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Neoadjuvant treatment in NSCLC

CHEST trial reports: induction chemo+surgery vs. surgery in early stage NSCLC

J Clin Oncol. 2012 Jan 10;30(2):172-8. Epub 2011 Nov 28. Randomized Phase III Study of Surgery Alone or Surgery Plus Preoperative Cisplatin and Gemcitabine in Stages IB to IIIA Non-Small-Cell Lung Cancer. Scagliotti GV, Pastorino U, Vansteenkiste JF, Spaggiari L, Facciolo F, Orłowski TM, Maiorino L, Hetzel M, Leschinger M, Visseren-Grul C, Torri V. University of Turin, Department of Clinical and Biological Sciences, S. Luigi Hospital, Regione Gonzole 10, 10043 Torino, Italy; giorgio.scagliotti@unito.it. **PURPOSE** This study aimed to determine whether three preoperative cycles of gemcitabine plus cisplatin followed by radical surgery provides a reduction in the risk of progression compared with surgery alone in patients with stages IB to IIIA non-small-cell lung cancer (NSCLC). **PATIENTS AND METHODS** Patients with chemotherapy-naïve NSCLC (stages IB, II, or IIIA) were randomly assigned to receive either three cycles of gemcitabine 1,250 mg/m² days 1 and 8 every 3 weeks plus cisplatin 75 mg/m² day 1 every 3 weeks followed by surgery, or surgery alone. Randomization was stratified by center and disease stage (IB/IIA v IIB/IIIA). The primary end point was progression-free survival (PFS). **Results** The study was prematurely closed after the random assignment of 270 patients: 129 to chemotherapy plus surgery and 141 to surgery alone. Median age was 61.8 years and 83.3% were male. Slightly more patients in the surgery alone arm had disease stage IB/IIA (55.3% v 48.8%). The chemotherapy response rate was 35.4%. The hazard ratios for PFS and overall survival were 0.70 (95% CI, 0.50 to 0.97; P = .003) and 0.63 (95% CI, 0.43 to 0.92; P = .02), respectively, both in favor of chemotherapy plus surgery. A statistically significant impact of preoperative chemotherapy on outcomes was observed in the stage IIB/IIIA subgroup (3-year PFS rate: 36.1% v 55.4%; P = .002). The most common grade 3 or 4 chemotherapy-related adverse events were neutropenia and thrombocytopenia. No treatment-by-histology interaction effect was apparent. **CONCLUSION** Although the study was terminated early, preoperative gemcitabine plus cisplatin followed by radical surgery improved survival in patients with clinical stage IIB/IIIA NSCLC.

Editor's commentary: The CHEST trial was initially designed to enroll 712 pts to answer the question of the value of neoadjuvant or induction chemotherapy in surgical patients, but only accrued 270 before closure. Over the course of the trial, several RCTs demonstrating the effectiveness of **adjuvant** chemotherapy reported and the data monitoring board terminated enrollment into CHEST. So, in effect, this is really only a partially completed trial. Read the accompanying editorial for an excellent synopsis of this field. It is rare that one comes across a trial that claims such positive results in the face of obvious methodology problems. The results in favor of the induction+surgery arm are almost too good to be believable. Furthermore, the results are notably absent in the IB-IIA subgroups. There are marked difference in risk factors between the two arms including statistically significantly older pts, more men, and more pneumonectomies (25% vs. 15%) in the surgery only arm.

I strongly agree with the editorialist: the weight of evidence remains with postoperative adjuvant chemotherapy for these stage groups in NSCLC. Neoadjuvant treatment is only for selected patients; the majority of patients should be considered for postoperative treatment.

Survey shows oncologist incorporate surgery into treatment of IIIA NSCLC patients

J Thorac Oncol. 2012 Jan 10. Physician Preferences for Management of Patients with Stage IIIA NSCLC: Impact of Bulk of Nodal Disease on Therapy Selection. Tanner NT, Gomez M, Rainwater C, Nietert PJ, Simon GR, Green MR, Silvestri GA. Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, Medical University of South Carolina, Charleston, South Carolina; †Pulmonary and Sleep Center of the valley, Weslaco, Texas; ‡Division of Biostatistics and Epidemiology, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina; and §Division of Biostatistics and Epidemiology, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina; and ||Xcenda, Palm Harbor Abstract INTRODUCTION: Stage IIIA non-small cell lung cancer (NSCLC) constitutes a heterogeneous group of patients with predominant ipsilateral mediastinal (N2) disease. The spectrum of lymph node presentation has led to a host of trials involving various therapeutic combinations, and optimal management has been unclear. METHODS: In 2007 and 2008, 10 live research events surveyed the practice preferences of American medical oncologists using two hypothetical scenarios. The first scenario was of a stage IIIA NSCLC in the right upper lobe with a single enlarged (>1 cm) 4R lymph node found to be malignant by mediastinoscopy. The second was of a bulky stage IIIA NSCLC with multistation N2 pathologically positive nodes. RESULTS: In the first scenario, 373 (92%) of the oncologists incorporated surgery into their treatment plan. Only 34 (8%) offered chemoradiotherapy alone. Neoadjuvant chemotherapy, followed by surgery and then additional chemoradiotherapy (32%), was the most commonly offered treatment strategy. In the second scenario, 209 (52%) medical oncologists chose definitive chemoradiation. A total of 193 (48%) included surgery as part of the treatment plan. CONCLUSIONS: The current standard of care for IIIA N2 NSCLC recognized before treatment is concurrent chemoradiotherapy. This study demonstrated that a significant proportion of oncologists treating locally advanced lung cancer include surgery as part of the treatment plan more so in single versus multinodal disease. Since node positive locally advanced disease is such a common presentation for patients with lung cancer, well-designed clinical trials are needed to define the most advantageous treatment strategy for individual subsets of patients with stage IIIA disease. Commentary: In this study, 92% of surveyed oncologists would include surgery for a hypothetical patient with single node positive N2 disease amenable to resection. In the other scenario, 32% of oncologists said they would offer neoadjuvant chemotherapy followed by surgery and then postoperative radiation to a hypothetical patient with bulky, multistation disease.

Editor's commentary: This is an interesting survey that asked medical oncologists to treat two hypothetical stage IIIA, N2 NSCLC patients in an effort to clarify practice trends in IIIA treatment. What surprises me most about the findings is that such a large number of oncologists would incorporate surgery into the second scenario which included bulky, multi-station N2 disease: 32%. This certainly has not been my practice and I am not asked to consider surgery in these patients with any frequency.

Postoperative pneumonia

Molecular techniques identify high rate of CMV in NSCLC pts who develop postoperative infection

Ann Thorac Surg. 2011 Dec 27. Molecular Detection of Microorganisms in Distal Airways of Patients Undergoing Lung Cancer Surgery. D'Journo XB, Bittar F, Trousse D, Gaillat F, Doddoli C, Dutau H, Papazian L, Raoult D, Rolain JM, Thomas PA. Department of Thoracic Surgery and Diseases of the Esophagus, Aix-Marseille University and Assistance Publique-Hôpitaux de Marseille, Hôpital Nord, Marseille, France. BACKGROUND.: Whereas proximal airways of patients undergoing lung cancer surgery are known to present specific microbiota incriminated in the occurrence of postoperative respiratory complications, little attention has been paid to distal airways and lung parenchyma considered to be free from bacteria. We have hypothesized that molecular culture-independent techniques applied to distal airways should allow identification of uncultured bacteria, virus, or emerging pathogens and predict the occurrence of postoperative respiratory complications. METHODS.: Microbiological assessments were obtained from the distal airways of resected lung specimens from a prospective cohort of patients undergoing major lung resections for cancer. Microorganisms were detected using real-time polymerase chain reaction (PCR) assays targeting the bacterial 16S ribosomal RNA gene and Herpesviridae, cytomegalovirus (CMV), and herpesvirus simplex. All postoperative microbiological assessments were compared with the PCR results. RESULTS.: In all, 240 samples from 87 patients were investigated. Colonizing agents were exclusively Herpesviridae (CMV, n = 13, and herpesvirus simplex, n = 1). All 16S ribosomal RNA PCR remained negative. Thirteen patients (15%) had a positive CMV PCR (positive-PCR group), whereas the remaining 74 patients constituted the negative-PCR group. Postoperative pneumonia occurred in 24% of the negative-PCR group and in 69% of the positive-PCR group (p = 0.003). Upon stepwise logistic regression, performance status, percent of predicted diffusion lung capacity for carbon monoxide, and positive PCR were the risk factors of postoperative respiratory complications. The CMV PCR had a positive predictive value of 0.70 in prediction of respiratory complications. CONCLUSIONS.: When tested by molecular techniques, lung parenchyma and distal airways are free of bacteria, but CMV was found in a high proportion of the samples. Molecular CMV detection in distal airways should be seen as a reliable marker to identify patients at risk for postoperative respiratory complications.

Editor's commentary: Prevention of pneumonia in NSCLC patients undergoing resection is an important topic for surgeons taking care of lung resection patients. We have evolved an extensive protocol for our patients that includes preoperative oropharyngeal decontamination, early mobilization, adequate pain control, and careful postoperative monitoring for aspiration. These techniques have yielded good results over the years but clearly there is a persisting problem with respiratory morbidity in a small number of patients. This report identifies another potential means of addressing this problem.

Minimally invasive lobectomy is cost effective compared to open lobectomy

Ann Thorac Surg. 2011 Nov 28. Video-Assisted Thoracoscopic Lobectomy Is Less Costly and Morbid Than Open Lobectomy: A Retrospective Multiinstitutional Database Analysis. Swanson SJ, Meyers BF, Gunnarsson CL, Moore M, Howington JA, Maddaus MA, McKenna RJ, Miller DL. Division of Thoracic Surgery, Brigham and Women's Hospital and the Dana Farber Cancer Institute, Boston, Massachusetts. **BACKGROUND:** The Premier Perspective Database (Premier Inc, Charlotte, NC) was used to compare hospital costs and perioperative outcomes for video-assisted thoracoscopic surgery (VATS) and open lobectomy procedures in the United States. **METHODS:** Eligible patients underwent a lobectomy for cancer by a thoracic surgeon, by VATS or open thoracotomy and were captured in the database between third quarter of 2007 and through 2008. Multivariable logistic regression analyses were performed for binary outcomes. Ordinary least-squares regressions were used to estimate continuous outcomes. All models were adjusted for patient and hospital characteristics. **RESULTS:** A total of 3,961 patients underwent a lobectomy by a thoracic surgeon by open ($n = 2,907$) or VATS ($n = 1,054$) approach. Hospital costs were higher for open versus VATS; \$21,016 versus \$20,316 ($p = 0.027$). Adjustment for surgeon experience with VATS over the 6 months prior to each operation showed a significant association between surgeon experience and cost. Average costs ranged from \$22,050 for low volume surgeons to \$18,133 for high volume surgeons. For open lobectomies, cost differences by surgeon experience were not significant and both levels were estimated at \$21,000. Length of stay was 7.83 versus 6.15 days, for open versus VATS ($p = 0.000$). Surgery duration was shorter for open procedures at 3.75 versus 4.09 for VATS ($p = 0.000$). The risk of adverse events was significantly lower in the VATS group, odds ratio of 1.22 ($p = 0.019$) **CONCLUSIONS:** Lobectomy performed by the VATS approach as compared with an open technique results in shorter length of stay, fewer adverse events, and less cost to the hospital. Economic impact is magnified as the surgeon's experience increases.

Editor's commentary: As one would expect, VATS leads to better outcomes and cost effective results when compared to open procedures. I would expect that we will begin to see even better results as robotic lobectomy becomes more widely dispersed among thoracic surgeons. I think it is interesting to note that even in the VATS group, average length of stay is still over 6 days. Our median length of stay has been 3 days since the inception of the robotic technique.

Esophageal cancer

Hiatal hernia following esophagectomy: rare but important to identify

Ann Thorac Surg. 2011 Dec;92(6):2041-5. Hiatal hernia after esophagectomy: analysis of 2,182 esophagectomies from a single institution.

Price TN, Allen MS, Nichols FC 3rd, Cassivi SD, Wigle DA, Shen KR, Deschamps C. Division of General Thoracic Surgery, Mayo Clinic, Rochester, Minnesota 55905, USA. **BACKGROUND:** Esophageal resection is a complex operation often associated with morbidity. Hiatal hernia after esophagectomy is an unusual complication. We reviewed our experience with this complication. **METHODS:** From February 1988 through February 2009 we performed 2,182 esophagectomies. Fifteen (0.69%) patients experienced a hiatal hernia. We reviewed our prospective database for demographics, presentation, operative approaches, and outcomes. **RESULTS:** There were 14 men and 1 woman with a mean age of 59 years. Hernia developed after Ivor Lewis approach in 9, transhiatal in 5, and substernal colon interposition in 1. Presenting symptoms included pain in 7 patients, obstructive symptoms in 5, high chest tube output in 2, shortness of breath in 2, diarrhea in 1, and cough with dysphagia in 1. Two patients were asymptomatic. Radiographic studies revealed bowel in the left chest in 11 patients, right chest in 2, bilaterally in 1, and posterior mediastinum in 1. Hernia repair was through the abdomen in 14 patients and left chest in 1. All had reduction of the herniated contents and closure of the defect; 2 required mesh. There was no early mortality. Complications included wound infection, deep venous thrombosis, chylothorax, urinary retention, sacral decubiti, atrial arrhythmias, respiratory failure, and empyema. Mean follow-up was 34 months. Ten patients are still alive. There have been two hernia recurrences. **CONCLUSIONS:** Hiatal hernia after esophagectomy is rare. Repair can be accomplished with low mortality; however, there is substantial morbidity. Because of the increased risk of incarceration or strangulation, these herniae should be repaired. Long-term outcome is usually excellent.

Editor's commentary: I enjoyed reading this report since I have had the opportunity to care for three different patients with hiatal hernia following esophagectomy in the last year. Each of these three patients presented in different manners: one had colon strangulation and perforation; one had early postoperative hernia easily corrected with reoperation; and the last was dyspneic secondary to herniation of colon into the left chest, fixed by robotic hernia repair. Since it is so rare, it is not surprising that the diagnosis does not get considered early.

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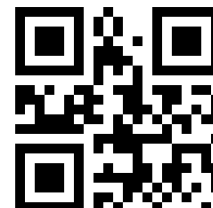
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