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Surgeon experience does not influence nodal upstaging during vats lobectomy: Results from a large prospective national database

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ABSTRACT

Background: Despite recent improvement in preoperative staging, nodal and mediastinal upstaging occur in about 5% to 15% of cN0 patients. Different clinical and tumor characteristics are associated with upstaging, whereas the role of the surgeon's experience is not well evaluated. This study aimed to investigate if operator experience might influence nodal upstaging during video-assisted thoracic surgery anatomical lung resection.
Methods: Clinical and pathological data from the prospective video-assisted thoracic surgery Italian nationwide registry were reviewed and analyzed. Patients with incomplete data about tumor and surgical characteristics, ground glass opacities tumors, cN2 to 3, and M+ were excluded. Clinical data, tumor characteristics, and surgeon experience were correlated to nodal and mediastinal (N2) upstaging using Pearson's χ^2 statistic or Fisher exact test for categorical variables and Mann–Whitney U and t tests for quantitative variables. A multivariable model was built using logistic regression analysis. Surgeon experience was categorized considering the number of video-assisted thoracic surgery major anatomical resections and years after residency.
Results: Final analysis was conducted on 3,319 cN0 patients for nodal upstaging and 3,471 cN0N1 patients for N2 upstaging. Clinical tumor-nodes-metastasis stage was stage I in 2,846 (81.9%) patients, stage II in 533 (15.3%), and stage III (cT3N1) in 92 (2.8%). Nodal upstaging occurred in 489 (13.1%) patients, whereas N2 upstaging occurred in 229 (6.1%) patients. Years after residency ($P = .60$ for nodal, $P = .13$ for N2 upstaging) and a number of video-assisted thoracic surgery procedures($P = .49$ for nodal, $P = .72$ for nodal upstaging) did not correlate with upstaging. Multivariable analysis confirmed cT-dimension ($P = .001$), solid nodules ($P < .001$), clinical tumor-nodes-metastasis ($P < .001$) and maximum standardized uptake values ($P < .001$) as factors independently correlated to nodal upstaging, whereas cT-dimension ($P = .005$), clinical tumor-nodes-metastasis ($P < .001$) and maximum standardized uptake values ($P = .028$) resulted independently correlated to N2 upstaging.
Conclusion: Our study showed that surgeon experience did not influence nodal and mediastinal upstaging during -assisted thoracic surgery anatomical resection, whereas cT-dimension, clinical tumor-nodes-metastasis, and maximum standardized uptake values resulted independently correlated to nodal and mediastinal upstaging.

Introduction

Lung cancer remains the leading cancer of death in the United States and Western countries, even if, in recent years, lung screening programs, minimally invasive techniques, and new chemotherapy options have improved survival.[1,2]

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In particular, the development of minimally invasive techniques such as video-assisted thoracic surgery (VATS) or robot-assisted thoracic surgery improved the quality of life of patients with non-small cell lung cancer (NSCLC) in terms of hospital stay and post-operative complication compared to thoracotomy.[3,4] However, the main goal of these techniques would be to ensure the same oncological and survival results of lung resections via thoracotomy, so different parameters were considered to assess the quality of VATS and robot-assisted thoracic surgery lobectomy. Two of those, nodal and mediastinal upstaging, were used to compare the appropriateness of the lymphadenectomy during VATS resection, with unclear results, especially when compared to thoracotomy.[5–8] Indeed, when a comparison between the 2 techniques is performed, it is hard to distinguish if the results may be due to a different surgeon's experience regarding the open and VATS approach. In particular, all studies focused their analysis on comparing the different techniques, but surgeon skills and experience in open or VATS were rarely considered.[5,9] On the other hand, the learning curve for VATS lobectomy may require time and cases and may affect the results also in terms of upstaging rate due to incomplete lymphadenectomy.[10,11]

This is a crucial point for patient management, considering that the presence of pathological nodal involvement changes the prognosis but also may lead to postoperative treatments that may significantly improve survival in case of limited nodal involvement.[12–14]

The purpose of this study is to analyze if surgeon experience may influence nodal upstaging using a large prospective national database on VATS lobectomy.

Materials and Methods

Data source

The Italian VATS Group database is a multicenter, prospective, web-based data system for collecting and reporting clinical, intraoperative, pathological, and survival data of patients who underwent VATS lobectomy or segmentectomy. When it was queried for the study aim, 58 participating centers were involved, and more than 14,000 cases were gathered. The current analysis was reviewed and approved for scientific merit and feasibility by the VATS Group Scientific Committee. Regarding the quality of the reported data, the Italian VATS Group database received awards from the European Society of Thoracic Surgeons in September 2017.[15]

Patients

Clinical and pathological data from the prospective VATS Italian nationwide registry were collected, reviewed, and analyzed from January 1, 2014, to December 31, 2019. All patients underwent VATS anatomical resection and lymphadenectomy (sampling or mediastinal radical lymph node dissection [MRLD]).

The extracted data regarded clinical, intraoperative, and pathological characteristics (see Table I and statistical analysis section for details).

Clinical and pathological information were reviewed and adapted according to the TNM Classification of Malignant Tumours, 8th edition.[16]

Inclusion criteria were defined as follows: pathological NSCLC, computed tomography (CT) scan with contrast/positron emission tomography, cN0 to cN1 patients, cN1 with preoperative mediastinal minimally invasive/invasive staging, lymph node assessment, and complete resection. Exclusion criteria were defined as follows: ground glass opacity nodules, incomplete preoperative staging

Table I
Clinical and pathological characteristics of the entire cohort (3,471 patients)

Variable	Frequency	Rate
Sex		
Male	2,159	62.2
Female	1,312	37.8
ECOG		
0	2,454	70.7
1	946	27.3
2–3	71	2.0
Teaching institution		
Yes	1,509	43.5
No	1,962	56.5
cN		
0	3,319	95.6
1	152	4.4
CT dimension		
<2 cm	1,160	33.4
2–3 cm	942	27.1
3–5 cm	1,054	30.4
>5 cm	304	8.8
T lung		
Left	1,414	40.7
Right	2,057	59.3
Tumor location		
Upper/middle lobes	2,253	64.9
Lower lobes	1,218	35.1
T lobe		
Lower	1,202	34.6
Lower + middle	12	0.3
Middle	195	5.6
Upper	2,052	59.1
Upper + middle	10	0.3
Nodule density		
Solid	2,772	79.9
Part solid GGO	699	20.1
PET		
No	270	7.8
Yes	3,201	92.2
cTNM		
Ia	2,313	66.6
Ib	533	15.4
IIa	409	11.8
IIb	124	3.6
III	92	2.7
Preoperative histology		
No	1,997	57.5
Yes	1,474	42.5
Continuous variables, median and range		
Age at surgery	70	17–88
cT SUV	6	0–30
Histology		
Adenocarcinoma	2,824	81.4
Squamous carcinoma	591	17
Other	56	1.6
pT		
pT1a–b	1,842	53.1
pT1c	630	18.2
pT2a	166	4.8
pT2b	542	15.6
pT3	291	8.4
pN		
pN0	2,907	83.8
pN1	335	9.7
pN2	229	6.6
Operator seniority (years after residency)		
<5	314	9
5–10	409	11.8
>10	2,748	79.2
First operator VATS lobectomy number		
0–20	651	18.8
21–50	686	19.8
>50	2,132	61.5
Surgical techniques		
Anterior Copenhagen	2,043	58.9

(*continued on next page*)

Table I (*continued*)

Variable	Frequency	Rate
Anterior D'Amico	567	16.3
Lateral Mc Kenna	87	2.5
Posterior acc. Walker	33	1
Gossot	97	2.8
Uniportal acc. Rivas	644	18.6
Type of resection		
Segmentectomy	254	7.3
Lobectomy	3,134	90.3
Bilobectomy	83	2.4
Lymph nodes dissection type		
Radical	2,003	57.7
Sampling	1,468	42.3
N2 resected		
<6	1,773	51.1
≥6	1,698	48.9
Total lymph nodes resected		
<10	1,482	42.7
≥10	1,989	57.3
Resected N2 stations		
<3	2,009	57.9
≥3	1,350	38.9
Conversion		
No	3,181	91.6
Yes	290	8.4
Nodal upstaging		
No	2,830	81.5
Yes	489	14.1
Mediastinal upstaging		
No	3,242	93.4
Yes	229	6.6
Continuous variables, median and range		
Operative time	175	30–450
N N1 resected	5	1–30
N N2 resected	5	1–41
Total resected lymph nodes	11	1–51

CT, computed tomograpy; *cTNM*, clinical tumor-nodes-metastasis; *ECOG*, Eastern Cooperative Oncology Group; *GGO*, ground glass opacities; *PET*, positron emission tomography; *SUV*, standardized uptake values; *VATS*, video-assisted thoracic surgery.

(missing brain, thorax, and abdomen CT or minimally invasive mediastinal staging not performed in cN1 patients), cN2 to cN3 patients, M+ patients, pneumonectomy, and benign disease.

Preoperative mediastinal staging in cN1 patients consisted of minimally invasive evaluation (endobronchial ultrasound-guided and/or endoscopic ultrasound and mediastinoscopy/mediastinotomy if needed).

Lymphadenectomy was chosen by the surgeon according to tumor stage, clinical characteristics, and own experience and categorized according to the European Society of Thoracic Surgeons guidelines[17] as follows:

- Node sampling was performed, removing 1 or more lymph nodes thought to be representative, which was guided by preoperative or intraoperative findings.
- Radical nodal dissection (MRLD), the entire mediastinal tissue containing the lymph nodes, was dissected and systematically removed within the anatomical landmarks.

Nodal upstaging was defined as the presence of pathological lymph node involvement involving N1 and/or N2 nodal station in clinical N0 patients (resulting in N1, N2, or N1–N2 metastases), whereas mediastinal (N2 only) upstaging was defined as the presence of pathological N2 involvement in patients clinically staged as N0 or N1. The stations 10, 11, 12, 13, and 14 were included in N1, whereas the stations 2, 3, 4, 7, 8, and 9 on the right side and the stations 2, 4, 5, 6, 7, 8, and 9 on the left side were considered as N2 stations.

In the database, surgeon experience was categorized considering the years after residency (0–5, 5–10, and more than 10) and considering the number of VATS lobectomies performed (0–20, 20–50, and more than 50) by the lead surgeon.

Statistical analysis

Applying a descriptive method, counts and percentages were reported for categorical variables, and the median (range) or mean (SD) for continuous variables. The normality distribution of data was assessed by Wilk–Shapiro tests and, where necessary, by QQ plots. At univariable analysis, baseline demographic, clinical characteristics intraoperative and pathological such as tumor dimension, location, density, clinical stage, clinical nodal involvement, operator experience in terms of years after residency and number of anatomical resections performed, kind of lymphadenectomy, number of resected lymph nodes and number of resected mediastinal stations were evaluated. The association between categorical variables and nodal upstaging or mediastinal upstaging was tested by Pearson χ^2 analysis. For continuous variables, the comparison between groups was performed by Student's t test or Mann–Whitney U test, when appropriate. The multivariate logistic regression model and Cox regression model were developed using stepwise regression (forward selection) to compare the predictive power of different factors. Enter limit and remove limit were $P = .10$ and $P = .15$, respectively. The odds ratio (OR) and the 95% CI were estimated for each significant variable. SPSS 21.0 software (IBM SPSS, Inc, Armonk, NY) was used for all calculations.

Results

The final analysis was conducted on 3,319 cN0 patients for nodal upstaging (presenting at the pathological exam pN1 or pN2 or pN1–2) and 3,471 cN0 + cN1 patients for N2 upstaging (presenting mediastinal stations nodal involvement at the pathological exam) (Supplementary Figure S1). The clinical and pathological characteristics of the entire cohort are reported in Table I. All patients underwent total body CT scans with contrast, and positron emission tomography was performed in 92.2% of cases.

MRLD was performed in the majority of cases (57.7%), whereas the median number of resected nodes and the median number of N2 resected nodes were 11 (1–51) and 5 (1–41), respectively. No differences were present considering the mean number of resected nodes between surgeons with >50 lobectomies compared to surgeons with <50 lobectomies: 12.1 ± 6.8 vs 11.7 ± 7.6 ($P = .094$). Nodal upstaging occurred in 489 (13.1%) patients, whereas N2 upstaging occurred in 229 (6.1%) patients. Regarding surgeon experience, most surgeries were performed by surgeons with more than 50 VATS lobectomies performed and more than 5 years after residency. Factors associated with nodal and mediastinal upstaging are reported in Table II.

In particular, surgeon experience did not correlate with nodal and mediastinal upstaging (Figures 1 and 2) without a significant difference in upstaging rate considering years after residency or the number of VATS lobectomies performed.

Conversely, tumor dimension and nodal assessment resulted significantly correlated to nodal and mediastinal upstaging, with a significantly higher nodal and mediastinal upstaging rate in case of number of resected nodes >10, number of N2 resected nodes >6, and MRLD. In detail, nodal and mediastinal upstaging resulted in 17% vs 11% and 7.5% vs 5.4% in MRLD compared to sampling (Figure 3).

This result was also confirmed considering the relationship between lymphadenectomy and upstaging according to surgeon experience in terms of lobectomies performed. Nodal upstaging

Table II
Univariable analysis for nodal and mediastinal upstaging

Variable	Nodal upstaging		*P* value	Mediastinal upstaging		*P* value
	No	Yes		No	Yes	
COPD			.91			.86
No	85.2% (2,129)	14.8% (369)		93.5% (2,438)	6.5% (169)	
Yes	85.4% (701)	14.6% (120)		93.1% (804)	6.9% (60)	
Teaching institutions			.46			.84
No	85.7% (1,602)	14.3% (268)		93.5% (1,834)	6.5% (128)	
Yes	84.7% (1,628)	15.3% (221)		93.3% (1,408)	6.7% (101)	
cT dimension			< .0001			< .0001
<2 cm	89.7% (1,016)	10.3% (117)		95.8% (1,111)	4.2% (49)	
2–3 cm	84.6% (763)	15.4% (139)		92.5% (871)	7.5% (71)	
3–5 cm	84% (837)	16% (160)		92.5% (975)	7.5% (79)	
>5 cm	73.6% (203)	26.4% (73)		90.1% (274)	9.9% (30)	
T lung			.10			.51
Left	84% (1,154)	16% (219)		93.1% (1,316)	6.9% (98)	
Right	86.1% (1,676)	13.9% (270)		93.6% (1,926)	6.4% (131)	
T lobe			< .0001			< .0001
Lower	84.5% (972)	15.5% (178)		92.8% (1,115)	7.2% (87)	
Lower + middle	44.4% (4)	55.6% (5)		66.7% (8)	33.3% (4)	
Middle	90.6% (173)	9.4% (18)		97.4% (190)	2.6% (5)	
Upper	85.5% (1,676)	14.5% (284)		93.6% (1,921)	6.4% (131)	
Upper + middle	55.6% (5)	44.4% (4)		80% (8)	20% (2)	
Nodule density			< .0001			.03
Solid	83.5% (2,200)	16.5% (435)		92.9% (2,576)	7.1% (196)	
Part solid GGO	92.1% (630)	7.9% (54)		95.3% (666)	4.7% (33)	
cTNM			< .0001			< .0001
cIA	88.4% (2,044)	11.6% (269)		95.2% (2,201)	4.8% (112)	
cIB	79.4% (423)	20.6% (110)		89.9% (479)	10.1% (54)	
cII	77.8% (318)	22.2% (91)		91.9% (376)	8.1% (33)	
cIII				89.1% (82)	10.9% (10)	
cN						< .001
cN0				93.8% (3,313)	6.2% (206)	
cN1				84.9% (129)	15.1% (23)	
Preoperative diagnosis			< .0001			.02
No	89% (1,194)	11% (147)		94.6% (1,307)	5.4% (74)	
Yes	82.7% (1,636)	17.3% (342)		92.6% (1,935)	7.4% (155)	
Operator seniority (years after residency)			.60			.13
<5	83.3% (245)	16.7% (49)		90.8% (285)	9.2% (29)	
5–10	85.9% (341)	14.1% (56)		94.1% (385)	5.9% (24)	
>10	85.4% (2,244)	14.6% (384)		93.6% (2,577)	6.4% (176)	
First operator VATS lobectomy number			.49			.72
0–20	86.4% (533)	13.6% (84)		92.8% (604)	7.2% (47)	
21–50	86% (565)	92% (14)		93.9% (644)	6.1% (42)	
>50	84.7% (1,732)	15.3% (313)		93.4% (1,994)	6.6% (140)	
Surgical techniques			.23			.17
Anterior Copenhagen	84.9% (1,664)	15,1% (297)		93.4% (1,909)	6.6% (134)	
Anterior D'Amico	87.6% (475)	12.4% (67)		93.3% (529)	6.7% (38)	
Lateral McKenna	79.5% (66)	20.5% (17)		88.5% (77)	11.5% (10)	
Posterior acc. Walker	80.6% (25)	19.4% (6)		100% (33)		
Gossot	89.7% (78)	10.3% (9)		96.9% (94)	3.1% (3)	
Uniportal acc. Rivas	84.9% (522)	15.1% (93)		93.2% (600)	6.8% (44)	
Resection			.001			.006
Segmentectomy	93.2% (234)	6.8% (17)		97.2% (247)	2.8% (7)	
Lobectomy	84.7% (2,537)	15.3% (457)		93.2% (2,922)	6.8% (212)	
Bilobectomy	79.7% (59)	20.3% (15)		88% (73)	12% (10)	
Tumor location			.24			.17
Upper/middle lobes	85.8% (1,848)	14.2% (306)		93.8% (2,114)	6.2% (139)	
Lower lobes	84.3% (982)	15.7% (183)		92.6% (1,128)	7.4% (90)	
Kind of lymphadenectomy						.02
Radical nodal dissection	83.0% (1,587)	17.0% (324)	< .001	92.2% (1,853)	7.5% (150)	
Sampling	88.3% (1,243)	11.7% (489)		94.6% (1,389)	5.4% (79)	
N2 resected nodes			.007			< .001
<6	86.9% (1,480)	13.1% (223)		95.4% (1,691)	4.6% (82)	
≥6	83.5% (2,830)	16.5% (266)		91.3% (1,551)	8.7% (147)	
Total resected nodes			.02			< .001
<10	85.9% (2,338)	14.1% (383)		94.1% (1,890)	5.9% (166)	
≥10	82.3% (492)	17.7% (106)		90.1% (572)	9.9% (63)	
No. of resected N2 stations			.10			.01
<3	85.9% (1,659)	14.1% (272)		94.1% (1,890)	5.9% (119)	
≥3	83.8% (1,074)	16.2% (208)		91.9% (1,240)	8.1% (110)	
Continuous variables						
Age surg			.003			.167
cT SUV			.000			.000
Operative time			.001			.053

COPD, chronic obstructive pulmonary disease; *cTNM*, clinical tumor-nodes-metastasis; *GGO*, ground glass opacities; *SUV*, standardized uptake values; *VATS*, video-assisted thoracic surgery.

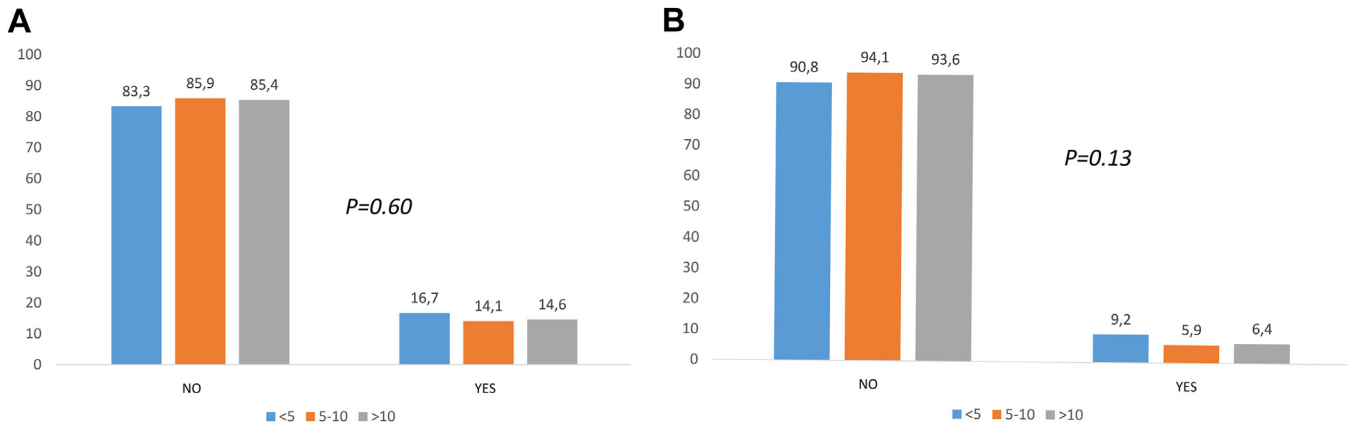

Figure 1. (A) Nodal and (B) mediastinal upstaging rate according to operator years after residency

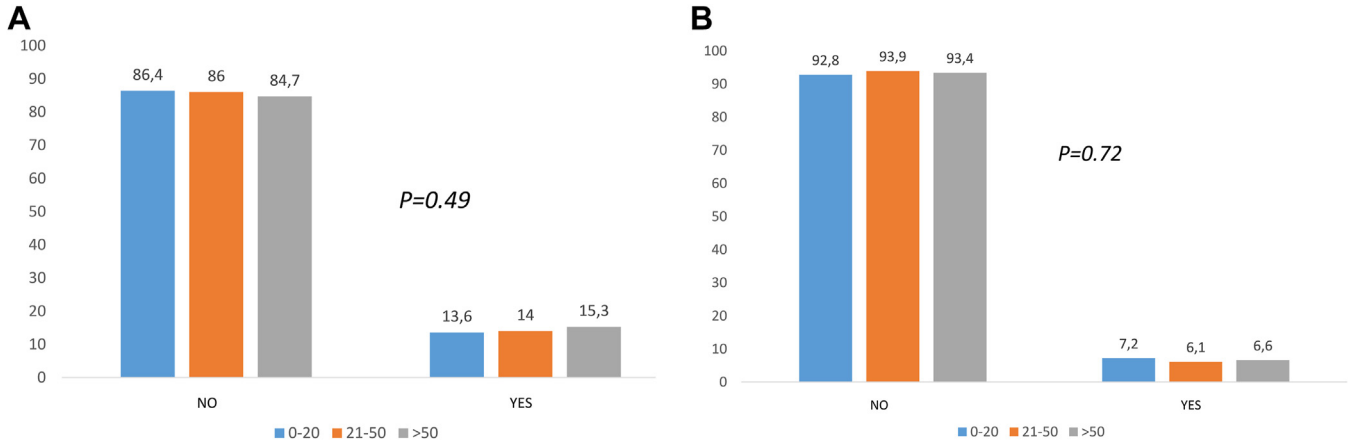

Figure 2. (A) Nodal and (B) mediastinal upstaging rate according to operator number of video-assisted thoracic surgery lobectomy performed.

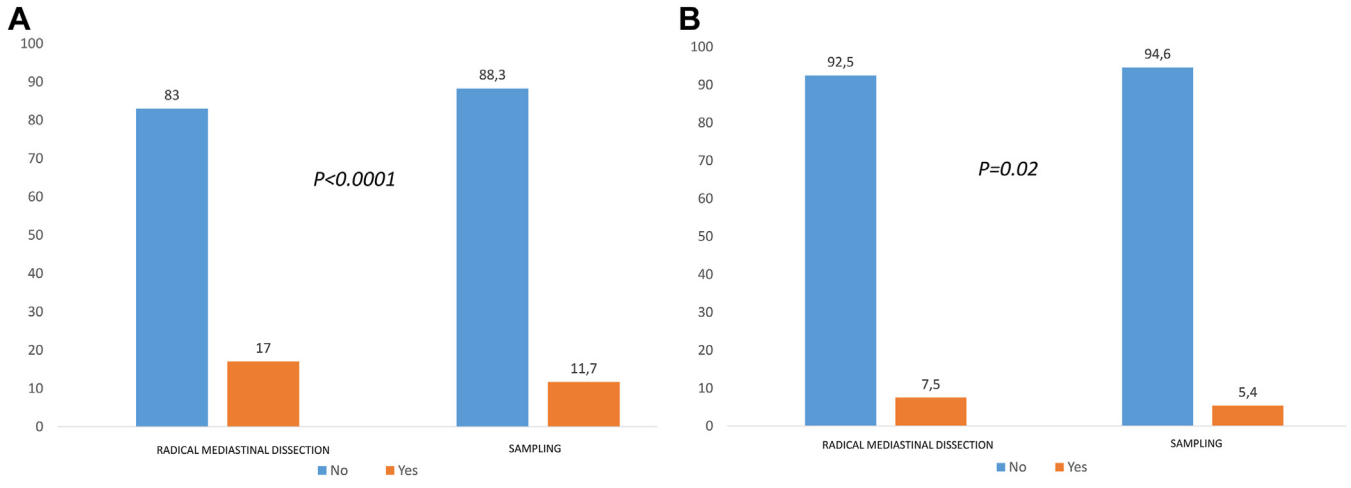

Figure 3. Mediastinal upstaging according to kind of lymphadenectomy.

rate was significantly higher in MRLD versus sampling in surgeons with >50 lobectomies and <50 lobectomies performed: 15.7% vs 11.4% ($P < .001$) and 14.3% and 9.3% ($P = .001$) respectively. Similarly, the difference remains significant also considering mediastinal upstaging in surgeons with >50 lobectomies and with <50 lobectomies performed—7.0% vs 5.2% ($P < .001$) and 7.1% vs 4.9% ($P < .001$), respectively.

Finally, upstaging rate significantly increased with tumor dimension, with nodal and mediastinal upstaging starting from 10.3% and 4.3% arriving at 26.4% and 9.9% in tumors with

dimensions less than 2 cm to the tumor with dimensions >5 cm, respectively ($P < .001$ for both outcomes) (Figure 4).

The multivariable model included tumor dimension, number of resected nodes, nodule density, and kind of lymphadenectomy for nodal upstaging, whereas clinical tumor-nodes-metastasis (cTNM), clinical *N*, number of mediastinal resected lymph nodes, nodule density, and kind of lymphadenectomy were considered in the multivariable model for mediastinal upstaging.

Multivariable analysis confirmed as factors independently associated with nodal upstaging the tumor dimension ($P = .001$), solid tumors ($P < .001$), and MRLD ($P = .001$), whereas cTNM ($P < .001$) and N2 resected nodes ≥6 resulted independently correlated to mediastinal upstaging (Table III).

Table III
Multivariable analysis reported independent prognostic factors

Nodal upstaging		
Variable	OR (95% CI)	*P* value
T dimension	-	.001
<2 cm (ref)	1.447(0.677–3.09)	.340
2-3cm	2.223 (1.044–4.737)	.038
>3 cm		
Nodule density	2.056(1.522–2.777)	< .001
Solid versus part solid		
Kind of lymphadenectomy	1.399 (1.138–1.779)	.001
Radical mediastinal dissection vs sampling		
Mediastinal upstaging		
cTNM	-	< .001
IA (ref)		
IB	4.466 (2.223–8.973)	< .001
IIA	2.671 (1.139–6.261)	.024
IIB	4.350 (2.503–7.561)	< .001
III	3.061 (0.947–9.887)	.062
N2 resected nodes	1.860 (1.403–2.465)	< .001
<6 vs ≥6		

cTNM, clinical tumor-nodes-metastasis; *OR*, odds ratio.

Discussion

In this study, we evaluated if surgeon experience may be related to nodal or mediastinal upstaging in patients who underwent VATS anatomical resection for NSCLC. The nodal upstaging rate and the N2 upstaging rate of 13% and 6%, respectively, align with literature data suggesting the quality of the database.[6–8]

Our results showed that surgeon experience, evaluated in terms of years after residency or the number of major VATS procedures performed, did not lead to different upstaging rates. To the best of our knowledge, this is the first study that investigated this issue, showing comforting results regarding the quality of the surgical and oncological outcomes in these patients.

Previously, other studies evaluated the potential role of the facilities and the skills present among the institutions involved in upstaging studies using different approaches.[5,8] In particular, Kneurtz et al suggested that the completeness of lymphadenectomy may be influenced by operator skills, experience, and instrumentation available. However, they did not report any information or analysis regarding the surgeon's experience or skills in VATS compared to the open approach. Similarly, Boffa et al[8] noted that the results comparing VATS to thoracotomy in upstaging rate changed according to the VATS institution volume. Using the Society of Thoracic Surgery database, they found a significant difference in upstaging rate comparing VATS to thoracotomy in the entire population, but when the analysis was limited to centers with a predominant VATS approach, no differences were reported. Similarly, Medbery et al[18] reported a significant difference in upstaging rate using the United States National Cancer Database comparing VATS to thoracotomy, but the difference dissipated in the subanalysis that considered institution/academic VATS programs. Again, Medbery and colleagues speculated that this result was due to the differences in surgeons' training in minimally invasive techniques. It is important to note that in these studies, the analysis was conducted considering the center volume/characteristics and not directly the surgeon's experience or the number of procedures. Regarding our analysis, it is important to underline that we used an ad hoc database and most of the participating institutions at the Italian Vats Group Registry present expertise and VATS development programs. For this reason, we can explain our results considering the database's nature and the participant center's expertise, whereas in previous studies based on other kinds of multi-centric databases,[5,8,18] these factors were not considered. It is interesting to note that using this cohort of patients, surgeons with less experience presented the same results as experienced and skilled surgeons, maybe due to appropriate training for surgeons approaching VATS lobectomy.

This result is hard to compare with other studies present in the literature, but it is similar to the study reported by Lee et al[19] that compared surgeons based on the first and the last 250 VATS lobectomies. In detail, there was a significant difference in terms of pN1/N2 lymph nodes among the 2 groups, but the statistical significance was lost after propensity matching on tumor characteristics. However, it was not reported if the nodal involvement was also present preoperatively or was a real upstaging. Conversely, other studies based on experience in gastrointestinal tumors reported a learning curve about lymphadenectomy in terms of

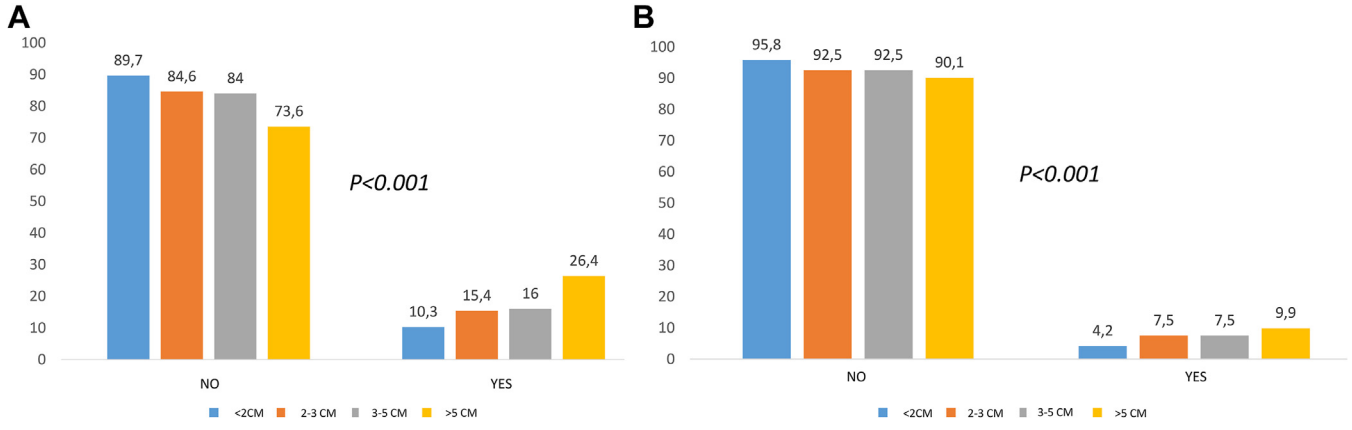

Figure 4. (A) Nodal and (B) mediastinal upstaging according to tumor dimension.

resected nodes, but the upstaging rate was not analyzed, confirming the paucity of information about this topic.[20,21]

Analyzing the different lymphadenectomy parameters, we found that MRLD type was independently associated with nodal upstaging, and the number of N2 resected nodes >6 was independently associated with mediastinal upstaging. Our results are in line with the Marulli et al paper,[22] which reported a significant correlation at multivariable analysis between a number of resected nodes >12 and nodal upstaging using the VATS group registry, whereas the kind of lymphadenectomy was significant in our study but only at univariable analysis. However, our study presents some differences. Firstly, we included more than 2 years of recruitment and so a higher number of patients. Second, we performed a more careful patient selection, especially in the case of cN1 involvement or T3 to T4 tumors, excluding patients with limited mediastinal investigation. Of the nature of the database, not all the participants may adhere to the actual mediastinal preoperative staging guidelines,[22,23] so we tried to limit this bias by introducing strict inclusion and exclusion criteria. However, we think that it is important to underline that the number of N2 resected nodes independently correlates to mediastinal upstaging.

A major part of the guidelines regarding the lymphadenectomy definition considered the number of the resected stations or the total number of resected lymph nodes, indicating the execution of the resection of almost 3 mediastinal stations and 6 to 10 lymph nodes in total.[17,24–26] Our study confirms the significant difference in mediastinal upstaging when 3 or more mediastinal stations are harvested, but we also think that the number of resected nodes should be better characterized. Indeed, for mediastinal upstaging, it is important to refer to a minimum number of mediastinal resected nodes that may also be considered for appropriate and tailored follow-up strategies in doubt of inappropriate lymphadenectomy. We preferred to include the number of resected N2 nodes in the multivariable model; for this reason, confirming that this parameter is strongly correlated to mediastinal upstaging and should be considered in this setting, even if further prospective ad hoc studies may give more information about this topic.

Our study confirmed that tumor dimension and TNM stage are independently correlated to nodal and mediastinal upstaging, respectively, confirming the increased risk of occult nodal metastases progressively when tumor size increases.[7,22] It is interesting to note that in our study, the biggest difference in upstaging rate regarded T1a to T1b versus T1c and T2 versus T3, whereas patients with T1c to T2 tumors presented a similar upstaging rate. According to these results, it is possible to speculate that patients with tumors of more than 2 cm may require a more extensive lymphadenectomy to reduce the risk of undetected nodal metastases, as well as in T1 tumors that exceed this dimension. On the other hand, we found that cTNM and not cN1 presence is independently correlated to mediastinal upstaging, suggesting that both parameters (tumor dimension and clinical nodal status) should be considered for the risk of occult mediastinal metastases and may lead to extensive and invasive preoperative mediastinal staging.

Study limitations

This study presents some limitations. First, it is a retrospective study, even if conducted using a prospective database. Second, considering the multicenter nature, different preoperative and surgical approaches are considered, and they are quite different among the different centers included. However, especially regarding the preoperative staging, we adopted strict inclusion criteria and exclusion criteria, not selecting patients without a clear execution of preoperative minimally or invasive mediastinal staging in case of large tumors or suspected N1 involvement.

Regarding the surgeon experience, some limitations regard the absence of information about the number of VATS lobectomies performed per year, and we can only use a categorization of the experience present in the database, reducing the possibility of deeper analysis. Moreover, most surgeons presented more than >50 lobectomies performed more than 10 years after residency, but this should be considered the picture of many countries, taking into account that VATS adoption has drastically increased in the last 10 to 15 years, and in the future, this number will be balanced and will permit new analysis testing also younger surgeons. Another limitation regarded the lack of information about the tumor location (central or peripheral), which is another factor correlated to nodal upstaging,[27] but no data on tumor location were present in the database. In the database, information about the diagnosis date is not reported, so it was not possible to know the delay in surgery. However, according to Italian law, patients should receive surgical treatment within 30 days of the diagnosis. Finally, the extent and the kind of lymphadenectomy were decided by the surgeon based on his knowledge and the adherence to the lymphadenectomy guidelines definition could not be confirmed despite the database quality assessment. For this reason, especially regarding the multivariable model for mediastinal upstaging, we preferred to include objective data such as the number of N2 resected nodes.

This study investigated if operator experience may influence the nodal and mediastinal upstaging rate in patients who underwent VATS anatomical resection for non-small cell lung cancer using a national ad hoc database. Surgeon experience in terms of years after residency and a number of VATS anatomical resection procedures did not correlate with upstaging. Tumor dimension, radical mediastinal lymphadenectomy, and solid nodules resulted independently correlated to nodal upstaging, whereas cTNM and number of N2 resected nodes >6 resulted independently correlated to mediastinal upstaging.

In conclusion, this study suggests that in centers formed in VATS resection, the surgeon experience does not influence upstaging rate; even further prospective studies are needed to validate these data.

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CRediT authorship contribution statement

Marco Chiappetta: Conceptualization, Data curation, Investigation. **Filippo Lococo:** Data curation, Formal analysis, Methodology. **Isabella Sperduti:** Formal analysis, Validation. **Diomira Tabacco:** Conceptualization, Methodology. **Carolina Sassorossi:** Conceptualization, Supervision, Validation, Writing – review & editing. **Carlo Curcio:** Conceptualization, Supervision, Validation. **Roberto Crisci:** Supervision, Validation, Visualization. **Elisa Meacci:** Conceptualization, Resources. **Federico Rea:** Conceptualization, Formal analysis, Investigation. **Stefano Margaritora:** Conceptualization, Software, Supervision.

Supplementary materials

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