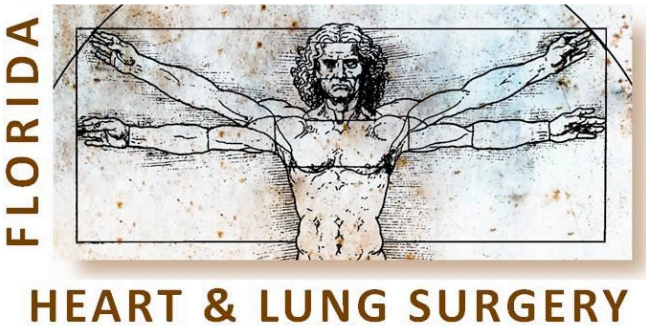
Review of Thoracic Surgical Oncology



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Editor's note: I am pleased to include my own peer reviewed publication in this month's review. Please see below.

NSCLC

Multi-center review shows robotic lobectomy equal to or better outcomes compared to open or VATS lobectomy

Ann Thorac Surg. 2014 Apr 11. Initial Multicenter Community Robotic Lobectomy Experience: Comparisons to a National Database. Adams RD1, Bolton WD2, Stephenson JE2, Henry G3, Todd Robbins E4, Sommers E5. BACKGROUND: In pulmonary lobectomy, video-assisted thoracoscopic surgery (VATS) offers advantages compared with open thoracotomy. However, various issues have limited its adoption, especially in community settings. Single surgeon studies suggest that completely portal robotic lobectomy (CPRL) may address such limitations. This multicenter study evaluates early CPRL experience in 6 community cardiothoracic surgeons' practices. METHODS: Perioperative data from each surgeon's initial 20, consecutive and unselected cases of CPRL were retrospectively gathered (total n = 120) and compared with the 2009 and 2010 Society of Thoracic Surgeons database for VATS (n = 4,612) and open (n = 5,913) lobectomy. The $\chi 2$ and t test procedures were used and significance was defined at the 95% confidence level ($p < 0.05$). RESULTS: One hundred sixteen lobectomies (96.7%) were completed robotically with a conversion rate of 3.3%. Preoperative patient characteristics were comparable across the CPRL, VATS, and open groups. The CPRL was equivalent to VATS on all intraoperative and postoperative outcomes, and resulted in significantly lower postoperative blood transfusion rates (0.9% vs 7.8%; $p = 0.002$), air leaks greater than 5 days (5.2% vs 10.8%; $p = 0.05$), chest tube duration (3.2 days vs 4.8 days; $p < 0.001$), and length of stay (4.7 days vs 7.3 days; $p < 0.001$) when compared with open. For these outcomes, results trended favorably for CPRL over VATS. CONCLUSIONS: This early CPRL experience reveals a minimally invasive lobectomy technique that is safe and reproducible in varied practice settings. Outcomes were equivalent between CPRL and VATS, trending in favor of robotics. The CPRL was superior in several measures compared with open. The absence of patient selection and low conversion rates suggest a broad applicability of this technique.

Editor's commentary: This is a retrospective review of six surgeons' initial experience with robotic lobectomy (including the editor's). This cohort of 116 patients was compared to the STS database results for VATS and open lobectomy. On the whole, outcomes for robotic lobectomy were better when compared to open lobectomy and comparable to VATS. This is one of the first peer reviewed publications to compare robotic results to the established alternatives. Of note,these good results were achieved across a variety of practice settings and hospitals.

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NSCLC

Why do women have better survival than men?

J Thorac Oncol. 2014 Mar;9(3):355-61. Survival in women with NSCLC: the role of reproductive history and hormone use. Katcoff H1, Wenzlaff AS, Schwartz AG. INTRODUCTION: Although lung cancer is the leading cause of cancer death in women, few studies have investigated the hormonal influence on survival after a lung cancer diagnosis and results have been inconsistent. We evaluated the role of reproductive and hormonal factors in predicting overall survival in women with non-small-cell lung cancer (NSCLC). METHODS: Population-based lung cancer cases diagnosed between November 1, 2001 and October 31, 2005 were identified through the Metropolitan Detroit Surveillance, Epidemiology, and End Results Registry. Interview and follow-up data were collected for 485 women. Cox proportional hazard regression models were used to determine hazard ratios (HRs) for death after an NSCLC diagnosis associated with reproductive and hormonal variables. RESULTS: Use of hormone therapy (HT) was associated with improved survival (HR, 0.69; 95% confidence interval, 0.54-0.89), adjusting for stage, surgery, radiation, education level, pack-years of smoking, age at diagnosis, race, and a multiplicative interaction between stage and radiation. No other reproductive or hormonal factor was associated with survival after an NSCLC diagnosis. Increased duration of HT use before the lung cancer diagnosis (132 months or longer) was associated with improved survival (HR, 0.54; 95% confidence interval, 0.37-0.78), and this finding remained significant in women taking either estrogen alone or progesterone plus estrogen, never smokers, and smokers. CONCLUSION: These findings suggest that HT use, in particular use of estrogen plus progesterone, and long-term HT use are associated with improved survival of NSCLC.

Editor's commentary: Women have better stage for stage outcomes than men in NSCLC. This paper examined a subset of the SEER database and examined reproductive variables such as age at first birth, number of children, age at first pregnancy, contraceptive use, use of hormonal therapy and other reproductive demographics. After controlling for stage, surgery, radiation, socioeconomic level, age, and race, the only reproductive variable associated with improved survival was hormonal therapy use. Interestingly, the type of hormonal therapy mattered: combination estrogen and progesterone users did better than estrogen only users, or women who had never taken hormonal therapy. In addition, it took 11 years of use or longer for the effect to become apparent. The authors surmise that progesterone receptor positive lung cancers may have a role in explaining this phenomenon.

NSCLC

First inherited lung cancer syndrome identified

J Thorac Oncol. 2014 Apr;9(4):554-8. Germline EGFR T790M Mutation Found in Multiple Members of a Familial Cohort. Yu HA1, Arcila ME, Harlan Fleischut M, Stadler Z, Ladanyi M, Berger MF, Robson M, Riely GJ. Abstract Activating mutations in epidermal growth factor receptor (EGFR) are present in a subset of lung cancers, and predict sensitivity to EGFR tyrosine kinase inhibitors. Acquisition of EGFR T790M is the most common mechanism of resistance to EGFR tyrosine kinase inhibitors and rarely is seen before treatment. Germline EGFR T790M mutations have been reported, although the penetrance and clinical significance of this mutation is unknown. We describe the identification of a patient with an EGFR T790M germline mutation and subsequent germline testing in her unaffected family members. Genetic testing revealed two additional EGFR T790M germline carriers, one of which was subsequently diagnosed with metastatic lung adenocarcinoma.

J Thorac Oncol. 2014 Apr;9(4):456-63. Hereditary Lung Cancer Syndrome Targets Never Smokers with Germline EGFR Gene T790M Mutations. Gazdar A1, Robinson L, Oliver D, Xing C, Travis WD, Soh J, Toyooka S, Watumull L, Xie Y, Kernstine K, Schiller JH. INTRODUCTION: Hereditary lung cancer syndromes are rare, and T790M germline mutations of the epidermal growth factor receptor (EGFR) gene predispose to the development of lung cancer. The goal of this study was to determine the clinical features and smoking status of lung cancer cases and unaffected family members with this germline mutation and to estimate its incidence and penetrance. METHODS: We studied a family with germline T790M mutations over five generations (14 individuals) and combined our observations with data obtained from a literature search (15 individuals). RESULTS: T790M germline mutations occurred in approximately 1% of non-small-cell lung cancer cases and in less than one in 7500 subjects without lung cancer. Both sporadic and germline T790M mutations were predominantly adenocarcinomas, favored female gender, and were occasionally multifocal. Of lung cancer tumors arising in T790M germline mutation carriers, 73% contained a second activating EGFR gene mutation. Inheritance was dominant. The odds ratio that T790M germline carriers who are smokers will develop lung cancer compared with never smoker carriers was 0.31 (p = 6.0E-05). There was an overrepresentation of never smokers with lung cancer with this mutation compared with the general lung cancer population (p = 7.4E-06). CONCLUSION: Germline T790M mutations result in a unique hereditary lung cancer syndrome that targets never smokers, with a preliminary estimate of 31% risk for lung cancer in never smoker carriers, and this risk may be lower for heavy smokers. The resultant cancers share several features and differences with lung cancers containing sporadic EGFR mutations.

Editor's commentary: Two independent reports and an accompanying editorial describe the first inherited lung cancer syndrome caused by somatic mutation in the EGFR gene. 14 members of the identified family in the second report faced a 31% risk of developing lung cancer, typically in non-smokers.

NSCLC

Introduction of PET scanning into lung cancer practice reduced rates of surgery and XRT: costs unaffected.

J Thorac Oncol. 2014 Apr;9(4):512-8. Redistribution of Health Care Costs after the Adoption of Positron Emission Tomography among Medicare Beneficiaries with Non-Small-Cell Lung Cancer, 1998-2005. Dinan MA1, Curtis LH, Carpenter WR, Biddle AK, Abernethy AP, Patz EF Jr, Schulman KA, Weinberger M. INTRODUCTION: Treatment patterns and cost implications of increased positron emission tomography imaging use since Medicare approval in 1998 are not well understood. We examined rates of surgery, radiotherapy, and chemotherapy and inpatient and total health care costs between 1998 and 2005 among Medicare beneficiaries with non-small-cell lung cancer. METHODS: Patients in this retrospective cohort study were 51,374 Medicare beneficiaries diagnosed with non-small-cell lung cancer between 1996 and 2005. The main outcome measures were receipt of surgical resection, radiotherapy, and chemotherapy and inpatient and total health care costs within 1 year of diagnosis. RESULTS: Between 1996-1997 and 2004-2005, the proportion of patients undergoing surgical resection decreased from 29% to 25%, the proportion receiving radiation therapy decreased from 49% to 43%, and inpatient costs decreased from $28,900 to $26,900. The proportion of patients receiving chemotherapy increased from 25% to 40% and total costs increased from $47,300 to $52,200 ($p < 0.001$ for all comparisons). Changes in use and costs remained after adjustment for shifting demographic characteristics during the study period. CONCLUSIONS: Adoption of positron emission tomography between 1998 and 2005 was accompanied by decreases in rates of surgery and radiotherapy and in short-term inpatient costs among Medicare beneficiaries with non-small-cell lung cancer, although there was an increase in chemotherapy and overall costs.

Editor's commentary: This paper analyzes the effects that the introduction of PET scanning had on treatment and costs on Medicare beneficiaries from 1998 to 2005. Not surprisingly, rates of surgery decreased from 29.1% to 24.7%. Use of XRT decreased as well. Use of chemotherapy increased from 25.1% to 40.4%. Overall costs increased from $47,335 to $52,209 on average. Note that this analysis does not include oral agents and chemotherapy given on an outpatient basis. One can easily surmise that chemotherapy costs are even greater in the present era given the availability and approval of oral agents, maintenance treatments, avastin, and second line chemotherapy. While PET scanning has avoided futile surgery in a small percentages of patients, there is currently no evidence in the literature that it has improved the cost efficiency of lung cancer treatment, or improved survival either.

NSCLC

Combining N1 and N2 classifications leads to better prognostic accuracy

Ann Thorac Surg. 2014 Apr;97(4):1156-62. Long-Term Survival of Patients With pN2 Lung Cancer According to the Pattern of Lymphatic Spread. Legras A1, Mordant P1, Arame A1, Foucault C1, Dujon A2, Le Pimpec Barthes F1, Riquet M3. N2 involvement has dramatic consequences on the prognosis and management of patients with non-small cell lung cancer (NSCLC). N2-NSCLC may present with or without N1 involvement, constituting non-skip (pN1N2) and skip (pN0N2) diseases, respectively. As the prognostic impact of this subclassification is still a matter of debate, we analyzed the prognosis of pN2 patients according to the pN1-involvement and the number of N2-stations concerned. METHODS: The medical records of consecutive patients who underwent surgery for pN2-NSCLC in 2 French centers between 1980 and 2009 were prospectively collected and retrospectively reviewed. Patients undergoing induction therapy, exploratory thoracotomy, incomplete mediastinal lymphadenectomy, or incomplete resections were excluded. The prognoses of pN1N2 and pN0N2 patients were first compared, and then deciphered according to the number of N2 stations involved (single-station: 1S, multi-station: 2S). RESULTS: All together, 871 patients underwent first-line complete surgical resection for pN2-NSCLC during the study period, including 258 pN0N2 (29.6%) and 613 pN1N2 (70.4%) patients. Mean follow-up was 72.8 ± 48 months. Median, 5- and 10-year survivals were, respectively, 30 months, 34%, and 24% for pN0N2 and 20 months, 21%, and 14% for pN1N2 patients ($p < 0.001$). Multivariate analysis revealed 3 different prognostic groups; ie, favorable in pN0N2-1S disease, intermediate in pN0N2-2S and pN1N2-1S diseases, and poor in pN1N2-2S disease ($p < 0.001$). CONCLUSIONS: Among pN2 patients, the combination of N1 involvement (pN0N2 vs pN1N2) and number of involved N2 stations (1S vs 2S) are independent prognostic factors. These results might be taken into consideration to sub-classify the heterogeneous pN2-NSCLC group of patients

Editor's commentary: In this report, the authors retrospectively analyzed survival of resected NSCLC by analyzing N1 involvement as well as N2. For example, if N1 nodes were negative, but a single station N2 node was identified, then this would be classified as N0N2. Not surprisingly, those patients with both N1 and N2 nodes positive did worse than those with N0N2 or "skip N2." It calls into question our current staging paradigm of reporting the "highest" station involved, even if lower stations are in truth, uninvolved.

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