

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 features a case presentation of resected Small Cell Lung Cancer and a mini-review of surgery in SCLC. I think we are probably underutilizing surgery for potentially operable SCLC: see what you think.

NSCLC

Report defines risk of second malignancies in survivors of Stage I NSCLC

J Thorac Oncol. 2012 Aug;7(8):1252-6. Stage I lung cancer survivorship: risk of second malignancies and need for individualized care plan. Surapaneni R, Singh P, Rajagopalan K, Hageboutros A. Department of Hematology and Oncology, Cooper Cancer Institute, Cooper University Hospital, Cooper Medical School of Rowan University, Camden, NJ. **BACKGROUND:** Survivors of stage I lung cancer are at increased risk of subsequent malignancies. Specific data on risk of subsequent malignancies are underreported in the literature. We studied the incidence of stage I lung cancer and the incidence of all second malignancies in survivors. **METHODS:** Data from the Surveillance, Epidemiology and End Results 9 database were analyzed to calculate the incidence of stage I lung cancer and subsequent malignancies from 1998 to 2007. The risk of subsequent malignancies is reported as a standardized incidence ratio (observed incidence [O]/expected incidence [E]). **RESULTS:** The incidence rate of stage I lung cancer increased slowly from 1988 (8, confidence interval [CI]: 7.6-8.4) to 2003 (9.2, CI: 8.9-9.6) and more rapidly from 2003 to 2007 (11.2, CI: 10.8-11.7). The risk of developing a second lung cancer is highest in the first year with the O/E at 6.78 (CI: 6.29-7.31) and continues to be high at 10 years (O/E 4.12; CI: 4.44-4.80). Laryngeal cancer has the highest incidence in the first year (O/E 9.78; CI: 7.51-12.51) and continues to be high at 10 years (O/E 3.55; CI: 1.77-6.34). For gastrointestinal cancers, there is increased risk of colon (O/E 1.33; CI: 1.22-1.44), esophagus (O/E 2.29; CI: 1.85-2.89), and stomach (O/E 1.43; CI: 1.15-1.75) cancers. The increased risk of bladder cancer (O/E 1.83; CI: 1.65-2.03) remains high even at 10 years after the diagnosis of stage I lung cancer. **CONCLUSIONS:** There is increasing incidence of stage I lung cancer. Survivors of stage I are at increased risk of certain second malignancies.

Editor's commentary: This is a fascinating report that quantifies the risk of developing a second cancer following curative resection for Stage I cancer. The highest risk for a second cancer is laryngeal cancer in the first year following lung resection (O/E=9.78), followed by a second lung cancer in the first year (O/E=6.78), and renal cancer in the first year (O/E=5.21). Overall, the risk for developing a second malignancy over the ten years following lung resection is highest for laryngeal cancer--higher than a second lung cancer. Other tumors associated with elevated risks are familiar: other head and neck cancer, esophageal cancer, renal cell, bladder and stomach. Interestingly, colon cancer is also slightly higher at an overall O/E=1.33.

Impact of PET scanning in NSCLC questioned

J Clin Oncol. 2012 Aug 1;30(22):2725-30. Stage migration, selection bias, and survival associated with the adoption of positron emission tomography among medicare beneficiaries with non-small-cell lung cancer, 1998-2003. Dinan MA, Curtis LH, Carpenter WR, Biddle AK, Abernethy AP, Patz EF Jr, Schulman KA, Weinberger M. Duke Clinical Research Institute, PO Box 17969, Durham, NC 27715; kevin.schulman@duke.edu. **PURPOSE** Previous studies have linked the use of positron emission tomography (PET) with improved outcomes among patients with non-small-cell lung cancer (NSCLC). However, this association may be confounded by PET-induced stage migration and selection bias. We examined the association between PET use and overall survival among Medicare beneficiaries with NSCLC. **PATIENTS AND METHODS** Retrospective analysis of Surveillance, Epidemiology, and End Results (SEER) -Medicare data was used to characterize changes in overall survival, stage-specific survival, and stage distribution among Medicare beneficiaries with NSCLC between 1998 and 2003. **Results** A total of 97,007 patients with NSCLC diagnosed between 1998 and 2003 met the study criteria. Two-year and 4-year survival remained unchanged, despite widespread adoption of PET. The proportion of patients staged with advanced disease increased from 44% to 50%. Upstaging of disease was accompanied by stage-specific improved survival, with 2-year survival of stage IV disease increasing from 8% to 11% between 1998 and 2003. PET was more likely to be administered to patients with less advanced disease (stages I through IIIA) and greater overall survival. **CONCLUSION** Overall survival among Medicare beneficiaries with NSCLC was unchanged between 1998 and 2003, despite widespread adoption of PET. The association between PET use and increased survival likely reflects an artifact of selection bias and consequent stage migration.

Editor's commentary: I think this study is somewhat misleading in its conclusions. Did anyone really think that PET scanning was going to improve absolute survival in NSCLC? In my opinion, the value of PET is the avoidance of ineffective or even harmful treatments administered to the wrong patients which may not be reflected in survival statistics. Nevertheless, the authors still demonstrate a trend toward better survival, even in Stage IV patients. Overall, the authors describe what we all know in our day-to-day practice: PET scanning usually upstages patients from better to worse stages, and once you get to Stage IV, survival goes to zero. Therefore, any survival benefit accrued from more accurate early staging is wiped out by the increased late stage proportion of patients (44 to 50% Stage IV), and hence negates any benefits in overall survival.

So what does this mean for the famous analogy "The Will Rogers Phenomenon" (ie; when the Okies left Oklahoma for California the average IQ of both states went up)?....I think we would have to add Colorado and Utah along the way and assume that once you get to California everybody's IQ becomes "0"!....

NSCLC

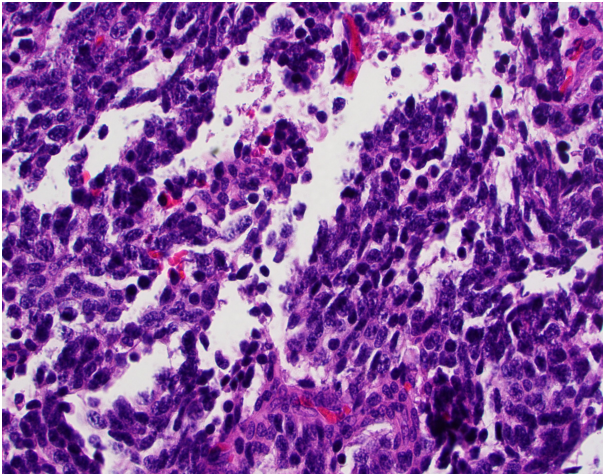
LLL NSCLC do worse than other anatomic sites

2012 Sep;42(3):414-9. Do tumours located in the left lower lobe have worse outcomes in lymph node-positive non-small cell lung cancer than tumours in other lobes? Kudo Y, Saji H, Shimada Y, Nomura M, Usuda J, Kajiura N, Ohira T, Ikeda N. Division of Thoracic Surgery, Department of Surgery, Tokyo Medical University, Tokyo, Japan. **OBJECTIVES:** Although an association between prognosis and lobar location of lung cancer, particularly the left lower lobe (LLL), has been suggested, the certainty of such association remains controversial. The purpose of this study was to evaluate the impact of tumour lobar location on surgical outcomes as an independent prognostic factor for survival in our non-small cell lung cancer (NSCLC) patient series. **METHODS:** We retrospectively reviewed 978 NSCLC patients who underwent complete resection in our hospital between 2000 and 2007. We statistically analysed the association between clinicopathological factors and clinical outcomes. **RESULTS:** Among the 978 patients reviewed, the NSCLC was located in the LLL in 143 (14.6%) patients, and lymph node involvement was identified in 210 patients (21.5%). The 5-year overall survival rates of patients whose NSCLC was located in the LLL and in other lobes (non-LLL) were 73.1 and 74.3%, respectively, and showed no significant association ($P = 0.86$). On the other hand, the 5-year survival rates of patients whose NSCLC occurred in the LLL ($n = 33$) and non-LLL ($n = 177$) and with lymph node metastasis were 32.7 and 57.7%, respectively, and showed a significant association ($P = 0.01$). Therefore, we performed a more detailed analysis on the 210 NSCLC patients with lymph node metastasis. On multivariate analysis, we found that LLL tumour ($P = 0.02$), tumour size >3 cm ($P = 0.02$) and N status ($P < 0.001$) were significant independent predictors for survival. **CONCLUSIONS:** LLL tumours with lymph node metastasis are strongly associated with mortality in NSCLC patients. The location of the primary tumour may contribute in determining the optimal management strategy and accurate prediction of prognosis.

Editor's commentary: Who knew?

Interesting case presentation: fully resected Small Cell Lung Cancer

A 61 yo WF former smoker was seen in a local facility for shortness of breath. A CXR, and subsequently a CT scan, was obtained that showed a 1.4 cm spiculated nodule in the LUL. PET scanning confirmed the suspicious nature of the lesion with an SUV calculated at 3.0. When seen for consultation, her shortness of breath had resolved and she was without symptoms. A recommendation for LUL lobectomy was made on the basis of the suspicious



nature of the lesion and the patient's smoking history. She underwent robotic assisted LUL lobectomy and was discharged from the hospital three days later.

Final pathology showed a 1.5 cm Small Cell Lung Cancer with lymphovascular invasion and two hilar lymph nodes positive for metastatic involvement. All margins were negative.

The consulting oncologist recommended adjuvant concurrent chemoradiation with cisplatin and etoposide.

The role of surgery in Small Cell Lung Cancer is broader than widely appreciated. Resection of PET positive lesions in smokers will result in a small number of previously undiagnosed

tumors as in the above case. In addition, patients with limited SCLC will, on occasion, demonstrate new lesions or have isolated lesions that represent NSCLC unresponsive to treatment directed at SCLC and may be amenable to resection. Mixed histopathologic lesion showing features of both SCLC and NSCLC are relatively common and should be resected if otherwise amenable to surgery.

I have included the abstract of a report from the University of Pittsburgh which reviewed the SEER database for Small Cell Lung Cancer staged in the TNM system as I or II. Of the 3566 patients identified, 25.1% of these patients underwent resection. Resections included: 67% lobectomies, 28% wedge resections, and 4.2% pneumonectomies. Median survival was 34 months for surgically treated patients vs. 16 months in non-surgical patients. Of note, 22.6% of surgically treated patients also received XRT and this was found to be a risk factor significantly associated with better survival.

It is interesting to consider how we came to abandon surgical resection for SCLC in the first place: the most influential report in this regard is the Medical Research Council randomized trial comparing surgery to XRT for SCLC included a complete resection rate of 48% and **no** resection in 52% of patients. There was a very high rate of pneumonectomy and high perioperative mortality rate as well. It certainly appears that surgical resection for SCLC should be reconsidered for operable TMN staged I and II.

Ann Thorac Surg. 2012 Sep;94(3):889-93. *Surgical Resection Should Be Considered for Stage I and II Small Cell Carcinoma of the Lung.* Weksler B, Nason KS, Shende M, Landreneau RJ, Pennathur A. Department of Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania. **BACKGROUND:** Small cell lung carcinoma (SCLC) is rarely treated with resection, either alone or combined with other modalities. This study evaluated the role of surgical resection in the treatment of stage I and II SCLC. **METHODS:** We queried the Surveillance, Epidemiology, and End Results (SEER) database for patients from 1988 to 2007 with SCLC. Survival was determined by Kaplan-Meier analysis and compared using the log-rank test. A Cox proportional hazard model identified relevant survival variables. **RESULTS:** We identified 3,566 patients with stage I or II SCLC. Lung resection was performed in 895 (25.1%), wedge resection in 251 (28.0%), lobectomy or pneumonectomy in 637 (71.2%), and lung resection not otherwise specified in 7 (0.78%). Median survival was 34.0 months (95% confidence interval [CI], 29.0 to 39.0 months) vs 16.0 months (95% CI, 15.3 to 16.7; $p < 0.001$) in nonsurgical patients. Median survival after lobectomy or pneumonectomy was 39.0 months (95% CI, 30.7 to 40.3) and significantly longer than after wedge resection (28.0 months; 95% CI, 23.2 to 32.8; $p = 0.001$). However, survival after wedge resection was still significantly longer than survival in nonsurgical patients ($p < 0.001$). Sex ($p = 0.013$), age, stage at diagnosis, radiotherapy, and operation (all $p < 0.001$) significantly affected survival. In the surgical patients, sex ($p = 0.001$), age ($p < 0.001$), final stage ($p < 0.001$), and type of resection ($p = 0.01$) were important determinants of survival. **CONCLUSIONS:** Surgical resection as a component of treatment for stage I or II SCLC is associated with significantly improved survival and should be considered in the management of early-stage SCLC.

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Contact us:

Florida Heart and Lung Surgery

4007 N. Taliaferro Ave; Suite C

Tampa, FL 33603

email: esommers@fhls.com tel: 813 238-0810

website: fhls.com



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Florida Heart and Lung Surgery
4007 N. Taliaferro Ave.; Suite C
Tampa, FL 33603