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Pathology in NSCLC

Pathologists miss up to 12% of positive N1 mets

J Clin Oncol. 2012 Jul 9. Incomplete Intrapulmonary Lymph Node Retrieval After Routine Pathologic Examination of Resected Lung Cancer. Ramirez RA, Wang CG, Miller LE, Adair CA, Berry A, Yu X, O'Brien TF, Osarogiagbon RU, Robert A. Ramirez, Christopher G. Wang, Laura E. Miller, and Raymond U. Osarogiagbon, University of Tennessee; Courtney A. Adair and Thomas F. O'Brien, Duckworth Pathology Group; Allen Berry, St Francis Hospital; and Xinhua Yu, University of Memphis, Memphis, TN. PURPOSE Pathologic nodal stage affects prognosis in patients with surgically resected non-small-cell lung cancer (NSCLC). Unlike examination of mediastinal lymph nodes (LNs), which depends on surgical practice, accurate examination of intrapulmonary (N1) nodes depends primarily on pathology practice. We investigated the completeness of N1 LN examination in NSCLC resection specimens and its potential impact on stage. PATIENTS AND METHODS We performed a case-control study of a special pathologic examination (SPE) protocol using thin gross dissection with retrieval and microscopic examination of all LN-like material on remnant NSCLC resection specimens after routine pathologic examination (RPE). We compared LNs retrieved by the SPE protocol with nodes examined after RPE of the same lung specimens and with those of an external control cohort. RESULTS We retrieved additional LNs in 66 (90%) of 73 patient cases and discovered metastasis in 56 (11%) of 514 retrieved LNs from 27% of all patients. We found unexpected LN metastasis in six (12%) of 50 node-negative patients. Three other patients had undetected satellite metastatic nodules. Pathologic stage was upgraded in eight (11%) of 73 patients. The time required for the SPE protocol decreased significantly with experience, with no change in the number of LNs found. CONCLUSION Standard pathology practice frequently leaves large numbers of N1 LNs unexamined, a clinically significant proportion of which harbor metastasis. By improving N1 LN examination, SPE can have an impact on prognosis and adjuvant management. We suggest adoption of the SPE to improve pathologic staging of resected NSCLC.

Editor's commentary: This report takes on one of the most difficult problems in oncology: the trustworthiness of the pathology report. Incomplete dissection of specimens for nodal examination has long been a complaint of surgeons. It takes time and effort to completely dissect and examine the nodal tissue contained within a lobectomy (or any) specimen; pathologist are human and busy like everybody else. This report confirms what we have long feared: reportedly negative specimens can harbor true metastatic N1 nodes in up to 12% of cases.

Accompanying editorial misses the mark It is expected that editorialists will infuse their pieces with a certain amount of opinion and bias, but it is rare that they include misleading information. Kemp Kernstein's accompanying editorial "A lobectomy by any other name" does a disservice to the readers of JCO by stating lobectomy for NSCLC should include "thorough evaluation of at least four mediastinal lymph node stations including one contralateral station..." This unreferenced personal opinion is simply not supported by the literature. I know of no evidence that contralateral lymph nodes should be sampled during routine lobectomy. ACOSOG Z032 proved that mediastinal dissection is not better than simple sampling. We also know that the negative predictive value of preoperative fusion PET/CT scanning in NSCLC is over 95%, and in the case of false negatives, the majority of these are N1 stations, NOT N2. In fact, it is far easier to make the case that mediastinal lymph node staging in early NSCLC carries more risk than benefits in this era.

AATS publishes guidelines for lung cancer screening

J Thorac Cardiovasc Surg. 2012 Jul;144(1):33-8. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. Jaklitsch MT, Jacobson FL, Austin JH, Field JK, Jett JR, Keshavjee S, MacMahon H, Mulshine JL, Munden RF, Salgia R, Strauss GM, Swanson SJ, Travis WD, Sugarbaker DJ. Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA. mjaklitsch@partners.org OBJECTIVE: Lung cancer is the leading cause of cancer death in North America. Low-dose computed tomography screening can reduce lung cancer-specific mortality by 20%. METHOD: The American Association for Thoracic Surgery created a multispecialty task force to create screening guidelines for groups at high risk of developing lung cancer and survivors of previous lung cancer. RESULTS: The American Association for Thoracic Surgery guidelines call for annual lung cancer screening with low-dose computed tomography screening for North Americans from age 55 to 79 years with a 30 pack-year history of smoking. Long-term lung cancer survivors should have annual low-dose computed tomography to detect second primary lung cancer until the age of 79 years. Annual low-dose computed tomography lung cancer screening should be offered starting at age 50 years with a 20 pack-year history if there is an additional cumulative risk of developing lung cancer of 5% or greater over the following 5 years. Lung cancer screening requires participation by a subspecialty-qualified team. The American Association for Thoracic Surgery will continue engagement with other specialty societies to refine future screening guidelines. CONCLUSIONS: The American Association for Thoracic Surgery provides specific guidelines for lung cancer screening in North America.

Editor's commentary: The American Association for Thoracic Surgery has published their version of guidelines for lung cancer screening. This set of guidelines is very similar to the previously published NCCN guidelines. They are more inclusive in the respect that they advocate screening based on overall lung cancer risk and, therefore, they include survivors of lung cancer who are at high risk for a metachronous cancers.

T3 NSCLC

Resection of T3 NSCLC can afford good long term survival

J Thorac Cardiovasc Surg. 2012 Aug;144(2):431-7. Epub 2012 Jun 19. Modern surgical results of lung cancer involving neighboring structures: A retrospective analysis of 531 pT3 cases in a Japanese Lung Cancer Registry Study. Kawaguchi K, Miyaoka E, Asamura H, Nomori H, Okumura M, Fujii Y, Nakanishi Y, Eguchi K, Mori M, Sawabata N, Yokoi K; Japanese Joint Committee of Lung Cancer Registry, Department of Thoracic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan. OBJECTIVE: The aim of the present study was to identify the modern surgical results of pathologic T3 lung cancer and to examine the heterogeneity of this group from the nationwide database. METHODS: The registered data of 11,663 cases from the Japanese Joint Committee of Lung Cancer Registry conducted in 2010 were analyzed, which included patients with resected lung cancer during 2004. Of these patients, 531 with invasive T3 lung cancer constituted the study population. RESULTS: Of the 531 patients, 466 were men and 65 women, with a mean age of 65.9 years. The 3- and 5-year survival rates and median survival time was 54.0%, 44.9%, and 46 months, respectively. A multivariate analysis showed incomplete resection, N2 disease, and no adjuvant therapy were independent prognostic factors of a poor outcome. However, pneumonectomy and N1 disease were not significantly associated with the prognosis. In terms of each involved structure, we detected 407 patients with T3 tumors involving the chest wall, 56 involving the mediastinal pleura, 45 with involvement of the bronchus within 2 cm of the carina, 31 involving the diaphragm, and 20 involving the pericardium. The corresponding 5-year survival rates were 43.2%, 40.1%, 55.2%, 42.6%, and 54.2%. CONCLUSIONS: The modern 5-year survival rates of patients with T3 lung cancer involving any neighboring structures have been 40% to 55%, and the current pT3 group was proved to have a relatively uniform prognosis.

Editor's commentary: This report from the Japanese Lung Cancer Registry details results with T3 patients including those with chest wall, pericardial, mainstem bronchus, and diaphragmatic involvement. The long term results are relatively good with survivals ranging from 40-55%. Not surprisingly, N2 disease, incomplete resection, and *no* adjuvant treatment were poor prognostic indicators.

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Surgery in Oligometastatic NSCLC

J Thorac Cardiovasc Surg. 2012 Aug;144(2):444-52. Epub 2012 Jun 17. Surgery for oligometastatic non-small cell lung cancer: Long-term results from a single center experience. Congedo MT, Cesario A, Lococo F, De Waure C, Apolone G, Meacci E, Cavuto S, Granone P. Department of General Thoracic Surgery, Catholic University of Sacred Heart, Rome, Italy. **OBJECTIVE:** The role of surgery in the multimodal therapy for selected stage IV oligometastatic non-small cell lung cancer (NSCLC) is still a forum of open discussion. **METHODS:** We have retrospectively analyzed the records of 53 patients with oligometastatic NSCLC who had been treated with curative intent in the period January 1997 to May 2010. **RESULTS:** The mean age and the male/female ratio were 61 years and 32:21, respectively. A single metastatic lesion was present in 45 (84.9%) subjects, in 2 patients there were 2 different anatomic sites involved, and in 8 patients there were 2 metastases in the same site. The most common involved sites were brain (39), followed by adrenal gland (7), bone (3), vertebrae (3), liver (1), and contralateral supraclavicular lymph node (1). Distant disease was completely resected in 42 patients; 10 patients were treated with exclusive chemotherapy and/or radiotherapy and 1 with local laser therapy. Twenty-nine patients had been administered concurrent chemoradiation in a neoadjuvant setting before the surgical treatment at the lung or both sites (primary/distant). The pulmonary resection was complete (R0) in 42 patients (79.2%). Overall, 1- and 5-year survivals were 73.1% and 24%, respectively (median follow-up, 28 months). Median overall survival, local disease-free survival, and distant disease-free survival, estimated using the Kaplan-Meier method, were respectively 19, 72, and 12 months. After stepwise multivariate analysis, the weight loss ($P < .001$), the completeness of pulmonary resection ($P = .0019$), and, interestingly, the performance of a positron emission tomography-computed tomography scan in preoperative staging ($P = .05$) maintained their independent prognostic value as overall survival determinants. **CONCLUSIONS:** Surgical treatment for selected stage IV NSCLC is feasible and safe. Furthermore, good survival can be expected in those patients in whom a complete resection of the primary tumor and radical control of the distant diseases are accomplished.

Editor's commentary: This is a fascinating report from an aggressive surgical group in Rome. They have shown reasonable short term and long term results in so called "oligometastatic disease." While surgery for the control of the primary has long been practiced in single brain lesions, this concept has now been extended to adrenal, bone, liver and N3 supraclavicular nodes. While the argument that this is a highly selected subset of metastatic NSCLC patients clearly is true, and I wouldn't argue against the fact that these patients would be expected to live longer relative to the entire population of metastatic NSCLC patients. However, in those patients who have yet to demonstrate widely metastatic disease, there is a growing empiric rationale for aggressive control of the primary, or metastases "generator."

Lymphadenectomy for NSCLC

Not all Stage IA patients need lymph node sampling

J Thorac Cardiovasc Surg. 2012 Aug 8. Prediction of pathologic node-negative clinical stage IA lung adenocarcinoma for optimal candidates undergoing sublobar resection. Tsutani Y, Miyata Y, Nakayama H, Okumura S, Adachi S, Yoshimura M, Okada M. Department of Surgical Oncology, Hiroshima University, Hiroshima, Japan. **OBJECTIVE:** Patients with pathologic node-negative early lung cancer may be optimal candidates for sublobar resection. We aimed to identify predictors of pathologic lymph node involvement in clinical stage IA lung adenocarcinoma. **METHODS:** The data from a multicenter database of 502 patients with completely resected clinical stage IA lung adenocarcinoma were retrospectively analyzed to determine the relationship between the lymph node metastasis status and tumor size on high-resolution computed tomography (HRCT) or maximum standardized uptake value (SUVmax) on [18F]-fluoro-2-deoxy-d-glucose positron emission tomography/computed tomography (FDG-PET/CT). Revised SUVmax was used to correct interinstitutional discrepancies. **RESULTS:** In multivariate analyses, either a solid tumor size on HRCT ($P = .001$) or an SUVmax on FDG-PET/CT ($P = .049$) was an independent predictor of lymph node metastasis. The predictive criteria of pathologic node-negative early lung cancer were a solid tumor size of less than 0.8 cm or an SUVmax of less than 1.5. Patients who met the predictive criteria of pathologic node-negative disease had less pathologic invasiveness, such as lymphatic, vascular, or pleural invasion ($P < .001$), and better disease-free survival ($P < .0001$) than those who did not, and 86 (40.4%) of the 213 patients with T1b (2-3 cm) tumors met the predictive criteria. **CONCLUSIONS:** Either a solid tumor size or an SUVmax was a significant independent predictor of nodal involvement in clinical stage IA lung adenocarcinoma. The pathologic node-negative status criteria of a solid tumor size of less than 0.8 cm on HRCT or an SUVmax of less than 1.5 on FDG-PET/CT may be helpful for avoiding systematic lymphadenectomy for clinical stage IA lung adenocarcinoma, even in cases of T1b (2-3 cm) tumor. and citation

Editor's commentary: This is a rather small subset of NSCLC patients (how many patients have a tumor less than 8mm or an SUV less than 1.5?) but I think this group will continue to grow. It is clear that we will be seeing a larger number of these patients as screening starts to kick in on a wider basis.

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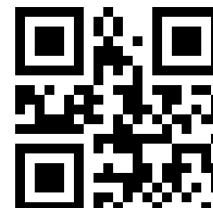
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