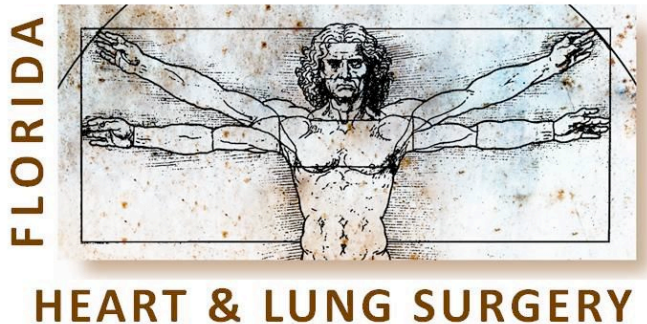# Review of Thoracic Surgical Oncology

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Edited by K. Eric Sommers, MD, FACS

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Editor's note: This month's review includes two case presentations of patients who were treated with SBRT for lung tumors who both came to salvage resection. I was surprised by the final pathologic findings in both cases. As we gain more experience with SBRT, it will be important to continue to review outcomes for these patients.

Thymic tumors

Recurrent thymoma improved with resection

Ann Thorac Surg. 2012 May 25. The Role of Surgical Management in Recurrent Thymic Tumors. Hamaji M, Allen MS, Cassivi SD, Nichols FC 3rd, Wigle DA, Deschamps C, Shen KR. Division of General Thoracic Surgery, Mayo Clinic, Rochester, Minnesota. BACKGROUND:There are few data on outcomes after surgical treatment for recurrent thymic tumors. The aim of this study is to analyze and compare long-term outcomes of treatments for recurrent thymic tumors. METHODS: Between January 1956 and December 2009, 344 thymic tumors were surgically resected (309 thymomas, 22 thymic carcinomas, 12 thymic carcinoids, and 1 thymolipoma). There were 48 recurrences (13.9%): 30 thymomas, 9 thymic carcinomas, and 9 thymic carcinoids. There were 27 men and 21 women with a median age of 51 years (range, 27 to 83). Retrospective chart review was performed. Relevant factors for recurrence as well as survival and progression-free interval were analyzed. RESULTS: The median follow-up interval from the initial operation was 83 months (range, 9 to 515). Recurrence adversely affected overall survival in surgically resected thymic tumors (p = 0.0014). In multivariate analysis, the initial Masaoka stage, incomplete resection, and World Health Organization histology were significant risk factors for recurrence. In multivariate analysis, only surgical management was associated with prolonged survival p = 0.0038) and improved progression-free interval (p = 0.0378) in recurrent thymoma. Five-year survival after recurrent thymoma was 54%. For recurrent thymic carcinoma, surgery did not improve survival. For these patients, chemotherapy was associated with improved progression-free interval after recurrence (p = 0.0295). There were no 5-year survivors of recurrent thymic carcinoma. CONCLUSIONS: Our data suggest that surgical management is associated with better outcome and is the treatment of choice for recurrent thymoma. For recurrent thymic carcinoma, surgical management has a very limited role, and chemotherapy appears to be a more effective treatment modality.

Editor's commentary: Recurrent thymoma is nearly always a local or regional issue and re-operation is frequently possible. This report confirms my bias which is to surgically remove disease that is accessible. Note, however, that thymic carcinoma is a different histology which is not nearly as amenable to multiple surgeries.

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Stage I NSCLC

Predicting recurrence in stage I resected NSCLC using molecular and clinical predictors

Ann Thorac Surg. 2012 May;93(5):1606-12. Clinical and molecular predictors of recurrence in stage I non-small cell lung cancer. Starnes SL, Pathrose P, Wang J, Succop P, Morris JC, Bridges J, Kupert EY, Anderson M. Department of Surgery, Division of Thoracic Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio. BACKGROUND: Patients with stage I lung cancer undergoing a complete resection have a 25% risk of recurrence. Factors predictive for recurrence are critically needed. In the present study, we prospectively examined clinical and molecular factors that may predict a poor outcome. METHODS: Patients with stage I non-small cell lung cancer undergoing surgical resection were enrolled into an institutional registry. Clinical demographics and outcomes data were prospectively collected. Patients who received neoadjuvant therapy or patients who died within 30 days of surgery were excluded from this analysis. Molecular factors involved in cell proliferation, cell cycle control, apoptosis, and angiogenesis were analyzed. The primary endpoint was recurrence-free survival. RESULTS: One hundred and two patients were enrolled between March 2006 and April 2009. There were 25 (25%) documented recurrences. In univariate analysis, male sex, increased tumor standard uptake value, tumor size, final pathology stage, arterial invasion, percent nuclear phosphorylated AKT, vascular endothelial growth factor score, negative cyclin D1 protein expression, and percent nuclear cyclin D1 expression were predictive of decreased recurrence-free survival. All factors with a p value of 0.1 or less were included in multivariate analysis. Male sex, final pathology stage, vascular endothelial growth factor score, and percent nuclear cyclin D1 expression were significant independent predictors for poor prognosis. CONCLUSIONS: Four clinical and molecular factors were associated with prognosis in a prospective study of stage I non-small cell lung cancer.

Editor's commentary This study reaffirms the importance of traditional predictors of survival such as final pathologic stage and male sex, but also adds two new molecular markers: VEGF and cyclin D1. In my opinion, the rate of recurrence (25% in this study) seems high for a PET era surgical study of fully resected stage I NSCLC. There was a significant majority of patients with IB disease vs IA, 56% vs. 44% which probably accounts for the relatively low overall survival.   This report highlights the need for better adjuvant treatment for high risk patients with NSCLC, even in early stages.

NSCLC

Adjuvant chemotherapy beneficial in elderly patients

J Clin Oncol. 2012 May 20;30(15):1813-21. Epub 2012 Apr 23. Adjuvant chemotherapy for non-small-cell lung cancer in the elderly: a population-based study in ontario, Canada. Cuffe S, Booth CM, Peng Y, Darling GE, Li G, Kong W, Mackillop WJ, Shepherd FA. Department of Medical Oncology, Princess Margaret Hospital, 610 University Ave, Toronto, Ontario, Canada M5G 2M9; sinead.cuffe@uhn.on.ca. Abstract PURPOSE Non-small-cell lung cancer (NSCLC) is predominantly a disease of the elderly. Retrospective analyses of the National Cancer Institute of Canada Clinical Trials Group JBR.10 trial and the Lung Adjuvant Cisplatin Evaluation (LACE) meta-analysis suggest that the elderly benefit from adjuvant chemotherapy. However, the elderly were under-represented in these studies, raising concerns regarding the reproducibility of the study results in clinical practice. PATIENTS AND METHODS By using the Ontario Cancer Registry, we identified 6,304 patients with NSCLC who were treated with surgical resection from 2001 to 2006. Registry data were linked to electronic treatment records. Uptake of chemotherapy was compared across age groups: younger than 70, 70 to 74, 75 to 79, and ≥ 80 years. As a proxy of survival benefit from chemotherapy, we compared survival of patients diagnosed from 2004 to 2006 with survival of those diagnosed from 2001 to 2003. Hospitalization rates within 6 to 24 weeks of surgery served as a proxy of severe chemotherapy-related toxicity. Results In all, 2,763 (43.8%) of 6,304 surgical patients were elderly (age ≥ 70 years). Uptake of adjuvant chemotherapy in the elderly increased from 3.3% (2001 to 2003) to 16.2% (2004 to 2006). Among evaluable elderly patients, 70% received cisplatin and 28% received carboplatin-based regimens. Requirements for dose adjustments or drug substitutions were similar across age groups. Hospitalization rates within 6 to 24 weeks of surgery were similar across age groups (28.0% for patients age < 70 years; 27.8% for patients age ≥ 70 years; P = .54). Four-year survival of elderly patients increased significantly (47.1% for patients diagnosed from 2001 to 2003; 49.9% for patients diagnosed from 2004 to 2006; P = .01). Survival improved in all subgroups except patients age ≥ 80 years. CONCLUSION Uptake of adjuvant chemotherapy for NSCLC increased in patients age 70 years or older following reporting of pivotal adjuvant chemotherapy trials, but it remained below that for patients younger than age 70 years. Adoption of adjuvant chemotherapy appears to be associated with significant survival benefit in the elderly (age ≥ 70 years), with tolerability apparently similar to that of patients who are younger than age 70 years.

Editor's commentary: While it seems self evident to us in Florida where so many of our patients are elderly, apparently the rest of the world is discovering that elderly patients can tolerate and benefit from adjuvant chemotherapy. What is particularly interesting about this report is that an overall 2.8% survival benefit was identified in this study even though only 16.2% of patients actually received treatment! Imagine the benefit if all eligible patients had been treated.

Interesting case presentations: PET changes following SBRT

Two cases illustrate the difficulty in evaluating lung lesions treated by SBRT following treatment. Case #1 involved a 65 yo WF with a history of T3N0 pancreatic cancer successfully treated with Whipple resection who subsequently developed a new RUL lung primary cancer. This was treated 7 months before presentation with SBRT. While PET scanning at 3 months post-treatment documented a decrease in activity, at 6 months, there was noted an increase in both size and SUV. Robotic assisted RUL lobectomy showed a NSCLC with no treatment effect noted on final pathology (despite initial radiographic response).

Case #2 involved a 64 yo WM with the history of a rectal carcinoma who was diagnosed with an isolated LLL lung metastases. This was treated with SBRT and follow up scanning in three months showed progression in both size and SUV. Removal of this lesion showed organizing pneumonia with extensive fibrosis, type 2 pneumocyte hyperplasia, and abundant alveolar macrophages. (See below). No evidence of tumor was detected despite radiographic progression.

As illustrated in these two cases, progression in PET findings following SBRT of lung tumors can be misleading. The time course of the changes is the important feature. In Case #1, there was interval decrease in activity followed by increase at six months. Case #2, however, showed increase at three months prompting referral. A report from MD Anderson identifies six months as the time period required before making reliable determination of PET changes after SBRT (see below).
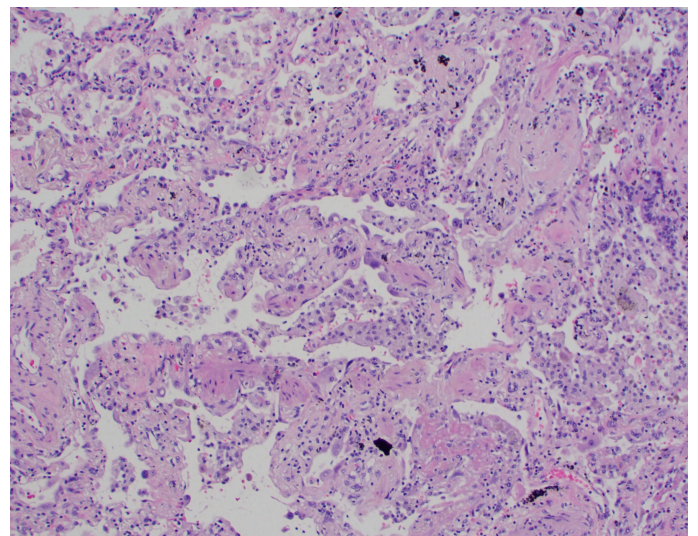
Abstract PURPOSE: We analyzed whether positron emission tomography (PET)/computed tomography standardized uptake values (SUVs) after stereotactic body radiotherapy (SBRT) could predict local recurrence (LR) in non-small-cell lung cancer (NSCLC). METHODS AND MATERIALS: This study comprised 128 patients with Stage I (n = 68) or isolated recurrent/secondary parenchymal (n = 60) NSCLC treated with image-guided SBRT to 50 Gy over 4 consecutive days; prior radiotherapy was allowed. PET/computed tomography scans were obtained before therapy and at 1 to 6 months after therapy, as well as subsequently as clinically indicated. Continuous variables were analyzed with Kruskal-Wallis tests and categorical variables with Pearson chi-square or Fisher exact tests. Actuarial local failure rates were calculated with the Kaplan-Meier method. RESULTS: At a median follow-up of 31 months (range, 6-71 months), the actuarial 1-, 2-, and 3-year local control rates were 100%, 98.5%, and 98.5%, respectively, in the Stage I group and 95.8%, 87.6%, and 85.8%, respectively, in the recurrent group. The cumulative rates of regional nodal recurrence and distant metastasis were 8.8% (6 of 68) and 14.7% (10 of 68), respectively, for the Stage I group and 11.7% (7 of 60) and 16.7% (10 of 60), respectively, for the recurrent group. Univariate analysis showed that SUVs obtained 12.1 to 24 months after treatment for the Stage I group (p = 0.007) and 6.1 to 12 months and 12.1 to 24 months after treatment for the recurrent group were associated with LR (p < 0.001 for both). Of the 128 patients, 17 (13.3%) had ipsilateral consolidation after SBRT but no elevated metabolic activity on PET; none had LR. The cutoff maximum SUV of 5 was found to have 100% sensitivity, 91% specificity, a 50% positive predictive value, and a 100% negative predictive value for predicting LR. CONCLUSIONS: PET was helpful for distinguishing SBRT-induced consolidation from LR. SUVs obtained more than 6 months after SBRT for NSCLC were associated with local failure. A maximum SUV greater than 5, especially at more than 6 months after SBRT, should prompt biopsy to rule out LR.

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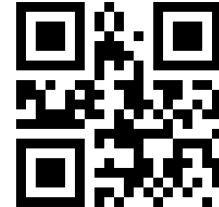
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