

Review of Thoracic Surgical Oncology

FLORIDA



HEART & LUNG SURGERY

Presented and distributed by Florida Heart and Lung Surgery

Edited by K. Eric Sommers, MD, FACS

May 2012, Vol 2: number 5.

Editor's note: Florida Heart and Lung Surgery is pleased to announce office hours in Leesburg to accommodate patients in the Ocala/Villages/Leesburg area.

Lung adenocarcinoma

Prognosis in lung adenocarcinoma predicted by histopathologic sub-types

J Clin Oncol. 2012 May 1;30(13):1438-46. The novel histologic international association for the study of lung cancer/american thoracic society/european respiratory society classification system of lung adenocarcinoma is a stage-independent predictor of survival. Warth A, Muley T, Meister M, Stenzinger A, Thomas M, Schirmacher P, Schnabel PA, Budczies J, Hoffmann H, Weichert W. Institute for Pathology, University Hospital Heidelberg, Im Neuenheimer Feld 220/221, D-69120 Heidelberg, Germany; arne.warth@med.uni-heidelberg.de.

PURPOSE Our aim was to analyze and validate the prognostic impact of the novel International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) proposal for an architectural classification of invasive pulmonary adenocarcinomas (ADCs) across all tumor stages. **PATIENTS AND METHODS** The architectural pattern of a large cohort of 500 patients with resected ADCs (stages I to IV) was retrospectively analyzed in 5% increments and classified according to their predominant architecture (lepidic, acinar, solid, papillary, or micropapillary), as proposed by the IASLC/ATS/ERS. Subsequently, histomorphologic data were correlated with clinical data, adjuvant therapy, and patient outcome. **Results** Overall survival differed significantly between lepidic (78.5 months), acinar (67.3 months), solid (58.1 months), papillary (48.9 months), and micropapillary (44.9 months) predominant ADCs ($P = .007$). When patterns were lumped into groups, this resulted in even more pronounced differences in survival (pattern group 1, 78.5 months; group 2, 67.3 months; group 3, 57.2 months; $P = .001$). Comparable differences were observed for overall, disease-specific, and disease-free survival. Pattern and pattern groups were stage- and therapy-independent prognosticators for all three survival parameters. Survival differences according to patterns were influenced by adjuvant chemoradiotherapy; in particular, solid-predominant tumors had an improved prognosis with adjuvant radiotherapy. The predominant pattern was tightly linked to the risk of developing nodal metastases ($P < .001$). **CONCLUSION** Besides all recent molecular progress, architectural grading of pulmonary ADCs according to the novel IASLC/ATS/ERS scheme is a rapid, straightforward, and efficient discriminator for patient prognosis and may support patient stratification for adjuvant chemoradiotherapy. It should be part of an integrated clinical, morphologic, and molecular subtyping to further improve ADC treatment.

Editor's commentary: Heterogeneity is the name of the game in lung adenocarcinoma. We are seeing more reports of tumor heterogeneity in prognosis and treatment response based on distinct radiographic, pathologic, and genomic profiles. This report details improved prognosis in the major IASLC/ATS/ERS histologic patterns lepidic predominant and acinar vs. solid/papillary and micro-papillary. Note that the majority of tumors contain multiple histologies within the same specimen and these results are based on the **predominate** histology.

Even with modern staging techniques, many patients are understaged on preoperative studies

Eur J Cardiothorac Surg. 2012 Apr 30. Stage migration: results of lymph node dissection in the era of modern imaging and invasive staging for lung cancer. Kirmani BH, Rintoul RC, Win T, Magee C, Magee L, Choong C, Wells FC, Coonar AS. Department of Thoracic Surgery, Papworth Hospital, Cambridge, UK. **OBJECTIVES:** Lung cancer staging has improved in recent years. Assuming that contemporary detailed preoperative staging may yield a lower rate of stage change after surgery, we were interested to determine the impact of our lymph node dissections performed at the time of surgical resection. **METHODS:** We retrospectively analysed a database in our surgical unit that prospectively captured information on all patients assessed and treated for lung cancer. We reviewed the data on patients who underwent lung cancer surgery with curative intent between January 2006 and August 2010 so as to reflect contemporary practice. Prior to potentially curative treatment, patients systematically underwent staging computerized tomography (CT), integrated positron emission tomography (PET) with CT and brain imaging. Enlarged and/or PET-positive nodes were subject to invasive evaluation to establish the nodal status in line with the current guidelines. This was performed by needle aspiration or biopsy usually with ultrasound guidance, endobronchial or endo-oesophageal ultrasound with needle biopsy; mediastinoscopy; mediastinotomy; video-assisted or open surgery. **RESULTS:** Three hundred and twelve lung cancer resections were performed (a mean age of 68 years [range 42-86] and a male-to-female ratio of 1.14:1). Despite thorough preoperative evaluations, 25.3% of patients had a change in nodal status after lung resection and lymph node dissection; of which 20.8% of patients had a nodal status upstaging. Occult N2 disease was identified in 31 (9.9%) of 312 patients. Patients with cT1 tumours showed a nodal upstaging of 12.3% compared with 25.3% in cT2 tumours. There was no difference in the rate of N2 disease for different tumour histological types. **CONCLUSIONS:** Despite systematic preoperative staging, there continues to be a high rate of nodal status change following surgical resection and lymph node dissection. If considering non-surgical treatments for the early stage lung cancer, the impact of this discrepancy should be considered. If not, errors in prognosis and in determining correct adjuvant treatment may arise.

Editor's commentary: This is a retrospective study that confirms what we all see in our day to day practices: understaging is common, particularly in N2 nodes and larger tumors. This is further re-inforcement that surgical staging is essential. On the other hand, patients who are found to have N2 disease AND negative preoperative PET scans do much better than clinically identified N2 patients.

Esophageal carcinoma

“Cured but wrecked” after esophagectomy

J Clin Oncol. 2012 May 10;30(14):1615-9. Influence of major postoperative complications on health-related quality of life among long-term survivors of esophageal cancer surgery. [Derogar M](#), [Orsini N](#), [Sadr-Azodi O](#), [Lagergren P](#). Upper Gastrointestinal Research, Department of Molecular Medicine and Surgery, Karolinska Institutet, Norra Stationsgatan 67, Level 2, SE-171 76 Stockholm, Sweden; maryam.derogar@ki.se. **PURPOSE** To evaluate the effect of major postoperative complications on health-related quality of life (HRQL) in 5-year survivors of esophageal cancer surgery. **PATIENTS AND METHODS** This study was based on the Swedish Esophageal and Cardia Cancer register with almost complete nationwide coverage and data on esophageal cancer surgery collected prospectively between 2001 and 2005. Patients who were alive 5 years after surgery were eligible. HRQL was assessed longitudinally until 5 years after surgery by using the validated European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire C30 and OES18. Linear mixed models were used to assess the mean score difference (MD) with 95% CIs of each aspect of HRQL in patients with or without major postoperative complications. Adjustment was made for several potential confounders. **Results** Of 153 patients who survived 5 years, 141 patients (92%) answered the 5-year HRQL questionnaires. Of these individuals, 46 patients (33%) sustained a major postoperative complication. Dyspnea (MD, 15; 95% CI, 6 to 23), fatigue (MD, 13; 95% CI, 5 to 20), and eating restrictions (MD, 10; 95% CI, 2 to 17) were clinically and statistically significantly deteriorated throughout the follow-up in patients with major postoperative complications compared with patients without major complications. Although problems with choking declined to levels comparable with patients without major postoperative complications, sleep difficulties and gastroesophageal reflux progressively worsened during follow-up. **CONCLUSION** The occurrence of postoperative complications exerts a long-lasting negative effect on HRQL in patients who survive 5 years after esophagectomy for cancer.

Editor's commentary: I have long seen patients putatively “cured” by trimodality therapy but who are made miserable by the chronic complications of dysphagia, fatigue, shortness of breath, or more severe postoperative complications. I call this the “cured but wrecked” syndrome. I have seen this phenomenon even after operation by the most experienced surgeons in the state, in both Tampa and Miami. These patients can be so miserable and depressed that they regret the decision to undergo surgery at all. Telling them they should be “happy” because they are cured of esophageal cancer doesn't mollify them, understandably. In my experience, it is not possible to predict these unfortunate individuals beforehand so I cannot give a strategy for avoiding this other than good informed consent that it is a rare but real possibility.

Another report of better survival with pleurectomy/decortication vs. extra-pleural pneumonectomy

Ann Thorac Surg. 2012 May;93(5):1658-67. Radical pleurectomy and intraoperative photodynamic therapy for malignant pleural mesothelioma. Friedberg JS, Culligan MJ, Mick R, Stevenson J, Hahn SM, Sterman D, Punekar S, Glatstein E, Cengel K. Division of Thoracic Surgery, University of Pennsylvania, Philadelphia, Pennsylvania. **BACKGROUND:** Radical pleurectomy (RP) for mesothelioma is often considered either technically unfeasible or an operation limited to patients who would not tolerate a pneumonectomy. The purpose of this study was to review our experience using RP and intraoperative photodynamic therapy (PDT) for mesothelioma. **METHODS:** Thirty-eight patients (42-81 years) underwent RP-PDT. Thirty five of 38 (92%) patients also received systemic therapy. Standard statistical techniques were used for analysis. **RESULTS:** Thirty seven of 38 (97%) patients had stage III/IV cancer (according to the American Joint Committee on Cancer [AJCC manual 7(th) Edition, 2010]) and 7/38 (18%) patients had nonepithelial subtypes. Macroscopic complete resection was achieved in 37/38 (97%) patients. There was 1 postoperative mortality (stroke). At a median follow-up of 34.4 months, the median survival was 31.7 months for all 38 patients, 41.2 months for the 31/38 (82%) patients with epithelial subtypes, and 6.8 months for the 7/38 (18%) patients with nonepithelial subtypes. Median progression-free survival (PFS) was 9.6, 15.1, and 4.8 months, respectively. The median survival and PFS for the 20/31 (64%) patients with N2 epithelial disease were 31.7 and 15.1 months, respectively. **CONCLUSIONS:** It was possible to achieve a macroscopic complete resection using lung-sparing surgery in 97% of these patients with stage III/IV disease. The survival we observed with this approach was unusually long for the patients with the epithelial subtype but, interestingly, the PFS was not. The reason for this prolonged survival despite recurrence is not clear but is potentially related to preservation of the lung or some PDT-induced effect, or both. We conclude that the results of this lung-sparing approach are safe, encouraging, and warrant further investigation.

Editor's commentary: Yet another report describing the superiority of radical pleurectomy/decortication over EPP in mesothelioma. I have had the opportunity of using this technique recently for an early mesothelioma and can attest that it is a much easier operation for the patient to recover from. It is quite tedious, however, for the surgeon but so is the alternative, EPP. I look forward to expanding my experience with this operation.

Screening for NSCLC

Analysis favorable for cost effective lung cancer screening

Health Aff (Millwood). 2012 Apr;31(4):770-9. An actuarial analysis shows that offering lung cancer screening as an insurance benefit would save lives at relatively low cost. [Pyenson BS](#), [Sander MS](#), [Jiang Y](#), [Kahn H](#), [Mulshine JL](#). Lung cancer screening is not established as a public health practice, yet the results of a recent large randomized controlled trial showed that screening with low-dose spiral computed tomography reduces lung cancer mortality. Using actuarial models, this study estimated the costs and benefits of annual lung cancer screening offered as a commercial insurance benefit in the high-risk US population ages 50-64. Assuming current commercial reimbursement rates for treatment, we found that screening would cost about \$1 per insured member per month in 2012 dollars. The cost per life-year saved would be below \$19,000, an amount that compares favorably with screening for cervical, breast, and colorectal cancers. Our results suggest that commercial insurers should consider lung cancer screening of high-risk individuals to be high-value coverage and provide it as a benefit to people who are at least fifty years old and have a smoking history of thirty pack-years or more. We also believe that payers and patients should demand screening from high-quality, low-cost providers, thus helping set an example of efficient system innovation.

Editor's commentary: This report is by far the most optimistic analysis of the cost-effectiveness of widespread screening for lung cancer to appear so far. The cost savings depend, however, on spreading the costs across all members of an insured population. Also, who is going to define "high-quality, low cost providers" and how?

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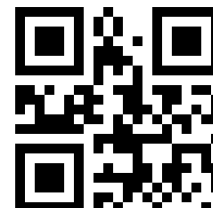
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