

Review of Thoracic Surgical Oncology

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Lung cancer screening

AATS issues lung cancer screening guidelines

J Thorac Cardiovasc Surg. 2012 Jul;144(1):25-32. Development of The American Association for Thoracic Surgery guidelines for low-dose computed tomography scans to screen for lung cancer in North America: Recommendations of The American Association for Thoracic Surgery Task Force for Lung Cancer Screening and Surveillance. Jacobson FL, Austin JH, Field JK, Jett JR, Keshavjee S, Macmahon H, Mulshine JL, Munden RF, Salgia R, Strauss GM, Sugarbaker DJ, Swanson SJ, Travis WD, Jaklitsch MT. Brigham and Women's Hospital, Harvard Medical School, Boston, Mass. **OBJECTIVE:** The study objective was to establish The American Association for Thoracic Surgery (AATS) lung cancer screening guidelines for clinical practice. **METHODS:** The AATS established the Lung Cancer Screening and Surveillance Task Force with multidisciplinary representation including 4 thoracic surgeons, 4 thoracic radiologists, 4 medical oncologists, 1 pulmonologist, 1 pathologist, and 1 epidemiologist. Members have engaged in interdisciplinary collaborations regarding lung cancer screening and clinical care of patients with, and at risk for, lung cancer. The task force reviewed the literature, including screening trials in the United States and Europe, and discussed local best clinical practices in the United States and Canada on 4 conference calls. A reference library supported the discussions and increased individual study across disciplines. The task force met to review the literature, state of clinical practice, and recommend consensus-based guidelines. **RESULTS:** Nine of 14 task force members were present at the meeting, and 3 participated by telephone. Two absent task force members were polled afterward. Six unanimous recommendations and supporting work-up algorithms were presented to the Council of the AATS at the 2012 annual meeting in San Francisco, California. **CONCLUSIONS:** Annual lung cancer screening and surveillance with low-dose computed tomography is recommended for smokers and former smokers with a 30 pack-year history of smoking and long-term lung cancer survivors aged 55 to 79 years. Screening may begin at age 50 years with a 20 pack-year history of smoking and additional comorbidity that produces a cumulative risk of developing lung cancer of 5% or greater over the following 5 years. Screening should be undertaken with a subspecialty qualified interdisciplinary team. Patient risk calculator application and intersociety engagement will provide data needed to refine future lung cancer screening guidelines.

Editor's commentary: These guidelines were developed by the AATS, a specialty organization of thoracic surgeons. They differ in a few significant ways from the previously issued NCCN and IASLC recommendations: the AATS is recommending lifelong annual screening rather than three consecutive years in recognition of the minimal risk of radiation dosing and the constant rate of new cancer detected each year of the NLST; the AATS guidelines recognize that 74 is not very old in terms of lung cancer diagnosis and treatment, and raises the older age limit to 79 years old; and the guidelines add surveillance screening for 5 year survivors of lung cancer. The preponderance of surgeons on this panel no doubt colors their recommendations, particularly the raising of the age limit for screening. Not surprisingly, this group recommends only experienced thoracic surgeons be included on screening panels, although, this has practical limitations based on the availability of such individuals in each community.

PET suv, lymphovascular invasion, among other traditional factors predict recurrence

Ann Thorac Surg. 2012 Jun;93(6):1813-21. Epub 2012 Apr 26. Tumor recurrence after complete resection for non-small cell lung cancer. Taylor MD, Nagji AS, Bhamidipati CM, Theodosakis N, Kozower BD, Lau CL, Jones DR. Division of Thoracic and Cardiovascular Surgery, Department of Surgery, University of Virginia, Charlottesville, Virginia. **BACKGROUND:** Long-term survival after R0 resection for non-small cell lung cancer (NSCLC) is less than 50%. The majority of mortality after resection is related to tumor recurrence. The purpose of this study was to identify independent perioperative and pathologic variables that are associated with NSCLC recurrence after complete surgical resection. **METHODS:** A retrospective examination was performed of a prospectively maintained database of patients who underwent resection for NSCLC from July 1999 to August 2008 at a single institution. Clinicopathologic variables were evaluated for their influence on time to recurrence. Cox's proportional regression hazard model examined the association of recurrence in NSCLC. **RESULTS:** A total of 1,143 patients met inclusion criteria and had complete follow-up information. Of these patients, 378 (33.1%) had recurrence of the primary cancer. Median follow-up was 24 months (range, 3-134 months). Preoperative tumor maximum standardized uptake value (SUV(max)) greater than 5 was associated with increased risk of recurrence (hazard ratio [HR], 1.81; $p = 0.01$). Preoperative radiation was independently associated with recurrence (HR, 1.98; $p = 0.05$) as well as the presence of pathologic stage II and stage III disease (stage II: HR, 2.53; $p = 0.05$; stage III: HR, 6.49; $p = 0.006$). Subgroup analysis found that sublobar resection was also associated with locoregional recurrence after resection (HR, 4.17; $p = 0.02$) and lymphovascular invasion of distant recurrence (HR, 4.21; $p = 0.002$). **CONCLUSIONS:** In the largest series reported to date on postresectional recurrence of NSCLC, SUV(max) greater than 5, increasing pathologic stage, and the administration of preoperative radiation were independently associated with NSCLC recurrence after resection. Sublobar resection was independently associated with locoregional recurrence, and lymphovascular invasion was associated with distant recurrence.

Editor's commentary: This retrospective study identified PET suv >5 as a risk factor for recurrence following R0 surgical resection. Lymphovascular invasion was also identified which is similar to several recent reports. Other well described risk factors for recurrence were also seen such as stage and sublobar resection, mostly wedge resection. This report raises the question of whether we should consider post-operative adjuvant (or even neoadjuvant) treatment for patients with high preoperative suv lesions on PET scanning.

Stage IIIA NSCLC

Meta-analysis does not support use of XRT in induction treatment of Stage IIIA NSCLC

Ann Thorac Surg. 2012 Jun;93(6):1807-12. Induction Chemoradiation Is Not Superior to Induction Chemotherapy Alone in Stage IIIA Lung Cancer. Shah AA, Berry MF, Tzao C, Gandhi M, Worni M, Pietrobon R, D'Amico TA. Department of Surgery, Duke University Medical Center, Durham, North Carolina. **BACKGROUND:** The optimal treatment strategy for patients with operable stage IIIA (N2) non-small cell lung cancer is uncertain. We performed a systematic review and meta-analysis to test the hypothesis that the addition of radiotherapy to induction chemotherapy prior to surgical resection does not improve survival compared with induction chemotherapy alone. **METHODS:** A comprehensive search of PubMed for relevant studies comparing patients with stage IIIA (N2) non-small cell lung cancer undergoing resection after treatment with induction chemotherapy alone or induction chemoradiotherapy was conducted using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) standards. Hazard ratios were extracted from these studies to give pooled estimates of the effect of induction therapy on overall survival. **RESULTS:** There were 7 studies that met criteria for analysis, including 1 randomized control trial, 1 phase II study, 3 retrospective reviews, and 2 published abstracts of randomized controlled trials. None of the studies demonstrated a survival benefit to adding induction radiation to induction chemotherapy versus induction chemotherapy alone. The meta-analysis performed on randomized studies ($n = 156$ patients) demonstrated no benefit in survival from adding radiation (hazard ratio 0.93, 95% confidence interval 0.54 to 1.62, $p = 0.81$), nor did the meta-analysis performed on retrospective studies ($n = 183$ patients, hazard ratio 0.77, 95% confidence interval 0.50 to 1.19, $p = 0.24$). **CONCLUSIONS:** Published evidence is sparse but does not support the use of radiation therapy in induction regimens for stage IIIA (N2). Given the potential disadvantages of adding radiation preoperatively, clinicians should consider using this treatment strategy only in the context of a clinical trial to allow better assessment of its effectiveness.

Editor's commentary: It has never been part of my practice to add XRT to induction treatment of IIIA disease and this paper supports that bias. Furthermore, in my opinion, the weight of evidence favors adjuvant over induction treatment as well, although, there are selected instances where I recommend induction.

Large series of thymic carcinoid tumors identifies size and proliferation index as prognostic predictors

Ann Thorac Surg. 2012 Jul;94(1):241-6. Primary neuroendocrine tumors of the thymus: a multicenter experience of 35 patients. Cardillo G, Rea F, Lucchi M, Paul MA, Margaritora S, Carleo F, Marulli G, Mussi A, Granone P, Graziano P. Department of Thoracic Surgery, Azienda Ospedaliera San Camillo Forlanini, Carlo Forlanini Hospital, Rome, Italy. **BACKGROUND:** Primary neuroendocrine tumors of the thymus (NETT) are rare tumors and represent a distinct category of tumors collectively displaying morphologic and biological neuroendocrine features. We sought to evaluate factors influencing long-term survival in patients with primary NETT. **METHODS:** From January 1990 to April 2011, 35 patients (27 male patients and 8 female patients) were surgically treated for primary NETT at 5 institutions. **RESULTS:** No operative (30-day) mortality occurred. Morbidity was 37.14% (13/35 patients). All patients were followed for a total of 2,703 months. Fourteen patients had associated paraneoplastic syndrome. Twenty-four patients are alive, 19 of whom are free of disease and 5 of whom continue to have disease. The median overall survival was 153 months. The overall 5-year and 10-year actuarial survival rates were 84.34% and 60.82%, respectively. The 10-year survival was evaluated according to histologic type (typical carcinoid, 77.92%; atypical carcinoid, 54.55%; large-cell neuroendocrine carcinomas, 0%; Masaoka staging (stage I, 100%; stage II, 66.67%; stage III, 61.9%; stage IVa, 25%; stage IVb, 0%), presence of paraneoplastic syndrome (no = 70.67%; yes = 32.14%), postoperative radiotherapy (yes = 39.71%; no = 85.71%), Surveillance, Epidemiology, and End Results (SEER) staging system (localized disease, 83.3%; regional disease, 53.3%; distant disease, 0%), tumor size (<7 cm = 90.9%; ≥7cm = 28.7%; $p = 0.0007$), and Ki67 expression, which was available in 23 patients (<10% = 85.71%; ≥10% = 0%; $p = 0.0037$). **CONCLUSIONS:** The prognosis of primary NETT is statistically significantly related to tumor size >7 cm and to the proliferation index (evaluated by Ki67 expression >10%). The histologic type of the neoplasm, the presence of a paraneoplastic syndrome, the Masaoka staging, the evidence of distant disease, and postoperative radiotherapy also impact prognosis.

Editor's commentary: Thymic carcinoid remains a difficult clinical problem: locally aggressive without good adjuvant treatment options. An experienced surgeon remains your best bet.

Esophageal Cancer

Neoadjuvant Rx improves survival vs. surgery alone

N Engl J Med. 2012 May 31;366(22):2074-84. Preoperative chemoradiotherapy for esophageal or junctional cancer. van Hagen P, Hulshof MC, van Lanschot JJ, Steyerberg EW, van Berge Henegouwen MI, Wijnhoven BP, Richel DJ, Nieuwenhuijzen GA, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, ten Kate FJ, Creemers GJ, Punt CJ, Plukker JT, Verheul HM, Spillenaar Bilgen EJ, van Dekken H, van der Slangen MJ, Rozema T, Biermann K, Beukema JC, Piet AH, van Rij CM, Reinders JG, Tilanus HW, van der Gaast A; CROSS Group. Department of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands. **BACKGROUND:** The role of neoadjuvant chemoradiotherapy in the treatment of patients with esophageal or esophagogastric-junction cancer is not well established. We compared chemoradiotherapy followed by surgery with surgery alone in this patient population. **METHODS:** We randomly assigned patients with resectable tumors to receive surgery alone or weekly administration of carboplatin (doses titrated to achieve an area under the curve of 2 mg per milliliter per minute) and paclitaxel (50 mg per square meter of body-surface area) for 5 weeks and concurrent radiotherapy (41.4 Gy in 23 fractions, 5 days per week), followed by surgery. **RESULTS:** From March 2004 through December 2008, we enrolled 368 patients, 366 of whom were included in the analysis: 275 (75%) had adenocarcinoma, 84 (23%) had squamous-cell carcinoma, and 7 (2%) had large-cell undifferentiated carcinoma. Of the 366 patients, 178 were randomly assigned to chemoradiotherapy followed by surgery, and 188 to surgery alone. The most common major hematologic toxic effects in the chemoradiotherapy-surgery group were leukopenia (6%) and neutropenia (2%); the most common major nonhematologic toxic effects were anorexia (5%) and fatigue (3%). Complete resection with no tumor within 1 mm of the resection margins (R0) was achieved in 92% of patients in the chemoradiotherapy-surgery group versus 69% in the surgery group ($P < 0.001$). A pathological complete response was achieved in 47 of 161 patients (29%) who underwent resection after chemoradiotherapy. Postoperative complications were similar in the two treatment groups, and in-hospital mortality was 4% in both. Median overall survival was 49.4 months in the chemoradiotherapy-surgery group versus 24.0 months in the surgery group. Overall survival was significantly better in the chemoradiotherapy-surgery group (hazard ratio, 0.657; 95% confidence interval, 0.495 to 0.871; $P = 0.003$). **CONCLUSIONS:** Preoperative chemoradiotherapy improved survival among patients with potentially curable esophageal or esophagogastric-junction cancer. The regimen was associated with acceptable adverse-event rates.

Editor's commentary: This was a well done randomized trial comparing neoadjuvant treatment with carboplatin/paclitaxel and 41Gy vs. surgery alone. The trial included both adenocarcinomas (75%) and squamous cell histology (23%) and had acceptable operative mortality of 4% in each group. Median overall survival was much better in the neoadjuvant group, 49.4 months vs 24.0 months in the surgery alone group. There was a phenomenally high anastomotic leak rate of 22% in the neoadjuvant group and 30% in the surgery alone group: far higher than any reported leak rate I have seen. (Since the mortality was good, it is likely this was artifactually elevated by the reporting requirements of the trial). A complete pathologic response was seen in 27% of the pretreated group, a subset known to have a good prognosis. Interestingly, surgical approaches included Ivor-Lewis, as well as transhiatal resection.

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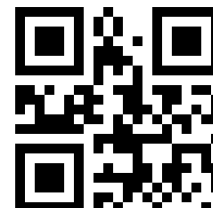
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