5;90.7]	69.6	[67.2;72.0]
6-15 days	147	4.5	[2.6;6.7]	86.2	[82.5;89.2]	67.9	[63.2;72.2]
More than 15 days	88	3.4	[0.7;6.8]	89.7	[83.6;93.7]	69.3	[61.2;76.2]
WHO - Performance Status at diagnosis							
0 – Asymptomatic	519	2.7	[1.3;4.2]	90.6	[87.8;92.8]	75.1	[71.2;78.6]
1 – Symptomatic but completely ambulatory	1,080	4.2	[3.0;5.4]	87.1	[85.1;89.0]	65.7	[62.8;68.4]
2 – Symptomatic, <50% in bed during the day	47	6.4	[0.0;14.9]	78.7	[64.1;87.9]	51.0	[36.1;64.2]
3&4 – Symptomatic, >50% in bed, but not bedbound/bedbound	11	16.7	[0.0;41.7]	NA (N < 20)		NA (N < 20)	
Missing	427	4.0	[2.2;6.0]	90.2	[86.9;92.8]	72.0	[67.4;76.2]

[a] One patient less in models on 60-day mortality because the patient was lost to follow-up within 60 days after surgery.
[b] The stage of the tumour is used as one covariate in the models in which pathological stage prevails over clinical stage, except when there is clinical prove of metastases.

resection, pneumonectomy). It can be assumed that larger centres perform more complex surgeries than smaller volume hospitals, which can influence their outcome. Also the intent of the surgery (curative intent, planned surgery vs. emergency situation …) could not be determined based on these data; for this reason, some patients with stage IV also underwent a major lung surgery. Second, analyses on the level of the individual surgeon were not possible. It is possible that a surgeon works in different centres and that several surgeons work in one centre. Some studies have revealed an impact of surgeon volume on postoperative mortality [8,28], irrespective of the surgical speciality, while others have found differences in outcome measures depending on the speciality of the surgeon [29,30]. In Belgium, there is only one recognition (general surgeon) but most surgeons who have a thoracic, cardiac or vascular practice follow an additional training. In the future, the training of surgeons will be more specialised. Additionally, mortality and survival are measures that can easily be understood and used to compare hospitals, but the underlying structural or procedural factors that cause the differences in outcomes remain unknown [31]. Besides volume of surgery, it is highly probable that the technical equipment and the skills of all teams (including oncologists, anaesthetists, and nurses) who took part in the management of patients highly contributed to better results. Finally, case mix was not fully taken into account. We used medication use as a proxy for three major comorbidities, but renal insufficiency also known to influence the treatment strategy and postoperative mortality could not be captured, as well as other factors such as lung function, smoking habits and socioeconomic status. However, we are convinced that far more data were used in this population-based study than previous comparable studies.

In conclusion, this study revealed a beneficial association of a higher surgical volume of the hospital on 60-day mortality and 1- and 3-year survival for NSCLC patients undergoing surgery in Belgium. Above a cut-off of 10 surgeries on an annual basis, no

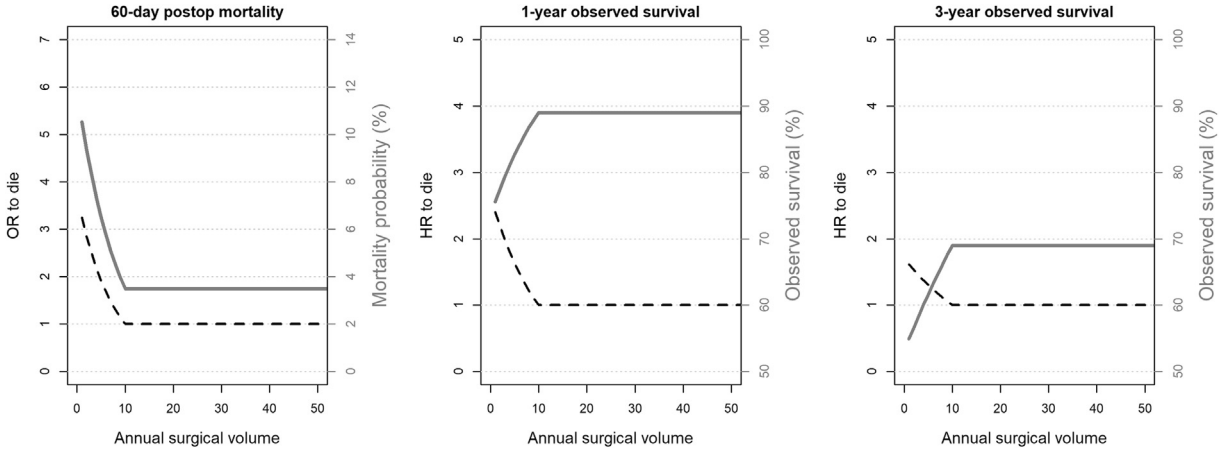

Fig. 3. Visualisation of the regression model results for outcome versus surgical volume on the odds/hazard ratio (dashed line, left axis) and probability scales (solid line, right axis). The odds/hazard ratios are relative to a large volume hospital (>10 surgeries).

Table 3
Unadjusted 60-day mortality and 1- and 3-year unadjusted observed survival (OS) by volume categorised as smaller or larger than 10 surgeries per year.

	Patients treated with major lung surgery	60 d mortality[a]		1-year OS		3-year OS	
	N	%	CI	estimate	CI	estimate	CI
Annual surgical volume							
≤10	354	5.6	[3.4;8.2]	85.0	[80.9;88.3]	66.9	[61.8;71.6]
>10	1730[a]	3.5	[2.7;4.4]	89.0	[87.4;90.4]	69.2	[67.0;71.4]

[a] One patient less in models on 60-day mortality because the patient was lost to follow-up within 60 days after surgery.

further improvement in survival with a higher volume was observed. Based on the results of this study in a Belgian context, we recommend to refer patients who can potentially benefit from surgery to higher surgical volume hospitals.

Conflict of interests

Dr. Wauters reports personal fees from KCE, outside the submitted work. For the remaining authors none were declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2019.05.017.

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