

Review of Thoracic Surgical Oncology

FLORIDA



HEART & LUNG SURGERY

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Edited by K. Eric Sommers, MD, FACS

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Editor's note: This month's review includes a case presentation of pulmonary artery sarcoma, a rare thoracic surgical challenge.

Metastasectomy for colon cancer

Mediastinal lymph node involvement in colon cancer metastasectomy prognostic for long term survival

Ann Thorac Surg. 2012 Dec;94(6):1796-800. Is lymph node dissection required in pulmonary metastasectomy for colorectal adenocarcinoma? Hamaji M, Cassivi SD, Shen KR, Allen MS, Nichols FC, Deschamps C, Wigle DA. Division of General Thoracic Surgery, Mayo Clinic, Rochester, Minnesota. **BACKGROUND:** The aim of this study was to clarify the clinical outcome and significance of mediastinal lymph node dissection (LND) during pulmonary resection of metastases from colorectal adenocarcinoma. **METHODS:** A retrospective chart review was performed. Between April 1985 and December 2009, 518 patients underwent 720 pulmonary metastasectomies for metastatic colorectal adenocarcinoma. Relevant factors were analyzed with the χ^2 or Fisher exact test and the Mann-Whitney test. Survival and lymph node (LN) recurrence-free period after pulmonary metastasectomy were analyzed with Kaplan-Meier and Cox proportional hazards methods. **RESULTS:** The overall 5-year and 10-year survival rate after pulmonary metastasectomy were 47.1% and 27.7%, respectively. The only significant prognostic factor for survival after pulmonary metastasectomy was mediastinal LN metastasis ($p = 0.047$ in univariate and 0.0028 in multivariate analysis); 199 patients did not undergo LND, 279 patients underwent LND that were negative, and 40 patients underwent LND that contained 1 or more positive mediastinal LN for metastases. The sensitivity of positron emission tomographic scan for detecting mediastinal LN metastases was only 35%. Although long-term survivors were present, systematic LND was not a significant factor for prolonged survival ($p = 0.26$) in the positive LND group. **CONCLUSIONS:** Mediastinal LN metastases are a significant negative prognostic factor for survival after pulmonary metastasectomy for metastatic colorectal cancer. Computed tomography and positron emission tomography based imaging, as well as preoperative carcinoembryonic antigen levels have poor sensitivity for detecting malignant mediastinal LN in this setting. Systematic mediastinal LND should be performed for prognostic purposes during pulmonary metastasectomy for colorectal metastases.

Editor's commentary: This is a provocative, retrospective study from the Mayo Clinic. After controlling for traditional predictors of survival like number of mets, disease free interval, and stage of primary, the authors found that mediastinal lymph node involvement was the only multivariate predictor of survival. Close readers of the *Review* will note that we reviewed a report from MD Anderson in our last issue on metastasectomy for colon mets which did not use lymph node mets in its analysis. Five year survival in both reports are similar, 55.4% in the MD Anderson report, and 47.1% in this report.

Resected NSCLC patients with EGFR mutations have improved survival vs wild type

J Thorac Oncol. 2012 Dec;7(12):1815-22. Distinct Clinical Course of EGFR-Mutant Resected Lung Cancers: Results of Testing of 1118 Surgical Specimens and Effects of Adjuvant Gefitinib and Erlotinib. D'Angelo SP, Janjigian YY, Ahye N, Riely GJ, Chaft JE, Sima CS, Shen R, Zheng J, Dycoco J, Kris MG, Zakowski MF, Ladanyi M, Rusch V, Azzoli CG. *Department of Medicine, Division of Solid Tumor Oncology, Thoracic Oncology Service; and Departments of †Epidemiology and Biostatistics, ‡Surgery, and §Pathology, Memorial Sloan-Kettering Cancer Center and Weill Cornell Medical College, New York, New York. BACKGROUND: EGFR and KRAS mutations are mutually exclusive and predict outcomes with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) treatment in patients with stage IV lung cancers. The clinical significance of these mutations in patients with resected stage I-III lung cancers is unclear. METHODS: At our institution, resection specimens from patients with stage I-III lung adenocarcinomas are tested for the presence of EGFR or KRAS mutations during routine pathology analysis such that the results are available before consideration of adjuvant therapy. In a cohort of 1118 patients tested over 8 years, overall survival was analyzed using multivariate analysis to control for potential confounders, including age, sex, stage, and smoking history. The impact of adjuvant erlotinib or gefitinib was examined in an independent data set of patients exclusively with EGFR mutation, in which date of recurrence was recorded. RESULTS: In the overall population, we identified 227 KRAS (25%) and 222 EGFR (20%) mutations. Patients with EGFR-mutant lung cancers had a lower risk of death compared with those without EGFR mutations, overall survival (OS) HR 0.51 (95% confidence interval [CI]: 0.34-0.76, $p < 0.001$). Patients with KRAS-mutant lung cancers had similar outcomes compared with individuals with KRAS wild-type tumors, OS HR 1.17 (95% CI: 0.87-1.57, $p = 0.30$). A separate data set includes only patients with EGFR-mutant lung cancers identified over 10 years ($n = 286$). In patients with resected lung cancers and EGFR mutation, treatment with adjuvant erlotinib or gefitinib was associated with a lower risk of recurrence or death, disease-free survival HR 0.43 (95% CI: 0.26-0.72, $p = 0.001$), and a trend toward improved OS. CONCLUSIONS: Patients with resected stage I-III lung cancers and EGFR mutation have a lower risk of death compared with patients without EGFR mutation. This may be because of treatment with EGFR TKIs. Patients with, and without KRAS mutation have similar OS. These data support reflex testing of resected lung adenocarcinomas for EGFR mutation to provide prognostic information and identify patients for enrollment on prospective clinical trials of adjuvant EGFR TKIs.

Editor's commentary: this is a large (>1000 pts) retrospective study from Memorial Sloan-Kettering that compared survival of surgically resected patients with EGFR mutations vs. wild type tumors. Treatment with TKIs was associated with a trend toward improved survival. This report certainly adds evidence for a strategy of adding or substituting a TKI to the adjuvant treatment of resected, high risk patients.

Mesothelioma

Tomotherapy for mesothelioma following decortication/pleurectomy

J Thorac Oncol. 2012 Dec;7(12):1862-6. Tomotherapy after pleurectomy/decortication or biopsy for malignant pleural mesothelioma allows the delivery of high dose of radiation in patients with intact lung. Minatel E, Trovo M, Polesel J, Rumeileh IA, Baresic T, Bearz A, Del Conte A, Franchin G, Gobitti C, Drigo A, Dassie A, Pagan V, Trovo MG. Departments of *Radiation Oncology, †Epidemiology and Biostatistics, ‡Nuclear Medicine, and §Medical Oncology, Centro di Riferimento Oncologico di Aviano, Italy; ||Department of Medical Oncology, Pordenone General Hospital, Pordenone, Italy; and Departments of ¶Medical Physics and #Surgery, Centro di Riferimento Oncologico di Aviano, Italy. INTRODUCTION: This study aimed to assess the safety of high doses of radiation delivered with tomotherapy to the intact lung after radical pleurectomy/decortication or biopsy for malignant pleural mesothelioma (MPM). METHODS: Twenty-eight patients were enrolled in this prospective study and underwent adjuvant or definitive tomotherapy after radical pleurectomy/decortication ($n = 20$) or pleural biopsy ($n = 8$) for MPM. The dose prescribed to the planning target volume, defined as the entire hemithorax, including chest-wall incisions and drain sites and excluding the intact lung, was 50 Gy delivered in 25 fractions. All patients underwent fluorodeoxyglucose-positron emission tomography for staging after surgery. Any fluorodeoxyglucose-avid areas or regions of particular concern for residual disease were given a simultaneous boost of radiotherapy to 60 Gy. Specific lung dosimetric parameters were reported. Toxicity was graded using the modified Common Toxicity Criteria version 3.0. RESULTS: The median follow-up was of 19 months (range, 6-29 months). Five patients (17.8%) experienced severe respiratory symptoms corresponding to grade 2 pneumonitis in three cases, and grade 3 pneumonitis in two cases. No fatal respiratory toxicity was reported. Contralateral lung V5 was strongly correlated with the risk of pneumonitis. Patients who developed grade 2 and 3 pneumonitis had a higher contralateral lung V5 (mean $V5=32\%$) than those without pneumonitis (mean $V5=17\%$) ($p=0.002$). Other two grade 3 toxicities were registered: one severe pain to the chest wall, and one severe thrombocytopenia. CONCLUSIONS: Tomotherapy allows the safe delivery of high dose of radiation to the hemithorax of MPM patients with intact lung.

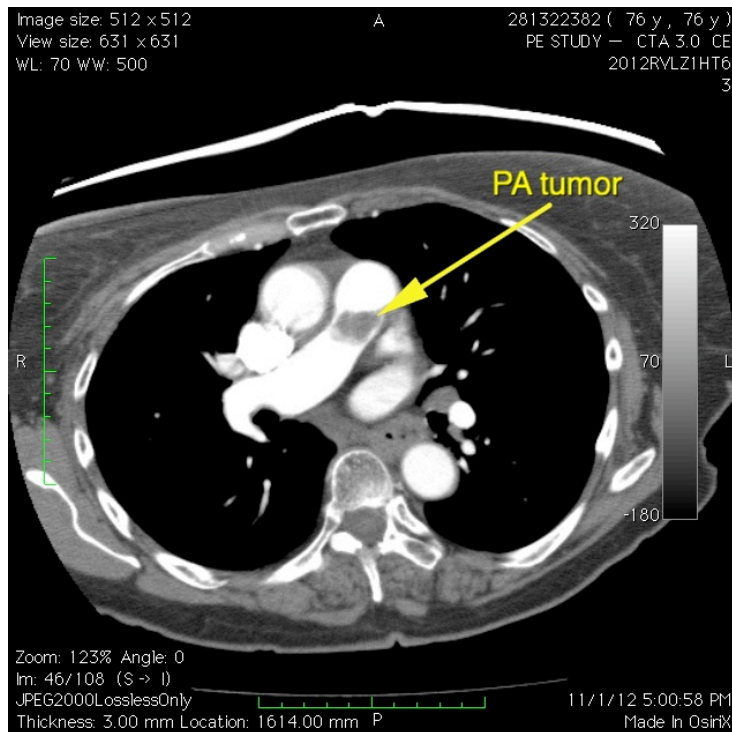
Editor's commentary: This report caught my attention because I have been re-evaluating extra-pleural pneumonectomy in the treatment of malignant mesothelioma in favor of decortication/pleurectomy in selected patients. So far, I have seen a better quality of life and in one patient, who received adjuvant Alima based chemotherapy, NED status. So naturally if adjuvant XRT can be given to bolster these results: great. This report however falls short in my opinion. Almost 20% of patients experienced severe respiratory symptoms from pneumonitis. This limits the possible applicability for routine adjuvant use of XRT, whether tomotherapy or not.

Interesting case presentation:

Pulmonary Artery Sarcoma

A 61 yo WF with a recent history of breast cancer was found to have an abnormal PET scan with a lesion localized to the mediastinum. Subsequent work up, including CT scanning and cardiac MRI, confirmed that this abnormality originated from the posterior wall of the main pulmonary artery, extending into the right main pulmonary artery. Appearance on CT scanning was consistent with a pulmonary artery mass, most likely a primary tumor such as a sarcoma. (See below left).

Based on these findings, a preoperative diagnosis of primary pulmonary artery sarcoma was entertained and resection by median sternotomy with cardiopulmonary bypass was recommended. (See below right). Intraoperative findings and frozen section were consistent with sarcoma. Involvement of the main PA extended into the bifurcation as well



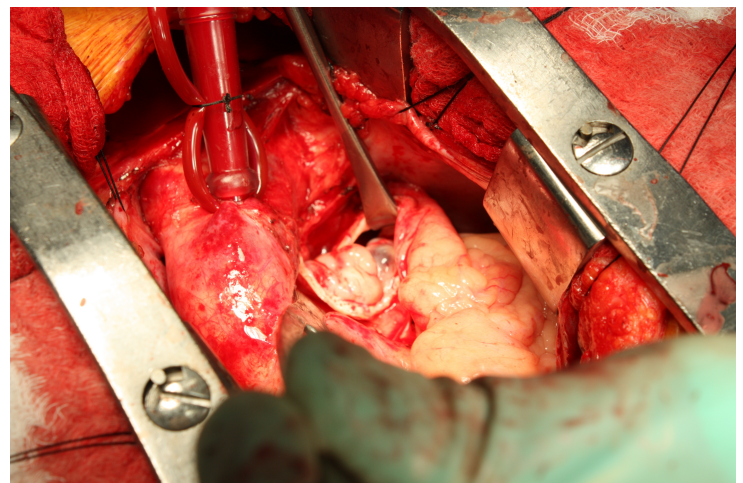
as the left and right main branches (below lower left) and required complete resection with reconstruction using woven Dacron grafts. The patient was discharged and recovered uneventfully. Postoperative XRT is planned.

Final pathology showed a high grade sarcoma, grade 3, with 41 mitotic figures/ HPF. The additional margin was found to be positive for endothelial surface growth.

Review by Dr. Allen Patrick Burke at the University of Maryland concluded: "The tumor has features of leiomyosarcoma. The location filling the lumen indicates intimal derivation. The in-situ growth in the margin is unusual and not well documented in the literature."

Primary pulmonary artery sarcomas are rare tumors, usually identified after causing symptoms relating to obstruction of right ventricular outflow or occlusion of one of the branch PAs. Overall prognosis is poor.

Ref: Am J Surg Pathol. 2008 Dec; 32(12): 1751-61.



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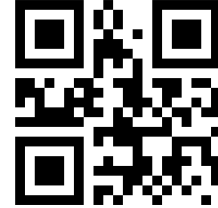
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