



Surgery without preoperative histological confirmation of lung cancer: what is the current clinical practice?

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Background: There are discordances in the guidelines regarding the need to acquire histological diagnosis before surgical treatment of (presumed) lung cancer. Preoperative histological confirmation is always encouraged in this setting to prevent unnecessary surgery or when sublobar resection for small-sized tumors is considered. The aim of this retrospective cohort study was to assess the proportion of patients undergoing lung cancer resection in the Netherlands without preoperative pathological confirmation, based on the intraoperative pathological diagnosis (IOD) rate, and to determine characteristics that may influence IOD frequency.

Methods: Data on 10,226 patients, who underwent surgical treatment for lung cancer from 2010 to 2015, were retrieved from the Netherlands National Cancer Registry. We registered an IOD when the date of diagnosis equaled the date of the first surgical intervention. Tabulations and multivariable logistic regression were used to identify predictive parameters for IOD.

Results: 36% of surgical procedures were classified as IOD, and decreased with increasing tumor size and extent of surgery (57% for segmentectomy, 39% for lobectomy and 11% for pneumonectomy). IOD was more frequently observed in adenocarcinoma (41%), varied between hospitals from 13% to 66% and was less common when patients were referred from a hospital where thoracic surgery was not performed. Previous history of cancer did not affect IOD.

Conclusions: More than one-third of patients with suspected lung cancer in the Netherlands was operated without preoperative histological confirmation. There was significant variation in IOD rates between different hospitals, which deserves further detailed analysis when striving for uniform surgical quality of care for patients with lung cancer.

Keywords: Intraoperative pathological diagnosis; preoperative histological confirmation; lung cancer surgery; lung cancer diagnosis

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Introduction

There is strong agreement amongst guidelines that surgical resection forms the cornerstone of curative treatment for patients with early-stage lung cancer (1-5). However, discordances exist regarding the need to acquire pathological diagnosis before planned surgical resection (*Table 1*). For example, the European Society for Medical Oncology (ESMO) guidelines on early non-small cell lung cancer (NSCLC) recommend to acquire pathological diagnosis before any curative treatment, unless an experienced multidisciplinary group decides the risks of obtaining pathology to be unacceptable (4). Conversely, the United States (US)-based National Comprehensive Cancer Network (NCCN) guidelines recommend that patients with a strong clinical suspicion of early-stage lung cancer do not require a biopsy before surgery (5); however, an intraoperative tissue diagnosis is still necessary before performing intended curative resection, usually through intraoperative frozen section (FS) procedure. Comparably, the American College of Chest Physicians (ACCP) and British Thoracic Society (BTS) have advocated upfront surgery when the clinical probability of malignancy is high, either >65% (6) or >70% (3).

Whether preoperative pathological confirmation of lung cancer diagnosis is indispensable is an interesting debate. Case series have reported risks of 5–20% of finding benign disease (thus ultimately undergoing unnecessary surgery) when patients were operated without preoperative pathological diagnosis (7-13). Moreover, with a rising trend of utilizing sublobar resections to treat small-sized early-stage lung cancer (14), accurate pathological classification beforehand will become increasingly important. After all, high-risk histological subtypes such as solid or micropapillary adenocarcinoma are associated with local recurrence in patients who have undergone limited resections when compared to lobectomy (15), and the diagnostic accuracy of intraoperative FS on these high-risk histologic features is still debatable (16).

With conflicting recommendations from available guidelines, it is reasonable to assume this will lead to variation in lung cancer surgical care. Recent studies have reported important quality gaps in treatment delivery (17) and unwarranted care variation (18), leading to significant variation in preoperative cardiopulmonary assessment practices (19) and surgical resection rates (20). Whether there are also differences in preoperative diagnostic testing, leading to variation in proportion of patients being operated without

a preoperative pathological diagnosis, remains to be clarified.

In our current study, we assessed the proportion of patients undergoing lung cancer resection being operated in the Netherlands without preoperative pathological confirmation, based on the rate of “intraoperative pathological diagnosis” (IOD). Furthermore, we attempted to determine factors that are predictive for IOD, as well as variations in these rates in the Netherlands, with specific interests for patients with small-sized early-stage disease and undergoing sublobar resection. Our hypothesis is that IOD rate will be higher in small peripheral tumors that are resected by smaller anatomical resections. Mainly because of the difficulty to reach these tumors with current diagnostic tools. And we also can assume that conflicting recommendations in the guidelines will lead to a significant IOD rate variation in the Netherlands.

We present the following article in accordance with the STROBE reporting checklist (available at <https://dx.doi.org/10.21037/jtd-21-617>).

Methods

This study was designed as a retrospective cohort study, including all surgical treated patients in the Netherlands using data from a national wide database. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Data used in this study was obtained from the Netherlands National Cancer Registry (NNCR), after approval by the NNCR Privacy Review Board. In accordance with the regulations of the Central Committee on Research involving Human Subjects, this type of study does not require approval from an ethics committee in the Netherlands.

All registered patients in the NNCR with invasive primary lung cancer who underwent an anatomical resection, diagnosed between 2010 and 2015 were evaluated for inclusion in this study.

The NNCR collects data on all cancer patients diagnosed in the Netherlands, based on notification of newly diagnosed malignancies by the national automated pathology archive and of hospital discharge diagnoses. Information on demographics, diagnosis, staging, and treatment is extracted routinely from the medical records by specially trained NNCR personnel and not by the care takers themselves, in order to minimize the chance of bias. Clinical and postsurgical stage information was recorded according to the 7th edition of the TNM Classification of Malignant Tumours from the International Union against

Table 1 Guidelines recommendations on the need of preoperative diagnosis prior to surgical resection

Society	Year	Recommendation
NCCN (5)	2020	❖ Patients with a strong clinical suspicion of stage I or II lung cancer (based on risk factors and radiologic appearance) do not require a biopsy before surgery
ESMO (4)	2017	❖ In patients with clinical stages I–III lesions, a pretreatment pathological diagnosis is recommended prior to any curative treatment. <ul style="list-style-type: none"> • An exception to the requirement for a pretreatment diagnosis can be made if an experienced multidisciplinary group decides that the risks of obtaining pathology may be unacceptable in a patient in whom the likelihood of malignancy is high based on clinical and imaging findings
BTS (3)	2015	❖ Offer people surgical resection as the favoured option where the risk that the nodule is malignant is >70% <ul style="list-style-type: none"> • Consider image-guided biopsy where the risk of malignancy is assessed to be between 10% and 70%; other options are excision biopsy or CT surveillance guided by individual risk and patient preference
Oncoline - Comprehensive Cancer Centre the Netherlands (2)	2015	❖ The diagnosis of non-small cell lung cancer is preferably obtained preoperatively. <ul style="list-style-type: none"> • When this is not feasible, intraoperative rapid diagnosis through frozen section examination should be available • After confirmation of malignancy, extended resection during the same surgical procedure can be performed
ACC (1)	2013	❖ In the individual with a solid, indeterminate nodule that shows clear evidence of malignant growth on serial imaging, nonsurgical biopsy is recommended and/or surgical resection unless specifically contraindicated <ul style="list-style-type: none"> ❖ In the individual with a solid, indeterminate nodule that measures >8 mm in diameter, surgical diagnosis is recommended in the following circumstances: <ul style="list-style-type: none"> • When the clinical probability of malignancy is high ($\geq 65\%$) • When the nodule is intensely hypermetabolic by PET or markedly positive by another functional imaging test • When nonsurgical biopsy is suspicious for malignancy • When a fully informed patient prefers undergoing a definitive diagnostic procedure. ❖ In the individual with a solid, indeterminate nodule measuring >8 mm in diameter who chooses surgical diagnosis, we recommend thoracoscopy to obtain a diagnostic wedge resection.

NCCN, national comprehensive cancer network; ESMO, European society for medical oncology; BTS, british thoracic society; ACC, American college of chest physicians.

Cancer. The date of diagnosis is recorded as the date of retrieval of cytology specimens or histological specimen, mentioned in the pathology report that first confirmed the diagnosis of cancer. Whether diagnosis resulted from FS analysis during surgery or by later examination of the resection specimen, cannot be distinguished. Lung surgery for benign lesions is not recorded. Hospitals of diagnosis and treatment are recorded separately.

In 2010, 92 hospitals treated patients with lung cancer, while 58 hospitals performed lung surgery. Fifteen of the

58 hospitals stopped performing lung surgery during the study period. Patients who were younger than 18 years of age, or with cancer located in the main bronchi, operated abroad or in any of the hospitals that discontinued lung surgery, were excluded from this study. Patients with synchronous or metachronous tumors were excluded in order to keep a homogeneous population. Patients who underwent wedge resection were also excluded because in the NNCR database it was not recorded whether the procedure was performed with diagnostic or with curative intend.

Study variables

Age was categorized in 4 subgroups. Pathology was coded according to the ICD-O-3 morphology classification and was categorized in 5 subgroups: small cell lung cancer, squamous cancer, adenocarcinoma, large cell carcinoma not otherwise specified (NOS), and other tumors including neuroendocrine tumors, carcinoids, and sarcomatoid lesions. Type of surgery was categorized into segmentectomy, lobectomy, bilobectomy, and pneumonectomy. IOD was designated when the date of diagnosis equaled the date of the first operation. IOD could be achieved by an intraoperative frozen section or by definitive pathological examination after the surgery. This could not be distinguished because the data regarding a frozen section with pathological examination or an intraoperative cytological examination is not recorded in the NNCR. History of previous cancer was included as a parameter, excluding diagnoses of non-melanoma skin cancer. A separate parameter designates that diagnosis and surgery did not occur in the same hospital.

Statistical analysis

Statistical analyses were performed using Stata 14 (©Copyright 1996–2017 StataCorp LLC). The proportion of patients with intraoperative diagnosis was tabulated, this was also done for the sub analysis of patients undergoing sublobar resection. Missing data were included as separate categories. Differences between subgroups were tested for significance with chi-square statistics. Multivariable analysis was performed using hierarchical logistic regression, including the hospital of surgery as the first level variable.

The hierarchical model accounts for clustering of patients within hospitals and allows assessment of residual variation in IOD rate between hospitals.

The significance of predictive factors was assessed with the log-likelihood test and significant ($P < 0.05$) parameters are represented by odds ratios (OR) and a 95% confidence interval (CI). Posterior Bayes estimates of the odds ratios for the involved hospitals were plotted against hospital resection volume. The hospital resection volume is defined as the number of anatomical parenchymal resections performed for lung cancer in a hospital.

Results

A total of 10,226 patients in 43 hospitals were included in our analysis (Table 2). The median age was 66 years and 57% were men. Adenocarcinoma was the most common pathological subtype (52%) and small cell lung cancer comprised only 1.4% of cases. Lobectomy comprised 83% of all operations and segmentectomy was only performed in 1.7% of cases. Clinical T-stages 1a (0–2 cm) and 1b (2–3 cm) were diagnosed in 24% and 17% respectively. Of all patients, 16% were previously diagnosed with another type of cancer and 25% were transferred from the hospital of diagnosis to another hospital for lung cancer surgery.

Intraoperative pathological diagnosis

Cytological or histological diagnosis was not available before the start of surgery for more than one-third of the patients (36%) (Table 2). This proportion remained stable over time from 38% in 2010–2011 to 35% in 2014–2015, and was not affected by age or sex. The IOD proportion decreased with

Table 2 Proportion of IOD in patients who underwent lung cancer surgery

	Cohort, N=10,226	N [%] with IOD	P value	OR	95% CI
Age					
18–59	2,638	923 [35]	0.39	NS	–
60–69	3,992	1,437 [36]			
70–79	3,171	1,142 [36]			
80+	425	140 [33]			
Gender					
Men	5,831	1,924 [33]	<0.001	NS	–
Women	4,395	1,714 [39]			

Table 2 (continued)

Table 2 (continued)

	Cohort, N=10,226	N [%] with IOD	P value	OR	95% CI
Pathology					
Adeno	5,305	2,175 [41]	<0.001	1	
Squamous	3,450	932 [27]		0.73	0.66–0.81
Small cell	144	66 [46]		1.27	0.88–1.85
Large cell	607	194 [32]		0.8	0.65–0.98
Other	720	245 [34]		0.72	0.60–0.87
Lobe					
Upper	6,071	2,307 [38]	<0.001	1	
Middle	478	186 [39]		0.92	0.74–1.14
Lower	3,288	1052 [32]		0.81	0.73–0.90
NOS	389	74 [19]		0.77	0.57–1.04
Year					
2010–2011	3,111	1,182 [38]	0.01	1	
2012–2013	3,442	1,170 [34]		0.79	0.71–0.89
2014–2015	3,673	1,286 [35]		0.87	0.77–0.97
Type of surgery					
Segmentectomy	173	99 [57]	<0.001	1.77	1.25–2.51
Lobectomy	8,476	3,306 [39]		1	
Bilobectomy	686	144 [21]		0.58	0.47–0.72
Pneumonectomy	891	98 [11]		0.28	0.22–0.36
cT					
1a	2,483	1,465 [59]	<0.001	3.34	2.94–3.80
1b	1,701	697 [41]		1.62	1.41–1.86
2a	2,619	760 [29]		1	
2b	998	180 [18]		0.61	0.51–0.74
3	1,637	278 [17]		0.58	0.49–0.68
4	400	56 [14]		0.53	0.38–0.72
X	388	198 [51]		2.70	2.13–3.43
cN					
0	8,507	3,233 [38]		1	
1	1,081	270 [25]		0.77	0.66–0.91
2/3	638	115 [18]		0.47	0.37–0.59
Previous cancer					
Yes	1,648	626 [38]	0.01	ns	–
No	8,578	3,002 [35]			
Referred for lung surgery ^a					
No	7,625	2,974 [39]	<0.001	1	
Yes	2,601	702 [27]		0.60	0.53–0.90

^a, patients were analyzed in another hospital than the hospital of surgery. IOD, intraoperative pathological diagnosis; OR, odds ratio; CI, confidence interval; NS, not significant; NOS, not specified/missing; cT, clinical T stage; cN, clinical N stage; X, missing/unknown.

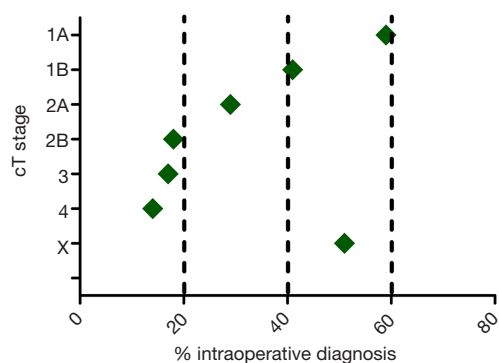


Figure 1 Proportion of IOD in relation to the clinical T (cT) stage. IOD, intraoperative pathological diagnosis; cT, clinical T.

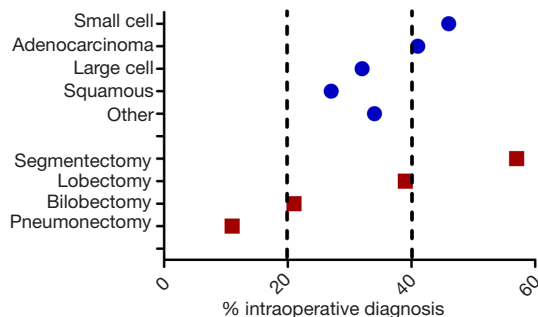


Figure 2 Proportion of IOD in relation to the histological cancer type (blue circles) and the extent of resection (red squares). IOD, intraoperative pathological diagnosis.

tumor size, being 59% for T1a, 41% for T1b, and only 17% and 14% for T3 and T4 tumors respectively (Figure 1). Regarding differences between pathological subtypes, IOD was highest (46%) for small cell carcinoma; the frequency of IOD was more common in adenocarcinoma (41%) than in other non-small cell lung cancer subtypes (Figure 2). IOD varied significantly with different extent of surgical resection, being 57% for segmentectomy, 39% for lobectomy, and 11% for pneumonectomy (Figure 2). A history of previous cancer had no influence on the IOD proportion, but the IOD proportion was significantly lower if patients were not diagnosed in the hospital of surgery (27% versus 39%, $P < 0.001$).

A small group of patients ($N = 173$) underwent a segmentectomy. Sub-analysis showed that adenocarcinoma was the most common pathological diagnosis in this group (65%) with an IOD rate of 57% (Table 3). Squamous cell carcinoma was diagnosed in 14% with a high IOD rate of

72%. A total of 18 patients (10%) had a tumor classified T2b or higher, with a IOD rate of 44% in this group. In 9% ($N = 16$) of the cases the N stage was 1 or higher with an IOD rate of 31%.

Multivariable analysis revealed the independent predictive impact of pathology, tumor localization, year of diagnosis, type of surgery, TNM stage, and patient referral (Table 2). Controlling for the independent prognostic factors, residual variation in IOD rate between hospitals was considerable ($P < 0.001$). Odds ratios ranged from 0.23 to 3.98, reflecting proportions of IOD ranging from 13% to 66%. IOD proportions were significantly higher in 18 hospitals and lower in 14 hospitals, compared to the national average (Figure 3).

Discussion

Our study has shown that over one-third of patients who had undergone lung cancer resection were operated without a preoperative definitive diagnosis in current Dutch clinical practice. IOD rate decreased with increasing tumor size and extent of surgery. Furthermore, there was significant variation in the rate of IOD, varying from 13–66% between the Dutch surgical centers during the study period.

Our findings are roughly comparable with the scarcely reported data on this matter. Population-based registries have documented rates of approximately 30% of cases without pathological confirmation of their lung cancer diagnosis, regardless of treatment strategy (21). For lung cancer patients undergoing operative treatment specifically, various small single-institutional studies reported that 27–36% of patients who had undergone surgery for (ultimately) confirmed lung cancer were operated without preoperative pathological diagnosis (9,22). To the best of our knowledge, this is the first nationwide population-based registry describing the rate of lung cancer patients undergoing surgical treatment without a preoperative definitive diagnosis.

The lack of a definite preoperative diagnosis, leading to IOD, generates various potential risks and problems during lung cancer surgery. First of all, there is an obvious possibility that a patient with a suspicious pulmonary nodule without definitive diagnosis might be operated for benign disease, thus resulting in an unnecessary surgical procedure and related morbidity and risks in hindsight. Due to our methodology, utilizing data from the NNCR where patients with benign diagnoses were already excluded, this risk cannot be estimated in our current study. However, the rate

Table 3 Subanalysis of IOD rate in patients who underwent segmentectomy for lung cancer (N=173)

	N	N [%] with IOD
Pathology		
Adenocarcinoma	111	63 [57]
Squamous cell carcinoma	25	18 [72]
Small cell carcinoma	3	1 [33]
large cell carcinoma	7	2 [29]
Other	27	14 [52]
cT		
1a	96	65 [68]
1b	39	20 [51]
2a	20	5 [25]
≥2b	18	8 [44]
cN		
0	157	93 [54]
1/2/3	16	5 [31]

IOD, intraoperative pathological diagnosis; cT, clinical T stage; cN, clinical N stage.

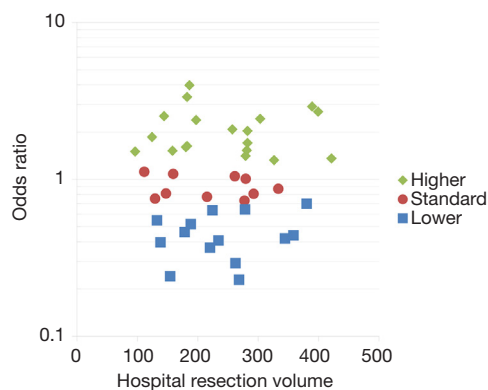


Figure 3 OR of the IOD proportion, in relation to hospital resection volume. Grouped in standard OR, higher and lower than the standard OR. IOD, intraoperative pathological diagnosis; OR, odds ratio.

of unnecessary surgery was not the focus of our analysis, and this (often trivialized) risk has already been reported in other investigations, varying from 5–20% in case series published in the last decade (7–13). For example, a recent study on 129 patients undergoing surgical intervention with pulmonary nodules found incidentally or by lung cancer screening (13), 75–80% were <2 cm, and <10% received percutaneous needle biopsy preoperatively. However, this diagnostic approach led to 17% “unnecessary surgery”

with an ultimately benign diagnosis. Correspondingly, recent reports have documented an accuracy of 85% of experienced radiologists to estimate the likelihood of malignancy of nodules <2 cm based on CT-imaging, with or without additional help from risk prediction models (23). Although this seems to align with beforementioned guideline recommendations to accept upfront surgery when the clinical probability of malignancy is >65–70% (3,6), these rates of ultimately unnecessary surgery undeniably challenge the physician’s ability to make a reliable lung cancer diagnosis solely based on clinical and radiologic data.

Secondly, the lack of a preoperative diagnosis requires the acquirement of an intraoperative diagnosis, usually through wedge resection and FS examination, before anatomic pulmonary resection can be justified (3). However, not all pulmonary nodules are suitable for this approach. In a recent Japanese case series with 199 patient undergoing lung resection without preoperative definitive diagnosis, 98 (49%) underwent upfront direct lobectomy without FS, because wedge resection was deemed not feasible due to size and/or depth of the nodule (24); ultimately, six of these patients (6%) had benign disease as final pathological diagnosis (24). Even when diagnostic wedge resection is feasible, various problems can arise hampering real-time intraoperative decision-making related with FS examination. Although the concordance rate between intraoperative FS

results and final pathology diagnosis has been reported to be appropriate (25,26), rates of false-negative and indeterminate FS diagnosis have been reported as high as 12–18% (27,28), and errors of intraoperative FS procedures are reported to have significant clinical impact (25). Furthermore, in the setting of a previous malignancy, the intraoperative differentiation between primary NSCLC or pulmonary metastasis might be problematic, while being essential in determining the extent of resection. Remarkably, the rate of IOD in our study was similar in patients with and without a history of previous cancer, suggesting that surgeons do not necessarily feel the need for this differentiation beforehand.

Thirdly, various additional challenges arise specifically in the setting of small-sized tumors while considering a potential sublobar resectional strategy when a preoperative definitive diagnosis is not available. Technically, a wedge resection necessary for confirming the cancer diagnosis might obscure intersegmental planes and complicate a following segmentectomy. Conversely, an upfront segmentectomy is technically more challenging than wedge resection, and is associated with higher surgical morbidity (29,30) and mortality (31), exposing the patient to unnecessary surgical trauma and risks in the case of an ultimately benign diagnosis. Moreover, several adenocarcinoma subtypes [such as micropapillary adenocarcinoma (31)] and tumors with high-risk histologic features [such as “tumor spread through air space” (16)] are known to have an inferior prognosis after sublobar resection (15,16,32), and lobectomy is therefore recommended. However, when a preoperative diagnosis is not available, the indispensable intraoperative FS examination has been associated with a diagnostic accuracy of only 68–85% in identifying predominant histologic subtype (25,33). Additionally, various studies have documented low sensitivity for FS in diagnosing high-risk morphology, often caused by sampling error largely affected by tumor heterogeneity (16,34). Consequently, errors in intraoperative FS examination are factual and well reported (28,33), and could potentially have significant negative clinical impact (15). Therefore, an accurate preoperative pathological diagnosis with subtyping is essential to guide the surgeon in choosing the optimal intraoperative strategy regarding extent of resection, especially for smaller sized tumors and/or adenocarcinomas (32,35). Interestingly, in our study, we observed an opposite clinical practice that lower T-stage, smaller sized tumors, adenocarcinoma, or undergoing segmentectomy were factors significantly associated with a higher IOD rate.

Naturally, the beforementioned drawbacks of IOD should be balanced against the hazards and accuracy of preoperative invasive diagnostic procedures. Traditionally, these non-surgical biopsies can be obtained through guidance with bronchoscopy, ultrasound, computed tomography (CT), and more recently through electromagnetic navigation bronchoscopy (ENB) and cone-beam-CT based navigation bronchoscopy (3). For CT-guided transthoracic lung biopsy, major complication rate relatively high with a 19–25% risk of pneumothorax requiring drainage in 4.3–5.6% (36). The introduction of navigation bronchoscopy-guided biopsy is associated with a much lower risk of pneumothorax (2–3%) (37). In our country however, navigation bronchoscopy is not widely implemented and is routinely used in our center alone since late 2017. Since the yield of image guided navigation bronchoscopy is increasing and in some centers matches the yield of TTNA, this is a promising strategy to implement (38,39).

There were several important limitations to our current explorative study. First of all, the study was performed using data obtained from the NNCR, including only patients with a cancer diagnosis. With the absence of patients with benign pathology, we could not explore the effect of the lack of a preoperative diagnosis on the proportion of patients undergoing ultimately futile surgery, or properly assess any correlation with preoperative workup or postoperative outcome. In potential upcoming future studies on this matter, we plan to use data from population-based and nationwide surgical databases on general thoracic surgery to address the beforementioned issues.

The clinical implications of the high incidence of IOD and the remarkably large variation of this occurrence remain speculative at this moment. However, several prospects in impending trends in lung cancer practice should be considered in this regard. As advocated earlier, the negative effects of IOD would theoretically be most important in smaller-sized tumors, especially adenocarcinomas, particularly when considering a sublobar resectional strategy. With the advent of lung cancer screening with low-dose CT (40–42), a large number of patients with small pulmonary nodules will be detected and presented to multidisciplinary team meetings. In previous lung cancer screening trials, 49–81% of patients who will undergo surgical resection of these nodules do not have a preoperative diagnosis (43,44). Furthermore, while 73–91% presented with clinical stage I disease, only 18–48% were treated by sublobar resections (43,44). Comparably, the percentage of sublobar resections in our study is fairly low as well. Surgeons may not be familiar or comfortable yet

performing sublobar resections, besides awaiting for more evidence supporting these resections. Although lobectomy has long been the standard resection for most patients with resectable lung cancer (45), randomized trials are currently assessing the results of sublobar resections for NSCLC ≤ 2 cm when compared to standard lobectomy (12,46,47). The outcome of these trials could have significant impact on guidelines recommendations on the extent of surgical resection in these smaller sized tumors, especially with favorable histopathology, substantially increasing the number of patients in whom a sublobar resectional strategy could be considered. With the complex interplay between tumor size, pathology subtyping, and extent of resection on oncological outcome (48), the oncological and surgical communities should maximize efforts diminishing the current variations in care, unifying discordances in preoperative diagnostic algorithms, hopefully leading to more uniform perioperative decision-making regarding the extent of surgical resection, ultimately offering the best patient-tailored surgical care for individuals with NSCLC.

Another limitation of our study is the lack of data about the performed preoperative diagnostic workup. Unfortunately, these records were not included in the available NCCR dataset, and the exact utilization of invasive diagnostic procedures before surgery remains to be clarified. Notwithstanding this paucity of data, it is clear that the currently practiced diagnostic strategy only leads to a definitive preoperative diagnosis in only 64% of cases, with a wide variation of 33–87% between Dutch centers. This seems to be at variance with the recommendations by the Dutch guidelines (2), stating that “the diagnosis of non-small cell lung cancer is preferably obtained preoperatively”, which is in line with other international documents on this matter, including the ESMO guidelines (4). However, other international standards advise the opposite, with the NCCN (5) recommending that “patients with a strong clinical suspicion of stage I or II lung cancer (based on risk factors and radiologic appearance) do not require a biopsy before surgery”. In this regard, to diminish unwarranted variation in lung cancer care, international and national consensus should be advocated on this matter. As such, regional and national data, such as provided in our current study, should be examined as a benchmark for future reference.

Conclusions

In conclusion, our current study presents the first available nationwide population-based numbers on IOD rates in

patients undergoing lung cancer surgery in the Netherlands, offering data for benchmarking purposes. The significant variation in these rates deserves additional attention in order to initiate uniform surgical quality of care for patients with lung cancer, especially when considering a sublobar resectional strategy.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). In accordance with the regulations of the Central Committee on Research involving Human Subjects, this type of study does not require approval from an ethics committee in the Netherlands.

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