Preoperative computed tomography–guided microcoil localization of small peripheral pulmonary nodules: A prospective randomized controlled trial

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Objectives: Growing, small, peripheral, pulmonary nodules in patients at high risk for lung cancer lead to requests for video-assisted thoracoscopic (VATS) resection for pathologic diagnosis. The purpose of this randomized controlled trial was to determine if preoperative localization using percutaneously placed computed tomography (CT)–guided platinum microcoils decreases the need for thoracotomy or VATS anatomic resection (segmentectomy/lobectomy) for diagnosis.

Methods: Patients with undiagnosed nodules of 15 mm or less were randomized to either no localization or preoperative microcoil localization. Coils were placed with the distal end deep to the nodule and the superficial end coiled on the visceral pleural surface with subsequent visualization by intraoperative fluoroscopy and VATS. Nodules were removed by VATS wedge excision using endostaplers. The primary outcome was a VATS wedge excision for pathologic diagnosis of the nodule without the need for either thoracotomy or VATS anatomic resection.

Results: Sixty patients were randomized and 56 underwent surgery between March 2010 and June 2012. Twenty-nine underwent microcoil localization and 27 did not. The baseline characteristics (age, sex, forced expiratory volume in the first second of expiration, nodule size/depth) were similar. The coil group had a higher rate of successful diagnosis with VATS wedge resection alone (27/29 vs 13/27; $P < .001$), decreased operative time to nodule excision (37 ± 39 vs 100 ± 67 minutes; $P < .001$), and reduced stapler firings (3.7 ± 2.0 vs 5.9 ± 31; $P = .003$) with no difference in total costs. Pathologic diagnoses included 14 benign nodules, 32 primary lung malignancies, and 10 metastases. There were no clinically significant complications related to the coil placement or wedge resection.

Conclusions: Preoperative CT-guided microcoil localization decreases the need for thoracotomy or VATS anatomic resection for the diagnosis of small peripheral pulmonary nodules. (J Thorac Cardiovasc Surg 2015;149:26-32)

See related commentry on pages 33-4.

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Detection and safe surgical resection of early lung cancer is the most promising strategy to improve lung cancer survival. The US National Lung Screening Trial showed that screening of patients at high risk for lung cancer with the use of low-dose thoracic computed tomography (CT) reduces mortality from lung cancer by 20%.[1] CT detection of nodule growth or an increase in the solid component of semisolid lung nodules in patients at risk for primary or secondary lung cancer raises the possibility of early lung cancer, causing anxiety for both patients and referring clinicians. Unfortunately, confident separation of benign from malignant small lung nodules cannot be reliably achieved using CT criteria[2] or positron emission tomography (PET)/CT scan analysis.[3] Pathologic diagnosis using needle or excision biopsy is usually required. Excision biopsy removes the entire nodule at 1 setting and eliminates the sampling error associated with needle biopsy, making it appealing to physicians and patients.

To reduce postoperative morbidity, excision biopsy is often performed using video-assisted thoracoscopic surgery (VATS) techniques. Nodules may be safely resected via minimally invasive techniques without the need for

Abbreviations and Acronyms
CT = computed tomography
PET = positron emission tomography
RCT = randomized controlled trial
VATS = video-assisted thoracoscopy

thoracotomy. Thoracoscopy may facilitate the diagnostic evaluation of potentially malignant lesions by allowing earlier excision biopsy. Patients with benign lesions benefit similarly by being spared an open thoracotomy. However, Suzuki and colleagues[4] reported that failure to visualize or palpate the nodule during unguided VATS occurred in 54% of patients, thus requiring conversion to thoracotomy. The conversion rate to thoracotomy increased to 63% when the nodule was 10 mm in diameter or less or greater than 5 mm from the pleural surface. There is particular difficulty in surgically locating low-density semisolid or ground-glass nodules because they are difficult to palpate, even at thoracotomy. To guide VATS wedge resection of these suspicious nodules, we developed a localizing technique that uses preoperative CT guidance to place commercially available fiber-coated microcoils with 1 end deep to the suspicious nodule and the other end in the pleural space. The safety and efficacy of the process was previously evaluated in a pig model[5] and in human feasibility trials,[6,7] which showed 97% accuracy and a low incidence of complications such as pneumothorax or hemothorax.

Based on this evidence, we carried out a prospective randomized controlled clinical trial. The primary outcome of the study was to determine the accuracy, safety, and total costs of open thoracotomy or VATS anatomic resection (segmentectomy or lobectomy) with preoperative CT-guided microcoil localization and VATS (experimental group) compared with VATS alone (control group) for pathologic diagnosis of small peripheral lung lesions.

METHODS

The study was approved by the institutional review boards of the University of British Columbia (CREB H09-02265) and Vancouver General Hospital (V10-0028). The randomized controlled trial (RCT) was registered with clinicaltrials.gov (NCT01028417). The CONSORT 2010 checklist of information was used to describe the design, methods, results, and conclusions of this randomized trial. A complete CONSORT diagram (Figure 1) is included. No industry funding was solicited or received for any equipment used in this study.

Sample Size Calculation, Study Duration, and Statistical Analysis

In our previous phase 1 study,[7] microcoil localization of small peripheral lung nodules enabled fluoroscopy-guided VATS resection of 97% of the nodules compared with a rate of less than 40% in historical controls.[4] The current study was powered to detect an absolute difference of 40% between the groups in reducing the rate of conversion to open thoracotomy or VATS segmentectomy or lobectomy from 50% to 10% for pathologic diagnosis of the target nodule. Twenty-eight patients were required in each group (power 90%; alpha, 0.05; beta, 0.10). Demographic, preoperative, perioperative, postoperative, pathologic, and cost data were collected. Means and standard deviations were reported for postoperative continuous data and proportions for categorical data. Independent samples *t* tests were performed on continuous data and χ^2 values were calculated for categorical data to test for any significant difference between the experimental and the control groups, including costs.

Randomization

Computer-generated block randomization was initiated by a data manager in the respiratory research group and placed in individual sealed envelopes, ensuring that both the surgeon and the thoracic research assistant interviewing potential candidates for the study were blind to the randomization code. Each envelope was opened in front of the patient on entry into the study after written informed consent was received.

Study Entry and Exclusion Criteria

Patients with known pulmonary nodules of 15 mm or less that were suspicious for cancer, who were referred by family physicians, respiratory physicians, oncologists, and radiologists after July 1, 2009, for possible VATS diagnostic wedge resection were assessed for eligibility. Patients eligible to enter the study had either a pulmonary nodule of 10 to 15 mm, or had a nodule less than 10 mm that was growing or increasing in density on serial CT. The patient had a contrast-enhanced thin-section CT scan of the chest and upper abdomen, which was assessed by an interventional chest radiologist (J.M.) and a thoracic surgeon (R.F.) with expertise in VATS and open lung resections to determine if the nodules were located in parts of the lung that were amenable to VATS wedge excision. The deepest part of the lesion had to be at least 2 cm away from major pulmonary arteries and veins to allow safe and adequate VATS excision. All patients were more than 18 years of age and mentally competent to give written informed consent.

Patients were excluded from the trial if they did not consent to participate in the study, if the radiologist and surgeon determined that the nodule was located too centrally to be safely excised using VATS wedge techniques, or if there was a history of previous ipsilateral thoracotomy. Patients with more than 3 nodules and patients with pulmonary hypertension were excluded from the study. If the patient was excluded, they received the current standard treatment, that is, needle biopsy, continued observation of the nodule at 3 to 6 monthly intervals, or excisional surgery (VATS or open thoracotomy).

If the eligibility criteria were met, patients were approached by a trained research assistant in a separate office from the thoracic clinic about study entry. They were informed of the risks and benefits of the procedure and all the alternatives for treatment. Written informed consent was obtained. Patients were then assigned to either the experimental group or the control group.

Surgical Procedure

Experimental group. As previously described,[7] preoperative localization of the lung nodule was carried out in the radiology department on the day of surgery using local anesthesia. CT-guided platinum microcoils (VortX-18; Diamond Shape; Boston Scientific, Cork, Ireland) were placed percutaneously through a 22-gauge needle with the distal end deep to the nodule and the superficial end coiled on the visceral pleural surface. The patient was then taken to the operating room, where under general anesthesia with lung isolation, the nodule and coil were removed by wedge excision with endostaplers (Endo GIA II, United States Surgical, Norwalk, Conn; Echelon Endostapler, Ethicon Endo-Surgery, Cincinnati, Ohio) using fluoroscopy and VATS visualization. If the lesion could not be excised using the VATS technique, the patient underwent an open