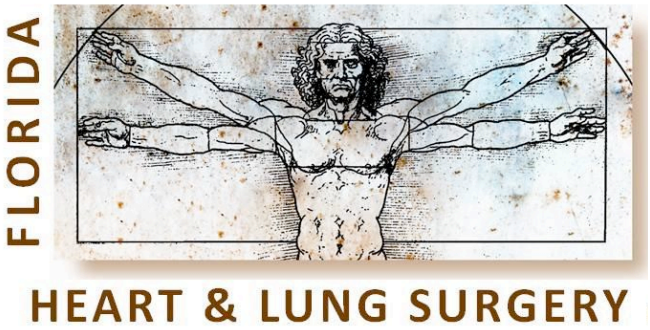
Review of Thoracic Surgical Oncology



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Editor's note: This month's review includes two reports attempting to identify high risk Stage I NSCLC patients. A literature review shows that there are many possible ways to stratify these patients--this month's review features a new commercial test which you will undoubtedly be hearing about. The real issue is treating these high risk patients and demonstrating improved survival, something that has not been done yet.

Thymoma

PET scanning in thymic tumors predictive of tumor behaviour and histology

Eur J Cardiothorac Surg. 2012 Dec;42(6):e152-6. The utility of [18F]-fluorodeoxyglucose positron emission tomography-computed tomography in thymic epithelial tumours. Fukumoto K, Taniguchi T, Ishikawa Y, Kawaguchi K, Fukui T, Kato K, Matsuo K, Yokoi K. Department of Thoracic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan. OBJECTIVES: Positron emission tomography using [(18)F]-fluoro-2-deoxy-d-glucose ((18)F-FDG-PET) plays an important role in many oncological settings. In this study, we assessed the utility of (18)F-FDG PET-CT for predicting the histologic type and stage of thymic epithelial tumours. METHODS: We retrospectively analyzed 58 patients with thymic epithelial tumours who underwent PET-CT before treatment and investigated the relationship between the histologic type based on the World Health Organization classification and the maximum standardized uptake value (SUV(max)) of each tumour. We also analyzed the relationship between the Masaoka tumour stage and the SUV(max). RESULTS: The study included 31 males and 27 females, ranging in age from 25 to 80 years (median: 62 years). The tumour histology of 44 tumours was thymoma and that of the remaining tumours was thymic carcinoma, including 11 squamous cell carcinomas and 3 carcinoids. The Masaoka tumour stage was as follows: Stage I in 8, Stage II in 24, Stage III in 18 and Stage IV in 8 patients. The patients were divided into three groups according to a simplified histologic classification: low-risk thymomas (types A, AB and B1, n = 23), high-risk thymomas (types B2 and B3, n = 21) and thymic carcinomas (n = 14). The SUV(max) of the thymic carcinoma group was significantly higher than those of the low-risk thymoma and high-risk thymoma groups (P < 0.001, respectively). No significant differences between the low-risk thymoma and high-risk thymoma groups were observed (P = 0.204). The SUV(max) of Stages III and IV thymomas showed a higher trend toward Stages I and II thymomas (P = 0.060). CONCLUSIONS: PET-CT is a useful modality for predicting the histologic type and tumour stage of thymic epithelial tumours.

Editor's commentary: This is a small study with relatively small subsets of tumor histology (only three thymic carcinoids for instance) but nevertheless, the authors were able to correlate PET SUVmax with behavior of the tumors. While low risk thymomas are usually cured by resection, high risk thymomas, thymic carcinomas and thymic carcinoids remain a challenge.

Lung mets in colon cancer

Predictors of recurrence in lung metastasectomy for colon mets identified

Ann Thorac Surg. 2012 Oct 10. Predictors of Recurrent Pulmonary Metastases and Survival After Pulmonary Metastasectomy for Colorectal Cancer. Blackmon SH, Stephens EH, Correa AM, Hofstetter W, Kim MP, Mehran RJ, Rice DC, Roth JA, Swisher SG, Walsh GL, Vaporciyan AA. Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, Texas; Department of Surgery, The Methodist Hospital, and Weill Cornell College of Medicine, Houston, Texas. BACKGROUND: Resection of pulmonary colorectal carcinoma metastases may provide long-term benefit, but patient selection remains controversial. The objective of this study was to identify preoperative predictors of survival and lung recurrence for patients undergoing resection of such lesions. METHODS. A prospectively collected database was retrospectively reviewed to identify patients who underwent their first colorectal carcinoma pulmonary metastasectomy. Two multivariate logistic analyses were performed to identify preoperative predictors of survival and lung recurrence. Preoperative factors, pathologic colorectal carcinoma stage, additional sites of metastases, timing of metastatic occurrence, and premetastasectomy disease-free interval were included in the univariate analyses. RESULTS: From January 2000 to December 2010, 229 patients met inclusion criteria. The mean age was 60 years, and 100 patients (43.7%) were women. The overall median time and 5-year survival rate were 70.1 months and 55.4%, respectively, after the first pulmonary metastasectomy. Median follow-up was 37.2 months. Age older than 60 years (hazard ratio [HR], 1.03; 95% confidence interval [CI], 1.005 to 1.052; p = 0.016), male sex (HR, 1.84; 95% CI, 1.089 to 3.094; p = 0.023), and more than three lung metastases (HR, 1.15; 95% CI, 1.024 to 1.282; p = 0.018) predicted survival at 5 years in one multivariate analysis. In the second, more than three lung metastases present at first metastasectomy (HR, 1.19; 95% CI, 1.071 to 1.321; p = 0.001) and the preoperative disease-free interval of less than 3 years (HR, 0.99; 95% CI, 0.973 to 0.997; p = 0.013) predicted lung recurrence. CONCLUSIONS: Older age, male sex, and more lung metastases predict poorer survival after resection of pulmonary colorectal cancer metastases. The number of lung metastases present at the first metastasectomy and the preoperative disease-free interval predicted recurrence in the lung. citation

Editor's commentary: In this report from MD Anderson, more lung mets at presentation, and shorter disease free interval prior to metastasectomy predicted recurrence and worse outcome. This conclusion agrees with intuition and experience. It has been interesting to see how much more frequently we are asked to consider metastasectomy for colon cancer compared to even a few years ago.

Esophageal cancer

XRT of no added benefit to resected T2N0 esophageal cancer

Ann Thorac Surg. 2012 Oct 11. The Role of Radiation Therapy in Resected T2 N0 Esophageal Cancer: A Population-Based Analysis. Martin JT, Worni M, Zwischenberger JB, Gloor B, Pietrobon R, D'Amico TA, Berry MF. Department of Surgery, Duke University Medical Center, Durham, North Carolina; Department of Surgery, University of Kentucky, Lexington, Kentucky. BACKGROUND: The prognosis of even early-stage esophageal cancer is poor. Because there is not a consensus on how to manage T2 N0 disease, we examined survival after resection of T2 N0 esophageal cancer, with or without radiation therapy. METHODS: Patients who underwent resection for T2 N0 squamous cell carcinoma or adenocarcinoma of the mid or distal esophagus, with or without radiation therapy, were identified using the Surveillance, Epidemiology and End Results cancer registry from 1998 to 2008. The 5-year cancer-specific survival (CSS) and overall survival (OS) after resection alone and combined resection with radiation therapy were compared using the Kaplan-Meier approach, risk-adjusted Cox proportional hazard models, and competing risk models. RESULTS: The 5-year OS of 490 T2 N0 patients was 40.3% (95% confidence interval [CI], 35.2% to 45.4%). Surgical resection alone was used in 267 patients (54%) and combined therapy in 223 (46%). The 5-year OS was 38.6% (95% CI, 31.7% to 45.5%) in patients undergoing resection only and 42.3% (95% CI, 34.7% to 49.6%) for combined therapy (p = 0.48). No difference in OS was found, even after risk adjustment (hazard ratio [HR], 1.14; 95% CI, 0.87 to 1.48; p = 0.35). However, in landmark studies with left truncation for 3 and 6 months, resection only showed better OS than combined therapy (HR, 1.33; 95% CI, 1.01 to 1.75; p = 0.04 vs HR, 1.36; 95% CI, 1.01 to 1.83; p = 0.04, respectively). No such difference for CSS was detected, even for the landmark study after 6 months (HR, 1.16; 95% CI, 0.98 to 1.39, p = 0.09). CONCLUSIONS: Combining radiation therapy with esophagectomy did not result in improved outcomes compared with esophagectomy alone for patients with T2 N0 esophageal cancer in the Surveillance, Epidemiology and End Results database.

Editor's commentary: This paper based on the SEER database confirms what most of us already practice: early stage esophageal cancer, fully resected and without lymph node involvement, does not require additional treatment with XRT.

14 gene expression assay predicts high risk for recurrence for completely resected NSCLC

Lancet. 2012 Mar 3;379(9818):823-32. A practical molecular assay to predict survival in resected non-squamous, non-small-cell lung cancer: development and international validation studies. Kratz JR, He J, Van Den Eeden SK, Zhu ZH, Gao W, Pham PT, Mulvihill MS, Ziaei F, Zhang H, Su B, Zhi X, Quesenberry CP, Habel LA, Deng Q, Wang Z, Zhou J, Li H, Huang MC, Yeh CC, Segal MR, Ray MR, Jones KD, Raz DJ, Xu Z, Jahan TM, Berryman D, He B, Mann MJ, Jablons DM. BACKGROUND: The frequent recurrence of early-stage non-small-cell lung cancer (NSCLC) is generally attributable to metastatic disease undetected at complete resection. Management of such patients depends on prognostic staging to identify the individuals most likely to have occult disease. We aimed to develop and validate a practical, reliable assay that improves risk stratification compared with conventional staging. METHODS: A 14-gene expression assay that uses quantitative PCR, runs on formalin-fixed paraffin-embedded tissue samples, and differentiates patients with heterogeneous statistical prognoses was developed in a cohort of 361 patients with non-squamous NSCLC resected at the University of California, San Francisco. The assay was then independently validated by the Kaiser Permanente Division of Research in a masked cohort of 433 patients with stage I non-squamous NSCLC resected at Kaiser Permanente Northern California hospitals, and on a cohort of 1006 patients with stage I-III non-squamous NSCLC resected in several leading Chinese cancer centres that are part of the China Clinical Trials Consortium (CCTC). FINDINGS: Kaplan-Meier analysis of the Kaiser validation cohort showed 5 year overall survival of 71·4% (95% CI 60·5-80·0) in low-risk, 58·3% (48·9-66·6) in intermediate-risk, and 49·2% (42·2-55·8) in high-risk patients (p(trend)=0·0003). Similar analysis of the CCTC cohort indicated 5 year overall survivals of 74·1% (66·0-80·6) in low-risk, 57·4% (48·3-65·5) in intermediate-risk, and 44·6% (40·2-48·9) in high-risk patients (p(trend)<0·0001). Multivariate analysis in both cohorts indicated that no standard clinical risk factors could account for, or provide, the prognostic information derived from tumour gene expression. The assay improved prognostic accuracy beyond National Comprehensive Cancer Network criteria for stage I high-risk tumours (p<0·0001), and differentiated low-risk, intermediate-risk, and high-risk patients within all disease stages. INTERPRETATION: Our practical, quantitative-PCR-based assay reliably identified patients with early-stage non-squamous NSCLC at high risk for mortality after surgical resection.

Editor's commentary: This report was actually published earlier in the year but I have included it now because I have been getting inquiries from the company behind this test, Pinpoint genomics (as I am sure you will too). To be honest, the value for such testing isn't really that it is possible to predict high risk subsets in early stage NSCLC: we can do that now. For instance, we know that tumors with lymphovascular invasion do worse stage for stage. What we all want is proof that treating high risk patients (how ever you define them) will improve survival.

Predicting recurrence in NSCLC

Histologic grade and PET SUVmax predictive of recurrence in NSCLC adenocarcinoma

Ann Surg Oncol. 2012 Oct;19(11):3598-605. FDG-PET SUVmax combined with IASLC/ATS/ERS histologic classification improves the prognostic stratification of patients with stage I lung adenocarcinoma. Kadota K, Colovos C, Suzuki K, Rizk NP, Dunphy MP, Zabor EC, Sima CS, Yoshizawa A, Travis WD, Rusch VW, Adusumilli PS. Thoracic Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA. BACKGROUND: We investigated the association between the newly proposed International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) classification and (18)F-fluorodeoxyglucose (FDG) uptake on positron emission tomography (PET), and whether the combination of these radiologic and pathologic factors can further prognostically stratify patients with stage I lung adenocarcinoma. METHODS: We retrospectively evaluated 222 patients with pathologic stage I lung adenocarcinoma who underwent FDG-PET scanning before undergoing surgical resection between 1999 and 2005. Patients were classified by histologic grade according to the IASLC/ATS/ERS classification (low, intermediate, or high grade) and by maximum standard uptake value (SUVmax) (low <3.0, high ≥3.0). The cumulative incidence of recurrence (CIR) was used to estimate recurrence probabilities. RESULTS: Patients with high-grade histology had higher risk of recurrence (5-year CIR, 29% [n = 25]) than those with intermediate-grade (13% [n = 181]) or low-grade (11% [n = 16]) histology (p = 0.046). High SUVmax was associated with high-grade histology (p < 0.001) and with increased risk of recurrence compared to low SUVmax (5-year CIR, 21% [n = 113] vs. 8% [n = 109]; p = 0.013). Among patients with intermediate-grade histology, those with high SUVmax had higher risk of recurrence than those with low SUVmax (5-year CIR, 19% [n = 87] vs. 7% [n = 94]; p = 0.033). SUVmax was associated with recurrence even after adjusting for pathologic stage (p = 0.037). CONCLUSIONS: SUVmax on FDG-PET correlates with the IASLC/ATS/ERS classification and can be used to stratify patients with intermediate-grade histology, the predominant histologic subtype, into two prognostic subsets.

Editor's commentary: So here is another report attempting to classify early stage NSCLC adenocarcinoma into high risk and low risk categories on the basis of histologic (IASLC/ATS/ERS) classification and PET SUVmax. We still need the **treatment** trial for these patients (see above).

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