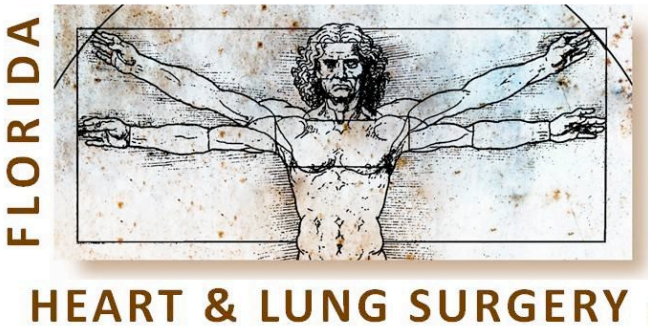
Review of Thoracic Surgical Oncology



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Editor's note: This month's Review features the National Lung Screening Trial published in the NEJM. The NLST was a massive undertaking that will influence the care of lung cancer patients for years to come. I was proud to participate in this effort while at Moffitt and contributed surgical care to several of the enrollees. Please spend a few moments reviewing the results of this very important trial. Go to www.nejm.org/doi/full/10.1056/NEJMoa1102873 or scan the QR code at the bottom of the page to view the full text article.

Lung Cancer Screening

NLST reports: Lung cancer mortality cut by 20% with CT scans but at a cost of a 96% false positive rate

BACKGROUND The aggressive and heterogeneous nature of lung cancer has thwarted efforts to reduce mortality from this cancer through the use of screening. The advent of low-dose helical computed tomography (CT) altered the landscape of lung-cancer screening, with studies indicating that low-dose CT detects many tumors at early stages. The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer

METHODS From August 2002 through April 2004, we enrolled 53,454 persons at high risk for lung cancer at 33 U.S. medical centers. Participants were randomly assigned to undergo three annual screenings with either low-dose CT (26,722 participants) or single-view posteroanterior chest radiography (26,732). Data were collected on cases of lung cancer and deaths from lung cancer that occurred through December 31, 2009.

RESULTS The rate of adherence to screening was more than 90%. The rate of positive screening tests was 24.2% with low-dose CT and 6.9% with radiography over all three rounds. A total of 96.4% of the positive screening results in the low-dose CT group and 94.5% in the radiography group were false positive results. The incidence of lung cancer was 645 cases per 100,000 person-years (1060 cancers) in the low-dose CT group, as compared with 572 cases per 100,000 person-years (941 cancers) in the radiography group (rate ratio, 1.13; 95% confidence interval [CI], 1.03 to 1.23). There were 247 deaths from lung cancer per 100,000 person-years in the low-dose CT group and 309 deaths per 100,000 person-years in the radiography group, representing a relative reduction in mortality from lung cancer with low-dose CT screening of 20.0% (95% CI, 6.8 to 26.7; P=0.004). The rate of death from any cause was reduced in the low-dose CT group, as compared with the radiography group, by 6.7% (95% CI, 1.2 to 13.6; P=0.02).

CONCLUSIONS Screening with the use of low-dose CT reduces mortality from lung cancer. (Funded by the National Cancer Institute; National Lung Screening Trial ClinicalTrials.gov number, NCT00047385.)

Scan with your QR reader to browse to the full text NEJM article

Editor's commentary: The NLST randomized over 53,000 patients to either three years of annual low dose CT scanning vs. three annual CXRs. The patients were then followed for an average of 3.5 years. The 20% reduction in mortality achieved by low dose CT screening is a phenomenal advance for any cancer, much less lung cancer.

The findings are consistent with clinical experience: the CT screened patients had more early stage cancers, and more bronchioalveolar cancers discovered. However, the expense and added procedural risk associated with the very high false positive rates will hamper widespread policy adoption of this approach. This trial is loaded with useful information and caveats:

-the huge number of false positives adds enormous costs in addition to the up-front costs of the scans themselves. (Keep in mind however that simple CXR screening in the other randomized arm also had a high rate of false positives). It remains to be seen if the payors will take this on as a covered benefit. Final policy recommendations will have to await cost-benefit analysis.

-over the period of screening, a cumulative total of 39.1% of CT screened patients had a positive result that required further work-up; 16% of CXR screened patients were positive over the three year screening period.

-the number of cancers identified did not change much from year 0 to year 2 which implies that screening would have to be ongoing: another additional cost.

-the entry criterion and definition of "heavy smoker" was not particularly exclusive in my experience: 30 pack/years active or quit within 15 years of the entry. I would imagine there are quite a few patients in all of our practices that meet this criterion. Furthermore, the trial only enrolled those over 55....there are millions of patients who meet this criterion who are less than 55 years old...what about them?

-60% of CT screened patients had surgery as part of their first line treatment vs. 44% of CXR screened patients.

-interestingly, patients in the CXR screened arm were more likely to have a cancer diagnosed in the follow up period than during the period of screening. On the other hand, CT screened patients were almost twice as likely to have their cancer detected during the screening period than in the follow up.

-24.5% of all patient deaths were from lung cancer in the enrolled population....this factoid re-enforces how prevalent death from lung cancer remains in this cohort of (relatively) heavy smokers.....

-over the entire time period of the study, there were 119 more cancers identified in the CT screening group which raises the topic of "indolent" lung cancer. In other words, it must be assumed that there are a near equivalent number of cancers in both groups but if CT scanning identified nearly 12% more tumors that did not subsequently emerge in the CXR group, then these must be indolent and non-life threatening. Some would argue that small BAC fall into this category. At any rate, it seems inherently dangerous to consider any lung cancer "indolent" but it certainly seems as if there may be a subset that may be worth identifying in future work.

Esophageal Cancer

Clinically staged T2N0 and T3N0 cancers harbor node positive disease in 60% of pathologic specimens

Ann Thorac Surg 2011;92:491-498. doi:10.1016/j.athoracsur.2011.04.004:

No consensus exists on the optimal treatment strategy for clinical T2-T3N0M0 esophageal cancer. This study was conducted to determine rates of nodal positivity (N +) and to evaluate results of treatment strategies in this cohort.

Methods: Surgically treated patients with cT2-T3N0M0 esophageal cancer were reviewed. Adequacy of lymph node dissection was assessed by guidelines applied to clinical stage. Survival was determined by Kaplan-Meier analysis. Univariate and multivariate analyses were done for predictors of N+ and survival.

Results: We identified 102 patients, 51 cT2N0 and 51 cT3N0, 39 (38%) of whom had induction therapy. Despite being clinically node negative, 61 patients (60%) had nodal metastases. Applied to cT classification, adequate nodal dissection was achieved in 64 patients (63%). Transthoracic esophagectomy was more likely than transhiatal esophagectomy to achieve adequate nodal dissection (69% versus 31%, p = 0.005). Adequate nodal dissection was more likely to document pN+ disease in both the surgery alone group (70% versus 50%, p = 0.13) and induction therapy group (71% versus 33%, p = 0.02). Five-year overall survival was 44% with surgery alone and 55% with induction therapy. On multivariate analysis, pN+ was the strongest predictor of overall survival (relative risk 2.73, confidence interval: 1.29 to 5.78).

Conclusions: Most cT2-T3N0M0 patients have pN+ disease. Despite induction therapy, more than 50% have persistent nodal disease. Transthoracic esophagectomy is more likely to detect pN+ disease and more likely to meet criteria of adequate nodal dissection than is transhiatal esophagectomy. Therefore, the majority of patients with cT2-T3N0M0 should be considered for neoadjuvant protocols and should be treated by transthoracic resection whenever possible.

Editor's commentary: A common theme in surgery for esophageal cancer is clinical understaging, even with EUS and PET. This report from Memorial-Sloan-Kettering shows an incidence of 60% occult nodal involvement in clinically staged N0 patients. They also show the usual Memorial predilection for maximal lymphadenectomy with some biased statements about transhiatal vs transthoracic resection approaches.

Pulmonary metastasectomy

Pulmonary metastasectomy gives good results across tumor types

J Thorac Oncol. 2011 Aug 24 Outcome after Pulmonary Metastasectomy: Analysis of 5 Years Consecutive Surgical Resections 2002-2006.

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INTRODUCTION: In this study, we analyze the results of management of pulmonary metastases in 5 years consecutive operations at our institution. We aim to define the patients who are most likely to benefit from surgery by investigating long-term survival and prognostic factors associated with prolonged survival. METHODS: The data on all consecutive patients between 2002 and 2006 were reviewed retrospectively. One hundred seventy-eight patients underwent 256 surgical resections for suspected pulmonary metastases from different primary malignancies. Prognostic factors analyzed included age, sex, surgical approach, surgical resection, number of metastases, distribution of metastases, disease-free interval, presence of synchronous metastases, recurrence of disease, prior liver resection (colorectal cancer), and tumor histology (sarcomas). RESULTS:Complete resection was achieved in 248 cases (96.8%). The mean follow-up was 61.6 months. Five-year survival with respect to primary malignancy was colorectal carcinoma (50.3%), sarcoma (21.7%), malignant melanoma (25.0%), renal cell carcinoma (51.4%), and miscellaneous malignancies (50.0%). Of the prognostic factors analyzed by univariate analysis, none was found to be significant in all the different groups of cancers. CONCLUSIONS: Pulmonary metastasectomy is a safe and effective treatment that may be associated with prolonged survival in highly selected patients. Low morbidity and mortality rates in contrast with the lack of any other effective treatment justify the aggressive approach of surgery. Thoracoscopic resection is a valid option in selected patients. In case of recurrence of pulmonary disease and if the patient fulfils the initial criteria for pulmonary metastasectomy, repeat surgery should be performed. Solid prognostic factors still need to be established.

Editor's commentary: Another report validating the usefulness of metastasectomy in various tumor histologies. VATS in selected patients also found to be useful, consistent with my experience.

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