BRIEF REPORT

A Brief Report on Survival After Robotic Lobectomy for Early-Stage Lung Cancer

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ABSTRACT

Introduction: Robotic-assisted surgery has become the first choice for several conditions since its introduction in clinical practice in 2000. However, the U.S. Food and Drug Administration has recently raised a warning against the use of robotic surgical approaches for the cure and prevention of cancer following the publication of two studies focused on endometrial cancer. We conducted an internal audit to retrospectively analyze our experience to assess the safety and feasibility of robotic-assisted surgery compared to open surgery.

Methods: We selected a 5-year period to guarantee at least 2 years of follow-up (2011–2016) and identified 1139 patients who underwent lobectomy for NSCLC in our division. The primary data set analyzed included 544 early-stage clinical N0 patients (348 open and 196 robotic surgeries). We compared 131 patients of each group individually matched, with demographic and clinical characteristics almost identical.

Results: No difference was observed between the cohorts, either in terms of recurrence-free survival (hazard ratio: 1.09; $p = 0.55$) or overall survival (hazard ratio: 0.86; $p = 0.36$). The 5-year recurrence of disease risk and overall survival were 24.9% and 83.2%, respectively, in the open group and 24.6% and 86.1%, respectively, in the robotic group.

Conclusions: These data underline that robotic-assisted lobectomy for early NSCLC is a safe and feasible technique with adequate long-term and progression-free survival compared to open surgery.

Keywords: Early-stage lung cancer; Robotic surgery; Safety

Introduction

Robotic-assisted surgery has become first choice for several conditions since its introduction in clinical practice in 2000.[1] Thanks to its features (e.g., precision, flexibility, noninvasiveness, etc.), minimally invasive robotic surgery has been developed and broadly adopted with good results.[1]

However, the U.S. Food and Drug Administration has recently raised a warning against the use of robotic surgical approaches for the cure and prevention of cancer.[2] This warning follows the publication of two studies focused on endometrial cancer that compared traditional open surgery to minimally invasive techniques.[3,4] Whereas the first study was only a retrospective analysis, the second one was a randomized trial between open and mini-invasive surgery; however, only 15% of the minimally invasive cases were performed by a robotic approach (49 robotic versus 269 laparoscopy procedures). Both studies showed that minimal invasive radical hysterectomy for early-stage endometrial cancer was associated with a lower rate of disease-free survival and overall survival compared to open surgery.

Nonetheless, a great debate has been raised regarding whether robotic-assisted surgery could be

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considered feasible and safe for oncologic patients.[5] Recently, Sheetz and Dimick[6] summarized the major concerns regarding robotic-assisted surgery: there are only small reports without rigorous controls and data about patient's prognosis are still missing. The consensus on the expensive cost of the approach suggests a higher insurance premium on patients who deserve greater attention. Furthermore, it is necessary to consider that robotic-assisted surgery could not be suitable for all the oncologic conditions, thus an experienced surgeon able to define risk/benefits ratio is essential to guarantee the best chances of healing.[6] In particular, thoracic oncology still lacks randomized prospective clinical trials comparing outcomes between open and robotic-assisted thoracic surgery for early-stage NSCLC, but only few retrospective studies show acceptable outcomes.

Following these reports, we directed an internal audit to retrospectively analyze our experience to assess the equivalence of robotic approach compared to open surgery, considering our 15-year experience in robotic surgery and more than 576 anatomical robotic-assisted resections performed (17% of all procedures).[7]

Materials and Methods

We selected a 5-year period between 2011 and 2016 to guarantee at least 2 years of follow-up, and identified 1139 patients who underwent lobectomy for NSCLC to assess the safety and efficacy of the robotic approach compared to open surgery. All patients underwent a preoperative evaluation including total-body computed tomography scan, fluorodeoxyglucose positron-emission tomography, and cardiorespiratory assessment; mediastinoscopy or endobronchial ultrasound-guided transbronchial needle aspiration was performed in case of clinical suspected lymph nodes involvement. At first, 595 patients were excluded from the analysis because they received neoadjuvant treatment, had advanced stages (e.g., clinical N2 patients or with distant metastasis at onset), underwent video-assisted surgery or extended resection, or had histology other than NSCLC (e.g., carcinoid tumors or benign tumors). The primary data set included 544 naive clinical N0 patients who underwent lobectomy for NSCLC in the 5-year period (348 open surgeries and 196 robot-assisted thoracic surgeries). Inclusion and exclusion criteria for the study are shown in Figure 1.

Results

Despite the strict selection criteria, patients in the robot-assisted thoracic surgery group showed significantly more favorable characteristics (higher frequency of screening-detected lung cancer and early-stage tumor, smaller tumor and negative nodal status at pathologic evaluation) and better performance status (Table 1) and showed a somewhat better survival (hazard ratio [HR]: 0.83; 95% confidence interval [CI]: 0.66–1.05; $p = 0.11$) than those in the open surgery group. The rate of robotic conversion to open surgery in our cohort was of 3.06% (6 cases among the 196 robotic surgery patients), which were due to lymph node infiltrating vascular structure precluding a safe dissection (three of six cases), vascular injury resulting in minor bleeding (two of six cases), technical issue (i.e., adherence; one of six cases).

Therefore, we individually matched 131 patients who received robot-assisted thoracic surgery with 131 patients who underwent open surgery and were in a similar age group (±10 years), sex, American Society of Anesthesiology score, pathologic T, pathologic N, and had equally been diagnosed through screening. The

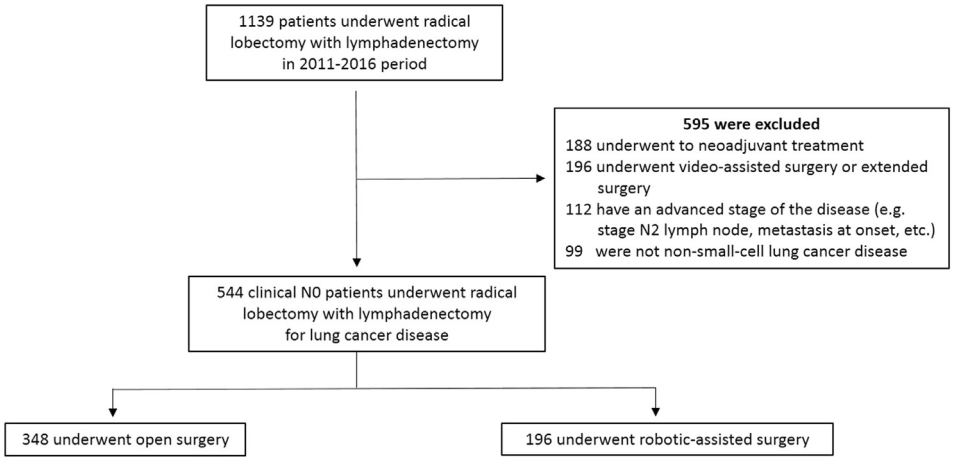

Figure 1. Study population.

Table 1. Patients' Demographic and Clinical Characteristics

	Unmatched			Matched*			
	Open	Robotic	p Value	Open	Robotic	p Value	†
	347	196		131	131		
Source							
Clinic	340	149		126	126		
Screening trial (COSMOS)	7	47	<0.0001	5	5	Matching	
Median age (range), years	68 (43-84)	67 (39-85)		69 (45-84)	69 (50-85)		
Age group, years							
<60	65	40		21	22		
60-64	56	36		18	15		
65-69	84	49		31	35		
70-74	73	42		38	36	Matching	
75-79	57	21		19	16	±10 years	
80+	12	8	0.61	4	7	0.89	0.99
Sex							
Male	213	128		84	84		
Female	134	68	0.36	47	47	Matching	
Obesity class							
Underweight	9	2		5	1		
Normal weight	177	97		60	63		
Overweight	113	69		46	51		
Obese	48	28	0.60	20	16	0.33	0.53
Smoking							
Never	69	33		25	23		
Former	151	75		61	58		
Current	126	88	0.15	44	50	0.76	0.92
Diabetes							
No	304	174		118	114		
Yes	41	22	0.82	12	17	0.34	0.35
Cardiac comorbidity							
No	121	79		49	48		
Yes	224	117	0.23	81	83	0.86	0.89
Pulmonary comorbidity							
No	302	176		114	116		
Yes	43	21	0.54	16	15	0.83	0.84
ASA score							
1	18	14		5	5		
2	243	149		108	108		
3	79	21	0.004	16	16	Matching	
Clinical stage							
Stage Ia	234	158		102	102		
Stage Ib	63	31		18	24		
Stage IIa	37	5		6	3		
Stage IIb	13	2	0.0006	5	2	0.37	0.61
Laterality							
Left	139	81		56	56		
Right	208	114	0.74	75	74	0.96	0.90
Site							
Upper lobe	218	123		84	86		
Medial lobe	18	14		8	10		
Lower lobe	107	58		37	34		
Multiple	4	1	0.70	2	1	0.87	0.97
Histology							
Adenocarcinoma	264	161		100	108		
Squamous	54	27		18	17		
Adenosquamous	13	3		6	3		
Other	16	5	0.23	7	3	0.40	0.71

(continued)

Table 1. Continued

	Unmatched			Matched*			
	Open	Robotic	p Value	Open	Robotic	p Value	†
Grade							
G1	41	21		16	13		
G2	135	84		57	54		
G3	166	89	0.68	55	63	0.63	0.80
Diameter, mm							
Median (range)	26 (5-92)	20 (5-75)		25 (6-68)	24 (6-75)		
<10	10	16		4	3		
10-19	95	74		42	40		
20-29	92	58		46	50		
30-49	122	41		36	33		
≥50	28	7	<0.0001	3	5	0.91	0.79
pT							
1	190	148		93	93		
2	107	36		29	29		
3	47	9		7	7		
4	3	3	<0.0001	2	2	Matching	
pN							
0	257	166		114	114		
1	48	17		11	11		
2	42	13	0.02	6	6	Matching	
Pathologic stage (8th edition)							
I	198	152		101	101		
II	99	26		20	20		
III	50	18	<0.0001	10	10	Matching	

*Matched on age (±10 years), sex, pT, pN, source (clinic, screening), ASA (1, 2, 3); information missing for: smoking (open = 1), diabetes (open = 1), cardiac comorbidity (open = 1), pulmonary comorbidity (open = 1), ASA score (open = 2, robotic = 2), laterality (robotic = 1), grade (open = 3, robotic = 1).
†McNemar test (dichotomous variables) or test of symmetry
ASA score, American Society of Anesthesiologist score; pT, pathological Tumour; pN, pathological Nodes.

demographic and clinical characteristics of patients in the two matched groups are almost identical (Table 1) and no operative mortality or in-hospital mortality occurred in both groups of patients. The major post-operative complications according to Clavien-Dindo classification (i.e., grade 3a or higher) were five in the open group (four pulmonary, one surgical) and six in the robotic group (one cardiac, three pulmonary, two surgical).[7] These major complications did not influence patient long-term outcome.

No difference was observed between the groups either in terms of recurrence-free survival (HR: 1.09; 95% CI: 0.83–1.42; $p = 0.55$) or overall survival (HR: 0.86; 95% CI: 0.63–1.19; $p = 0.36$) (Fig. 2). The 5-year recurrence of disease risk was 24.9% (95% CI: 17.4–34.8) in the open group and 24.6% (95% CI: 17.0–34.8) in the robot-assisted thoracic surgery group. The 5-year overall survival rates were 83.2% (95% CI: 74.8–89.0) in the open group and 86.1% (95% CI: 76.6–92.0) in robot-assisted thoracic surgery patients. All these data are in accordance with the literature previously published.[8]

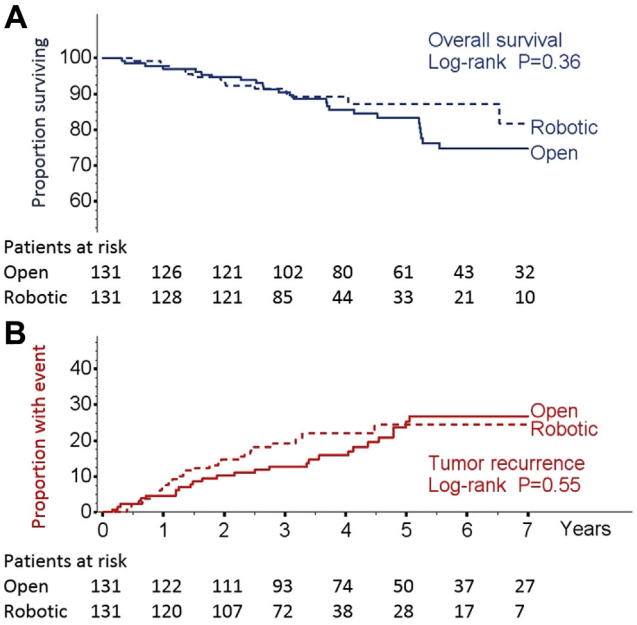

Figure 2. Overall survival (*A*) and disease-free survival (*B*) of cN0 patients matched (95% confidence intervals).

Discussion

Although this study is a retrospective evaluation with a limited number of patients, data suggest that robot-assisted thoracic surgery lobectomy for patients with early NSCLC is a safe and feasible technique with adequate long-term and progression-free survival. The result of our audit determined the equivalence of robotic approach compared to open surgery; thus, we will continue to perform robotic surgery in selected patients. Undeniably, robotic-assisted surgery is not an option for all lung cancer patients, but an appropriate preoperative evaluation of patients through benefits-risk assessment by experienced surgeon allows us to perform radical surgery with all the advantages of the robotic approach compared to conventional open surgery.

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