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ORIGINAL SCIENTIFIC REPORT

Pneumonectomy for Lung Cancer Treatment in The Netherlands: Between-Hospital Variation and Outcomes

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Abstract

Background Pneumonectomy in lung cancer treatment is associated with considerable morbidity and mortality. Its use is reserved only for patients in whom a complete oncological resection by (sleeve) lobectomy is not possible. It is unclear whether a patients' risk of receiving a pneumonectomy is equally distributed. This study examined between-hospital variation of pneumonectomy use for primary lung cancer in the Netherlands.

Methods Data from the Dutch Lung Cancer Audit for Surgery from 2012 to 2016 were used to study the use of pneumonectomy for primary lung cancer in the Netherlands. Using multivariable logistic regression, factors associated with pneumonectomy use were identified and the expected number of pneumonectomies per hospital was determined. Subsequently, the observed/expected ratio (*O*/*E* ratio) per hospital was calculated to study between-hospital differences.

Results Of the 8446 included patients, 659 (7.8%) underwent a pneumonectomy with a mean postoperative mortality of 7.1% ($n = 47$). Factors associated with receiving a pneumonectomy were age, gender, cardiac and pulmonary comorbidities, tumor side, size and histopathology. The pneumonectomy use in the Netherlands varied considerably between hospitals (IQR 5.5–10.1%). Three hospitals out of 51 performed significantly less pneumonectomies than expected (O/E ratio < 0.5) and three significantly more (O/E ratio > 1.7). In the latter group, severe complications were more frequent, taking other influencing factors into account (OR 1.51, 95% CI 1.05–2.19).

Conclusions There is a considerable between-hospital variation in pneumonectomy use in lung cancer treatment. To further optimize surgical lung cancer care, we suggest center-specific feedback on pneumonectomy use and the development of a risk-adjusted pneumonectomy indicator.

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Introduction

Anatomical parenchymal resection is the cornerstone in curative treatment for primary lung cancer. In certain cases, a complete oncologic resection cannot be obtained by a (sleeve) lobectomy and a pneumonectomy is considered the resection of choice. However, pneumonectomy is associated with considerable postoperative morbidity and mortality compared to less extensive resections and is an individual predictor of these negative outcomes [1–5]. Reduction in adverse outcomes of lung surgery may therefore be achieved by decreasing the number of pneumonectomies.

Several nationwide registries reported on the national pneumonectomy use [6–12]. Although the optimal target proportion of pneumonectomies is unclear and partly depends on casemix, differences in the threshold at which a pneumonectomy is performed may identify improvement potential. As suggested by Jakobsen et al. [6], the proportion of pneumonectomies could eventually function as a quality indicator in surgical lung cancer care.

To apply such a quality indicator, between-hospital variation in pneumonectomy use and possibilities for proper casemix adjustment first need to be studied. Therefore, the aim of this study was to investigate between-hospital variation in the use and outcomes of pneumonectomies for primary lung cancer in the Netherlands and to identify factors associated with pneumonectomy use.

Methods

Data source and study population

Data were derived from the Dutch Lung Cancer Audit for Surgery (DLCA-S) [13]. The DLCA-S is a nationwide mandatory registry including all patients undergoing surgery for lung cancer and is part of the multidisciplinary Dutch Lung Cancer Audit (DLCA), in which all major treatment disciplines evaluate care [13].

In the DLCA-S, data are collected on hospital level. Distinction on individual surgeon level is not possible. In cases of a surgeon operating in different hospitals, the procedure is attributed to the hospital where it was performed. Collected data include information on patient and tumor characteristics, diagnostic workup (e.g., discussion in a multidisciplinary meeting), surgical procedure, postoperative outcomes and pathology [14]. Independent onsite data verification processes are used to ensure data quality [15]. From 2015 on, there is a 100% coverage of NSCLC resection registration [14].

For this study, no ethical approval or informed consent was required under Dutch law.

Patients with a primary lung cancer resection between January 2012 and December 2016 were included. Minimum data registry criteria to be eligible for analyses included: age, gender, operation date, type of surgery, tumor side, postoperative histology and vital status 30 days after surgery and/or at time of discharge.

Wedge excisions were excluded for the analysis of anatomical resections, since these are considered oncologically insufficient. Primary lung cancer comprised a postoperative histology of: adenocarcinoma, squamous cell carcinoma, carcinoid, large cell carcinoma, small cell carcinoma and non-small cell carcinoma not otherwise specified.

Population characteristics and main outcomes

Analyzed patient characteristics were: age at time of surgery, gender, lung function, ECOG performance status and ASA classification. Preoperative lung function was analyzed as a composite measure of FEV1% (forced expiratory volume in 1 s percentage of normal) and DLCO% (diffusing lung capacity for oxygen percentage of normal), in three categories: FEV1% and DLCO% $\geq$ 80% or one of the values not registered (1), FEV1% or DLCO% $<$ 80% (2) and both FEV1% and DLCO% not registered (3). These cutoff values are in accordance with the evidence-based Dutch guideline [16, 17].

Disease characteristics and pre-surgical treatment characteristics were: tumor side, induction therapy (none/unknown, chemotherapy, radiotherapy and chemoradiotherapy), tumor stage (according to the seventh edition of the TNM staging system) and postoperative histology.

The outcomes assessed were postoperative mortality and postoperative complicated course. Postoperative mortality was defined as mortality within 30 days after surgery or during the primary hospital admission. Postoperative complicated course was defined as any complication leading to prolonged hospital stay ($\geq$ 14 days) and unplanned re-intervention or mortality and was used to reflect only severe complications.

Between-hospital variation in applying pneumonectomy

Between-hospital variation in applying pneumonectomy was studied by comparing the observed with the expected number of pneumonectomies per hospital. With a multivariable logistic regression model, after controlling for collinearity, patient and tumor characteristics associated with the risk of undergoing pneumonectomy were identified. Discriminative ability of the model was assessed by area under the ROC curve (AUC).

Subsequently, by using the coefficients of this multivariable model the expected 'pneumonectomy risk' per patient was calculated, which in turn was used to calculate the expected number of pneumonectomies on hospital level. Then, by dividing the number of observed by the number of expected pneumonectomies per hospital, the observed/expected ratio (*O*/*E* ratio) was calculated per hospital. An *O*/*E* ratio > 1 indicates that the hospital performed more pneumonectomies than expected based on the hospital population, whereas an *O*/*E* ratio < 1 indicates a lower pneumonectomy use than expected. Between-hospital variation in *O*/*E* ratio was displayed using a funnel plot, with 95% confidence intervals (95% CI) [18].

Hospital characteristics (e.g., case volume or type of hospital) were not included in the model since the chance of undergoing a pneumonectomy or a different resection type should not depend on that. If these factors would be included in the model, the effect can be distorted or even nullified [19].

Pneumonectomy/sleeve resection ratio

From 2015 on, the DLCA-S contains information on sleeve resections. Hypothesizing that sleeve lobectomies and pneumonectomies are performed in similar patient populations, a ratio between these two operation types could demonstrate differences in preference of indication per hospital.

Statistical significance was set at a threshold of 0.05, with P-values calculated by two-sided tests.

Statistical analyses were performed using SPSS (IBM SPSS Statistics for Macintosh, version 23.0).

Results

Population characteristics

A total of 8446 patients underwent a primary lung cancer resection and were eligible for analyses. Of them, 659 (7.8%) underwent pneumonectomy, 7226 (85.6%) (bi)lobectomy or anatomical segment resection and 561 (6.6%) wedge excision.

After excluding the wedge excisions, 7885 patients with an anatomical resection remained, of whom 8.4% (659) underwent pneumonectomy. These 7885 patients were divided over 51 hospitals, with a mean number of patients per hospital of 155, SD 97, range: 8–377.

Of patients with an anatomical resection, mean age was 66 years, 55.7% was male (*n* = 4395), 76.6% had an ECOG performance score 0–1 (*n* = 6040), 70.9% had an ASA score I–II (*n* = 5587), 6.3% received induction therapy (*n* = 498), 43.1% had a left-sided tumor (*n* = 3399), 81.5% had a pathological stage ≤ II (*n* = 6421) and 55.2% had an adenocarcinoma (*n* = 4352).

Table 1 displays the characteristics of all patients undergoing pneumonectomy. Compared to the total anatomical resection group, pneumonectomies were performed in slightly younger patients, more often of male sex, in more advanced disease stages, left-sided tumors and squamous cell carcinomas.

Of all anatomical resection, 5.3% (*n* = 417) was performed in hospitals with less than 20 resections a year (low volume considering the minimum annual volume standards set by the Association of Surgeons in the Netherlands), 56.0% (*n* = 4416) in hospitals with 20 to 49 resections a year and 38.7% (*n* = 3052) in hospitals with 50 or more resections a year. The pneumonectomies in these three hospital volume categories were, respectively, 8.9%, 7.9% and 8.9%.

Factors associated with pneumonectomy

Age, gender, cardiac and pulmonary comorbidities, tumor side, clinical tumor stage (cT) and histopathology are individual factors significantly associated with receiving a pneumonectomy (Table 2). The discriminative ability of a multivariable model with these factors was fairly good (AUC), 0.80, 95% CI 0.78–0.82.

Supplementary Fig. 1 visually demonstrates the association between cT and histopathology and the pneumonectomy proportion.

Between-hospital variation

The use of pneumonectomy as an anatomical resection for primary lung cancer per hospital ranged from 0.0 to 25.3% (national mean 8.4%). Fifty per cent of hospitals (interquartile range—IQR) performed a pneumonectomy in 5.5–10.1% of their patients.

Between-hospital variation remained after adjustment for relevant factors (Fig. 1). Out of 51 hospitals, three performed significantly more pneumonectomies than expected (*O*/*E* ratio > 1.7). Three performed significantly less pneumonectomies than expected, with an *O*/*E* ratio < 0.5; the percentage of pneumonectomies performed is > 50 less than expected. All six hospitals were middle-sized non-academic centers.

After adjustment for relevant factors [5], there were no significant differences in postoperative mortality and complicated course after a pneumonectomy performed in the three hospitals with more pneumonectomies (71 patients included) compared to the three hospitals with less pneumonectomies (19 patients included) than expected

Table 1 Population characteristics and postoperative outcomes of patients with primary lung cancer undergoing an anatomical parenchymal resection, stratified for resection type

	Pneumonectomy		(Bi)lobectomy and segmentectomy		*p*
	N	%	*N*	%	
Of total anatomical parenchymal resections	659	8.4	7226	91.6	–
Gender					< 0.001
Male	452	68.6	3943	54.6	
Female	207	31.4	3283	45.4	
Age mean [median] (± SD)	65 [66] (± 8.8)		66 [67] ± 9.4		
Age (years)					< 0.001
< 60	143	21.7	1681	23.3	
60–64	144	21.9	1256	17.4	
65–69	143	21.7	1491	20.6	
70–74	145	22.0	1433	19.8	
75+	84	12.7	1365	18.9	
Lung function					
FEV1% and DLCO% ≥ 80%	173	26.3	2358	32.7	0.004
FEV1% or DLCO% < 80%	443	67.2	4439	61.4	
Unknown	43	6.5	429	5.9	
Performance score*					0.063
< 2	489	74.2	5551	76.8	
≥ 2	35	5.3	260	3.6	
Unknown	135	20.5	1415	19.6	
ASA score					0.323
I–II	451	68.4	5136	71.1	
III+	186	28.2	1847	25.5	
Unknown	22	3.4	243	3.4	
Side					0.001
Left	408	61.9	2991	41.4	
Right	251	38.1	4235	58.6	
Induction therapy					< 0.001
No	589	89.3	6798	94.0	
Chemoradiotherapy	31	4.7	265	3.7	
Chemotherapy	1	0.2	137	1.9	
Radiotherapy	38	5.8	26	0.4	
Pathological stage					< 0.001
Stage I and occult	107	16.2	4155	57.5	
Stage II	266	40.4	1893	26.2	
Stage III+	255	38.7	939	13.0	
Unknown	31	4.7	239	3.3	
Pathological T stage					< 0.001
T1 (T0, Tis, Tx)	89	13.5	3087	42.7	
T2	274	41.6	2915	40.3	
T3	214	32.5	1048	14.5	
T4	80	12.1	152	2.2	
Unknown	2	0.3	24	0.3	
Postoperative histology					< 0.001
Adenocarcinoma	189	28.7	4163	57.6	
Squamous cell	410	62.2	2194	30.4	
Different**	60	9.1	869	12.0	
Postoperative mortality***	47	7.1	123	1.7	

*Performance score using ECOG/WHO. **Different: SCLC, carcinoid, adenosquamous, large cell (NET) and not otherwise specified. ***Defined as postoperative 30-day or in-hospital mortality

Table 2 Factors associated with receiving a pneumonectomy. Number of patients included: $N = 7885$

	Resection using pneumonectomy			
	Unadjusted*		Adjusted**	
	OR^	95% CI^	OR^	95% CI^
Age				
<60	Ref		Ref	
60–64	1.35	1.06–1.72	1.16	0.89–1.50
65–69	1.13	0.89–1.44	0.88	0.67–1.14
70–74	1.19	0.93–1.51	0.81	0.62–1.06
75+	0.72	0.55–0.96	0.47	0.34–0.64
Gender				
Male	Ref		Ref	
Female	0.55	0.46–0.65	0.72	0.60–0.87
Cardiac comorbidity				
No	Ref		Ref	
Yes	0.74	0.61–0.90	0.75	0.60–0.92
Pulmonary comorbidity				
No	Ref		Ref	
Yes	0.75	0.63–0.89	0.69	0.57–0.83
Lung function				
FEV1[a] or DLCO[b] ≥ 80%	Ref		NA	
FEV1 and DLCO < 80%	1.36	1.13–1.63	NA	
FEV1 and DLCO unknown	1.37	0.96–1.94	NA	
Side of tumor				
Left	Ref		Ref	
Right	0.44	0.37–0.51	0.43	0.36–0.52
Clinical T stage[c]				
≤T1	Ref		Ref	
T2	3.54	2.76–4.54	2.86	2.21–3.69
T3	8.23	6.36–10.64	6.75	5.18–8.80
T4	15.51	10.94–21.98	14.74	10.20–21.30
Unknown	4.08	2.75–6.04	3.78	2.52–5.65
Postoperative histology				
Adenocarcinoma	Ref		Ref	
Squamous cell carcinoma	4.12	3.44–4.93	3.58	2.94–4.35
Different[d]	1.52	1.13–2.06	1.49	1.09–2.03

^*OR* odds ratio, *CI* confidence interval. A confidence interval excluding 1.00 indicates *statistical significance*

*Univariable, **multivariable

[a]Forced expiratory volume in 1 s, percentage of expected

[b]Diffuse lung capacity for oxygen, percentage of expected

[c]According to TNM-7 staging

[d]Adenosquamous or large cell carcinoma

(mortality: OR 0.28, 95% CI 0.05–1.45, complicated course: OR 1.42, 95% CI 0.40–5.05).

When considering all anatomical resections, there were significantly more patients with a postoperative complicated course in the three hospitals with more pneumonectomies (430 patients included) compared to the three hospitals with less pneumonectomies (557 patients included) than expected (OR 1.51, 95% CI 1.05–2.19), after adjustment for relevant factors. There was no significant difference in postoperative mortality between these groups (OR 0.66, 95% CI 0.28–1.54).

Fig. 1 Funnel plot of between-hospital variation in the use of pneumonectomy (2012–2016). *O/E ratio: observed number of pneumonectomies divided by expected^ number of pneumonectomies. **O = E: the observed number equals the expected^ number of pneumonectomies. ^Expected number of pneumonectomies per hospital based on hospital population characteristics (age, gender, cardiac and pulmonary comorbidity, side of malignancy, clinical T stage, histopathology). Number of hospitals included $N = 51$; number of patients included $n = 7885$

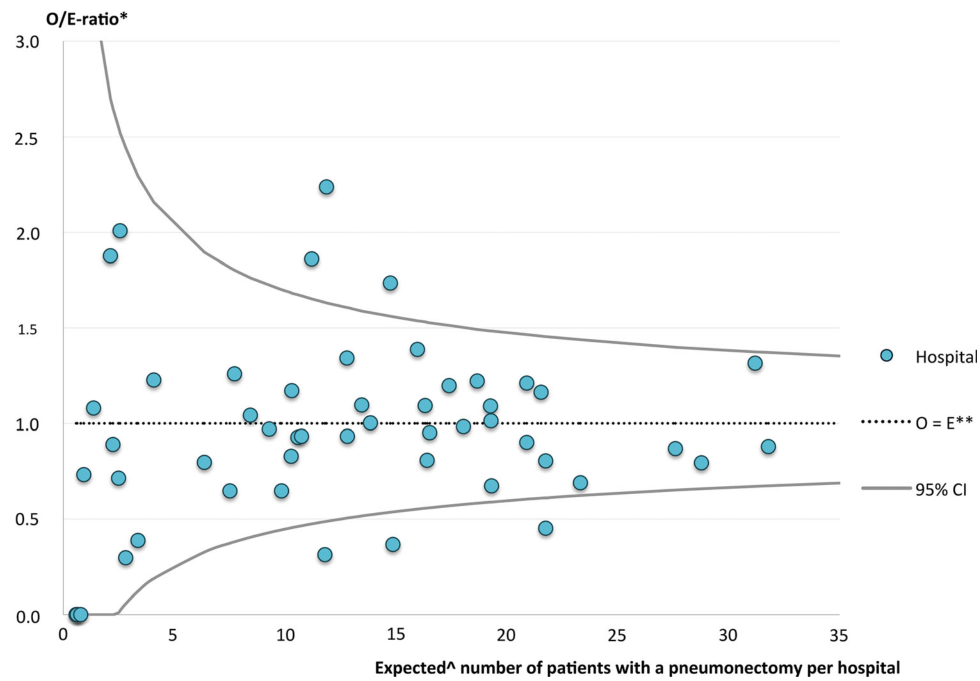
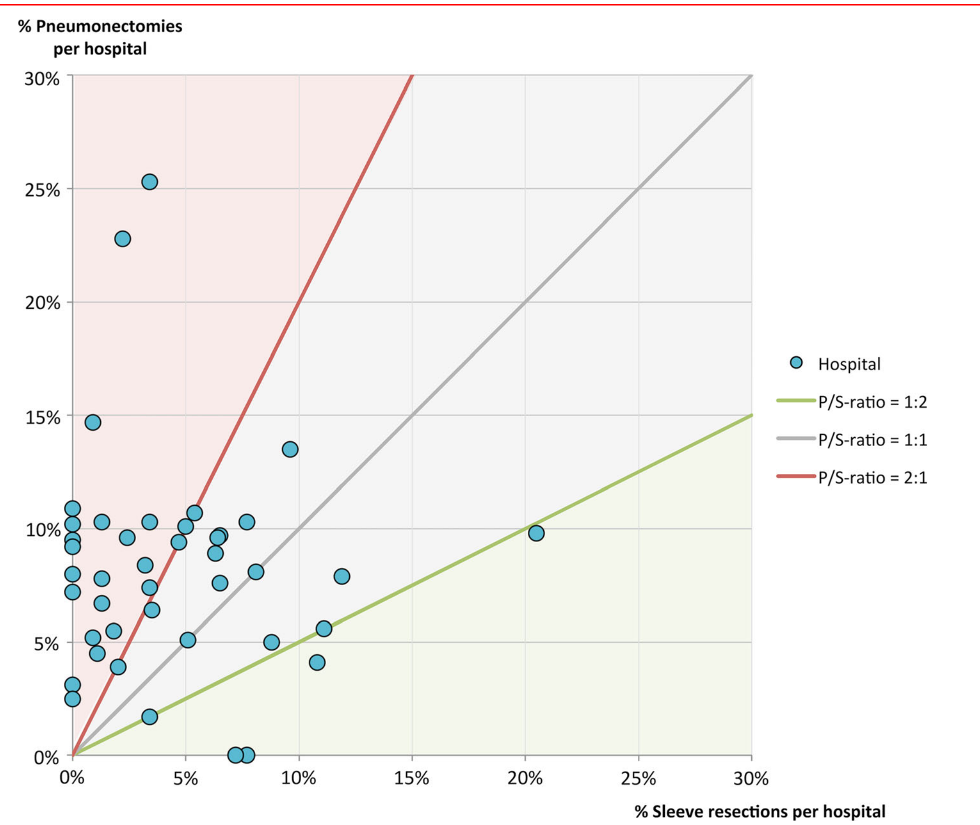


Fig. 2 Scatter of P/S ratio* per hospital (2015–2016). *P/S ratio: number of pneumonectomies divided by number of sleeve resections per hospitals. Number of hospitals included N = 42; number of patients included $n = 3790$



From 2015 on, the DLCA-S contains information on sleeve resections. Subgroup analysis of resections between 2015 and 2016 showed wide variation in the pneumonectomy/sleeve resection ratio per hospital (Fig. 2). Eight hospitals performed no sleeve resection and up to 10.9% pneumonectomies. Two hospitals performed up to 7.7% sleeve resections and no pneumonectomies.

Comment

This study is the first to report on both the national practice of pneumonectomy use and between-hospital variation by using Dutch nationwide registry data with center-specific information. Considerable between-hospital variation exists in the use of pneumonectomy for primary lung cancer in the Netherlands, even after adjustment for patient and disease characteristics.

National variation

In the current study, age, gender, cardiac and pulmonary comorbidities, tumor side, cT and histopathology were individual factors significantly associated with receiving a pneumonectomy. This is in line with previous studies, although the current study was the first to perform multivariable analyses [20, 21].

Between-hospital variation in pneumonectomy use in the Netherlands ranged from 0.0 to 25.3% (IQR: 5.5–10.1%). After adjustment for relevant factors, out of 51 hospitals, three hospitals performed significantly more and three significantly less pneumonectomies than expected based on predetermined patient/disease characteristics.

The proportion of severe postoperative complications was higher in the hospitals with significantly more pneumonectomies. There were no significant differences in postoperative mortality between the hospitals performing significantly more or significantly less pneumonectomies. However, pneumonectomy-related mortality and morbidity often express beyond the 30-day follow-up period [1, 8, 10]; thus, the outcomes reported in this study could be an underestimation.

The existence of between-hospital variation suggests that for individual patients the risk to receive a pneumonectomy, and its related morbidity, could depend on the hospital of choice. Pneumonectomies may be performed on lower thresholds in some hospitals, whereas others might perform sleeve lobectomies or no resection at all. Of course, one cannot simply assume that every sleeve resection is an averted pneumonectomy; however, the varying pneumonectomy/sleeve resection ratio does indicate that considerations per hospital vary. The proportion of pneumonectomies per hospital might also be influenced by the availability of alternative treatment strategies (e.g., chemo(radiotherapy) instead of surgery in T3/T4 tumors) or the preference of local multidisciplinary teams. Whether referral patterns or patient preferences influence the between-hospital differences could not be studied, since these data were not available from the DLCA-S. However, the fact that all six 'outlying' hospitals are medium-sized non-academic centers lowers the presumption of referral bias. In addition, potential bias was reduced by the casemix adjustment.

Unlike previous literature and the intuitive expectation that centers with a high pneumonectomy proportion would have better postoperative outcomes after a pneumonectomy, in this study no significant differences were observed in postoperative mortality and complicated course after a pneumonectomy performed in hospitals with a high versus low pneumonectomy proportion. This could suggest that high pneumonectomy proportions are rather an expression of varying treatment considerations per hospital than the result of referral to expertise centers. It can also be hypothesized that higher pneumonectomy percentages could be the result of more unplanned pneumonectomies due to intra-operative complications or a preoperatively underestimated tumor stage.

Centralization of care

In the past years, the number of hospitals providing surgical lung cancer care declined from 79 in 2005 to 43 hospitals in 2015, signifying a 45% reduction [14, 22]. In the current study, there were 42 hospitals performing sleeve resections or pneumonectomies in 2015–2016. In this period, there were 30 hospitals performing between 1 and 10 sleeve resections and 28 hospitals performing between 1 and 10 pneumonectomies. Although a considerable centralization has been achieved, a further centralization might be necessary for the technically difficult or high-risk procedures as sleeve resections or pneumonectomies, since it is know that volume could influence surgical outcomes [23].

International comparison

The pneumonectomy proportion in the Netherlands (7.8%) is lower than in most European countries (7.4–19.6%), but higher than in the USA (4.8%) (supplemental Table 1) [6–12]. A pneumonectomy proportion as high as 34.6% was reported by a regional cohort study from the Netherlands (1984–1992) [24]. More historical English and Danish registry data show a significant decrease in pneumonectomy proportion over time [6, 7]. The study by Jakobsen et al. reports a national decrease from 23% to 11% (2000–2007) [6]. Postoperative mortality after pneumonectomy in the Netherlands (7.1%) is similar to other European countries (5.9–8.0%), but slightly higher than in the USA (4.9%).

Making these international comparisons, one should keep in mind that studied populations differ. The Society of Thoracic Surgeons General Thoracic Surgery Database (GTSD) and the European Society of Thoracic Surgeons GTSD data included resections not only for primary lung cancer (87.0–94.5%), but also for metastasis (1.9–4.5%) and benign diseases (3.6–3.8%) [20]. Besides, the Dutch population is older and less frequently treated with induction therapy, and tumor (pT) stage is less frequently missing, though comparable to European and American populations [9, 20].

Although there are previous studies reporting on the national pneumonectomy proportion and regional variation, this study is the first to report between-hospital variation. What also distinguishes the current study from previous ones is the way data are collected and used, influencing data quality, completeness and analytic possibilities. Data for this study were collected using a national prospective audit system [13, 25]. The audit itself is designed and maintained by clinicians, therefore including clinically most relevant information. Clinicians receive weekly updated feedback information, thereby enhancing data quality. Participation in the audit is incorporated in the professional quality system, and registered data are regularly checked by external data verification, thereby stimulating unbiased information. This is in contrast to registries with a more voluntary nature or a pure retrospectively registration.

Study limitations

A limitation of the DLCA-S is that it does not provide information on non-operated patients; thus, resection rates cannot be calculated, nor could the indication for (not) operating be studied. In accordance with English and Danish registry data [6, 7], another study showed an increasing lung cancer resection rate in the Netherlands [26]. This, together with stable pneumonectomy rates and population characteristics during the existence of the DLCA-S, suggests that the relatively low pneumonectomy proportion in the Netherlands is not due to risk-averse behavior. The DLCA-S data 2012–2016 did not provide information whether a tumor is centrally located or extends beyond fissures. This is registered from 2017 onwards. Proxy information used in this study is tumor (T) stage and histopathology, since squamous cell carcinoma is more often centrally located [27]. Also, the DLCA-S does not provide information on the percentage of aborted procedures stratified by the extent of surgery. A probably underestimated percentage of 1.2 of all patients undergoing surgery for NSCLC in the DLCA-S with no resection in the end is reported previously [5].

Due to differences in definitions (e.g., mortality) and applied in- and exclusion criteria, it is challenging to generate true international comparisons. Consensus on key data items therefore should be a shared objective.

Future perspectives

Awareness among caregivers on pneumonectomy use in practice can increase by providing benchmarked information regarding the pneumonectomy proportion per hospital in indicator format.

National data can be used to evaluate current clinical practice and trigger improvement initiatives. In colorectal cancer surgery for example, data from the clinical audit led to a modification of the national guideline adjustment and led to remarkable changes in clinical practice [28].

In addition, indicator results and between-hospital variation can be used to support a more solid quality of care discussion. Adjustment for patient/disease characteristics can place this information in context.

The DLCA-S scientific committee will work toward providing caregivers with this information. Since a pneumonectomy remains necessary to obtain complete oncologic resection in certain cases, a percentage of 0.0 pneumonectomies is not aspired. What the ideal 'target' pneumonectomy proportion would be is not yet clear. This will be subject of debate for the DLCA-S scientific committee and affiliated professional associations. Another point of discussion will be whether further concentration of high-risk procedures into expertise centers (with expertise in sleeve resections, high volume and optimal postoperative care) may be beneficial. Organizing this optimal care, equally accessible to all patients, is a combined responsibility of healthcare government and caregivers.

Conclusions

This study demonstrates that there is a considerable nationwide between-hospital variation in pneumonectomy use in surgical lung cancer treatment, even after adjustment for patient and disease characteristics. Variation could be the result of varying treatment considerations or unplanned pneumonectomies. Nationwide registries and the development of specifically focused pneumonectomy indicators could be improvement tools to further optimize surgical lung cancer care.

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Compliance with ethical standards

Conflict of interest None declared for any of the authors.

Informed consent Not required for this study type under Dutch law.

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