The Prevalence of Nodal Upstaging During Robotic Lung Resection in Early Stage Non-Small Cell Lung Cancer

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Background. **Pathologic nodal upstaging can be considered a surrogate for completeness of nodal evaluation and quality of surgery. We sought to determine the rate of nodal upstaging and disease-free and overall survival with a robotic approach in clinical stage I NSCLC.**

Methods. **We retrospectively reviewed patients with clinical stage I NSCLC after robotic lobectomy or segmentectomy at three centers from 2009 to 2012. Data were collected primarily based on Society of Thoracic Surgeons database elements.**

Results. **Robotic anatomic lung resection was performed in 302 patients. The majority were right sided (192; 63.6%) and of the upper lobe (192; 63.6%). Most were clinical stage IA (237; 78.5%). Pathologic nodal upstaging occurred in 33 patients (10.9% [pN1 20, 6.6%; pN2 13, 4.3%]). Hilar (pN1) upstaging occurred in 3.5%, 8.6%, and 10.8%, respectively, for cT1a, cT1b, and cT2a tumors. Comparatively, historic hilar upstage rates of video-assisted thoracoscopic surgery (VATS) versus thoracotomy for cT1a, cT1b, and cT2a were 5.2%, 7.1%, and 5.7%, versus 7.4%, 8.8%, and 11.5%, respectively. Median follow-up was 12.3 months (range, 0 to 49). Forty patients (13.2%) had disease recurrence (local 11, 3.6%; regional 7, 2.3%; distant 22, 7.3%). The 2-year overall survival was 87.6%, and the disease-free survival was 70.2%.**

Conclusions. **The rate of nodal upstaging for robotic resection appears to be superior to VATS and similar to thoracotomy data when analyzed by clinical T stage. Both disease-free and overall survival were comparable to recent VATS and thoracotomy data. A larger series of matched open, VATS and robotic approaches is necessary.**

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Controversy still exists about the ideal approach to surgical resection of early stage non-small cell lung cancer (NSCLC). The ideal approach should minimize patient morbidity and allow return to usual activities in a reasonable period while maximizing the oncologic benefit. Minimally invasive approaches are optimally suited for resection of early stage lung cancer owing to benefits in patient recovery, but there have been no prospective randomized trials to evaluate the relative efficacy and oncologic equivalence of open versus minimally invasive techniques. Recent studies have attempted to assess the oncologic benefits of thoracotomy compared with video-assisted thoracoscopic surgery (VATS) lobectomy. In these studies, the prevalence of pathologic nodal upstaging is used as a surrogate measure for the completeness of nodal evaluation and, thus, the quality of surgery [1–3]. Each of these studies has shown VATS to have less nodal upstaging than thoracotomy, suggesting a difference in the completeness of nodal evaluation. However, none has demonstrated a difference in overall or disease-free survival [2–4].

A robotic approach to anatomic lung resection is the newest minimally invasive platform, and several studies have demonstrated its feasibility and safety [5–9]. In theory, three-dimensional high-definition visualization, platform stability, dexterity, and precision should facilitate a superior lymph node dissection [10], and many surgeons tout a superior lymphadenectomy anecdotally with robotic surgery compared with VATS. However, limited data exist regarding the oncologic effectiveness of robotic lung resection, overall survival, and disease-free survival [7]. We hypothesized that robotic anatomic lung resection would result in a higher rate of nodal

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Abbreviations and Acronyms

AJCC	=	American Joint Committee on Cancer
CT	=	computed tomography
EBUS	=	endobronchial ultrasonography
FNA	=	fine-needle aspiration
NSCLC	=	non-small cell lung cancer
PET	=	positron emission tomography
STS-GTD	=	Society of Thoracic Surgeons General Thoracic Database
VATS	=	video-assisted thoracoscopic surgery

upstaging than VATS and similar nodal upstaging compared with thoracotomy. Additionally, we hypothesized that overall survival and disease-free survival after robotics would be similar to recently published data comparing VATS to thoracotomy in early stage NSCLC.

Patients and Methods

We performed a multiinstitutional, retrospective review of consecutive patients who underwent a robotic lobectomy or segmentectomy for clinical stage I NSCLC at Hackensack University Medical Center (Hackensack, New Jersey), Swedish Cancer Institute (Seattle, Washington), and University of Alabama, Birmingham (Birmingham, Alabama) between 2009 and 2012. For cases performed in the years 2009 to 2011, version 2.081 of The Society of Thoracic Surgeons General Thoracic Surgery Database (STS-GTD) was used. The updated STS-GTD version (2.22) was used for cases performed in 2012. All patients were staged according to the American Joint Committee on Cancer (AJCC), seventh edition, guidelines [11]. The Institutional Review Board at each institution approved the study. Individual patient consent was waived by each institution's Institutional Review Board owing to the retrospective nature of the study.

The data element definitions were those outlined within the STS-GTD. Key specific elements included age, sex, body mass index, comorbidities, date of surgery, operative time, complications, intensive care unit stay, clinical and pathologic stage, laterality, lobe resected, and procedure performed. For cases performed in 2012, version 2.22 of the STS-GTD also includes data on clinical staging methods such as mediastinoscopy, endobronchial ultrasonography (EBUS) lymph node biopsy and positron emission tomography (PET), number of nodes resected, and hospital length of stay (LOS). These data were then supplemented with the site and date of first cancer recurrence, date of most recent follow-up, patient status (living or deceased), and cause of death.

Elements of AJCC, seventh edition, lung cancer staging were obtained as follows. Tumor size was measured on cross-sectional imaging to determine the clinical T stage (cT). Clinical node negative (cN0) status was defined as the patient having a negative PET or CT scan or both demonstrating lymph nodes that were less than 1 cm in short-axis dimension. A cN0 status was also assigned if a PET avid (standardized uptake value >1.5) or biopsy of lymph node greater than 1 cm was pathologically negative for malignancy by EBUS fine-needle aspiration (FNA) biopsy or mediastinoscopy or both. Pathologic node positive (pN1 or pN2) was assigned based on the highest N status only. Thus, patients who were pN2 could have had pN1 positive nodes but these were excluded from the pN1 data. Nodal specimens were labeled by station, and number of nodes were determined at each institution by the operating surgeon.

Follow-up was calculated from the date of discharge to the last clinic visit until the database closed on August 31, 2013. For patients lost to follow-up, status was verified by using the Social Security Death Registry and by contacting their referring or primary care physician. Recurrence of cancer was based on imaging showing progressive changes consistent with recurrence (increasing standardized uptake value activity) or biopsy of the identified area, or both. Date and site of highest level of recurrence was recorded as local (ipsilateral lung), regional (ipsilateral mediastinum or hilum), or distant (contralateral thorax, bone, brain, distant metastasis).

The choice of systematic lymph node sampling or complete lymphadenectomy was not mandated in this study. However, the participating surgeons all share a similar philosophy regarding the role of hilar and mediastinal nodal staging, with all patients undergoing systematic lymph node sampling or dissection at the discretion of the surgeon. Briefly, the specific robotic techniques utilized are as follows: completely portal four-arm technique [5]; a completely portal three-arm technique with 5 cm extraction incision [9]; and a three- or four-arm technique with a 3 cm to 4 cm non–rib spreading utility incision [9].

Statistical analysis was completed with the assistance of an experienced biostatistician. Groups were compared using χ^2 tests for categorical variables and two-sample t tests for continuous variables. A univariate and multivariate logistic regression analysis was used to calculate an odds ratio for the variables of interest that might predict the likelihood of upstaging. Disease-free survival and overall survival were compared using a log rank statistic, and survival curves were drawn according to the Kaplan-Meier method. All statistical analyses were conducted in Statistical Analysis Systems software 9.3 (SAS Institute, Cary, NC). Graphs were drawn using R (www.R-project.org).

Results

A total of 302 patients underwent robotic anatomic lung resection for clinical stage I NSCLC. This cohort was predominantly female, with relatively preserved pulmonary function, limited comorbidities, and good performance status. Patient characteristics are outlined in Table 1.

All patients were clinically staged with either a CT scan or a PET scan, and nearly 30% underwent invasive mediastinal staging by EBUS FNA, endoscopic ultrasonography FNA, or mediastinoscopy (Table 2). The most