[Indian J Chest Dis Allied Sci 2010;52:177-180]

Abstracts' Service

Implementation of a Management Guideline Aimed at Minimizing the Severity of Primary Graft Dysfunction After Lung Transplant

Judy Currey, David V. Pilcher, Andrew Davies, Carlos Scheinkestel, Mari Botti, Michael Bailey and Greg Snell

The Journal of Thoracic and Cardiovascular Surgery 2010;139:154-6

Objective. Primary graft dysfunction, a severe form of lung injury that occurs in the first 72 hours after lung transplant, is associated with morbidity and mortality. We sought to assess the impact of an evidence-based guideline as a protocol for respiratory and hemodynamic management.

Methods. Preoperative and postoperative data for patients treated per the guideline (n=56) were compared with those of a historical control group (n=53). Patient data such as ratio of arterial PO_2 to inspired oxygen fraction, central venous pressure, cumulative fluid balance, vasopressor dose, and serum urea and creatinine were measured and documented at specific times. Primary outcome was severity of primary graft dysfunction within the first 72 hours.

Results. Primary graft dysfunction grade was progressively lower in patients treated after introduction of the guideline (P=.01). Lower postoperative fluid balances (P=.01) and vasopressor doses (P=.007) were seen, with no associated renal dysfunction. There were no differences in duration of mechanical ventilation or mortality. Nonadherence to the guideline occurred in 10 cases (18%).

Conclusions. Implementation of an evidence-based guideline for managing respiratory and hemodynamic status is feasible and safe and was associated with reduction in severity of primary graft dysfunction. Further studies are required to determine whether such a guideline would lead to a consistent reduction in severity of primary graft dysfunction at other institutions. Creation of a protocol for postoperative care provides a template for further studies of novel therapies or management strategies for primary graft dysfunction.

Required Area of Lymph Node Sampling During Segmentectomy for Clinical Stage IA Non-small Cell Lung Cancer

Hiroaki Nomori, Yasuomi Ohba, Hidekatsu Shibata, Kenji Shiraishi, Takeshi Mori and Shinya Shiraishi

The Journal of Thoracic and Cardiovascular Surgery 2010;139:38-42

Objective. To investigate the required area of lymph node sampling during segmentectomy, especially for segmental nodes at the nonresected segments, we examined the distribution of sentinel nodes in patients with non-small cell lung cancer who underwent segmentectomy.

Methods. Ninety-four patients with clinical T1 N0 M0 non-small cell lung cancer were treated by using segmentectomy and dissection of lymph nodes with sentinel node identification using ^{99m}Tc-phytate. Anatomic locations of the segments were classified as either anterior or posterior, and correlations of anatomic location with the distribution of sentinel nodes at the segmental nodes were then examined.

Results. Of the 94 patients, segmental nodes at both the resected and nonresected segments could be dissected in 42 patients. Segmental sentinel nodes were found at the resected segments in 27 (64%) of these 42 patients, a frequency that was significantly higher than that (12/42 [29%]) seen at the nonresected segments (P=.001). Seven (47%) of the 15 patients with tumors in the anteriorly located segments had segmental sentinel nodes at the nonresected segments, a frequency that was significantly higher than that (4/24[17%]) seen in patients with tumours in the posteriorly located segments (P=.04).

Conclusion. The lymphatic flow from the anteriorly located segment can frequently go directly to the segmental lymph nodes of the posteriorly located segment, probably because the lobar bronchi locate at the posterior side in the thorax. Therefore segmental lymph nodes should be dissected at both the resected and nonresected segments during segmentectomy, especially for tumors in the anteriorly located segment.

Impaired Quality of Life After Pneumonectomy: Who is at Risk?

Francesco Leo, Paolo Scanagatta, Fernando Vannucci, Daniela Brambilla, Davide Radice and Lorenzo Spaggiari

The Journal of Thoracic and Cardiovascular Surgery 2010;139:49-52

Objective. After pneumonectomy, quality of life may be impaired in a proportion of patients because of the presence of symptoms causing severe limitations in daily activities. This is a prospective study on patients who have undergone pneumonectomy for cancer, assessing quality of life modifications 6 months after surgery.

Methods. Beginning in August 2006, candidates for pneumonectomy had their quality of life assessed by the European Organization for Research and Treatment of Cancer questionnaire (QLQ-C30+LC13) preoperatively and at 1, 3, and 6 months after surgery. Poor quality of life at 6 months was defined as global health values 10% or more below baseline values. The impact of several clinical variables was tested to discover predictors of poor postoperative quality of life.

Results. Forty-one of the 50 patients enrolled in the study had a complete quality of life follow-up by January 2008, representing the population of the study. Six months after pneumonectomy, global health showed a minimal impairment in the whole population (baseline 60.4 ± 26.5, at 6 months 56.3± 24.2, P=.15). Ten patients (24.4%) were identified as having poor quality of life at 6 months. Age of 70 years or more was identified as a significant risk factor for poor 6-month quality of life using multivariate analysis (odds ratio, 1.13; 95% confidence interval, 1-1.26). The baseline global health score was the strongest predictor of postoperative global health quality of life (odds ratio, 0.16; 95% confidence interval, 0.02-0.46; P=.0086).

Conclusions. The overall quality of life after pneumonectomy was impaired in 25% of surviving patients at 6 months after surgery; thus, this aspect of recovery should be routinely discussed with patients before pneumonectomy. Patients aged 70 years or more and those with low preoperative quality of life seem to be at risk for unsatisfactory quality of life after surgery.

Single-Dose Liposomal Amphotericin B for Visceral Leishmaniasis in India

Shyam Sundar, Jaya Chakravarty, Dipti Agarwal, Madhukar Rai and Henry W. Murray

The New England Journal of Medicine 2010;362:504-12

Background. Some 50% of patients with visceral leishmaniasis (kala-azar) worldwide live in the Indian state of Bihar. Liposomal amphotericin B is an effective treatment when administered in short courses. We wanted to determine whether the efficacy of a single infusion of liposomal amphotericin B was inferior to conventional parenteral therapy, consisting of 15 alternate-day infusions of amphotericin B deoxycholate.

Methods. In this open-label study, we randomly assigned 412 patients in a 3:1 ratio to receive either liposomal amphotericin B (liposomal-therapy group) or amphotericin B deoxycholate (conventional-therapy group). Liposomal amphotericin B (at a dose of 10 mg per kilogram of body weight) was given once, and patients were discharged home 24 hours later. Amphotericin B deoxycholate, which was administered in 15 infusions of 1 mg per kilogram, was given every other day during a 29-day hospitalization. We determined the cure rate 6 months after treatment.

Results. A total of 410 patients — 304 of 304 patients (100%) in the liposomal-therapy group and 106 of 108 patients (98%) in the conventional-therapy group — had apparent cure responses at day 30. Cure rates at 6 months were similar in the two groups: 95.7% (95% confidence interval [CI], 93.4 to 97.9) in the liposomal-therapy group and 96.3% (95% CI, 92.6 to 99.9) in the conventional-therapy group. Adverse events in the liposomal-therapy group were infusion-related fever or rigors (in 40%) and increased anemia or thrombocytopenia (in 2%); such events in the conventional-therapy group were fever or rigors (in 64%), increased anemia (in 19%), and hypokalemia (in 2%). Nephrotoxicity or hepatotoxicity developed in no more than 1% of patients in each group.

Conclusions. A single infusion of liposomal amphotericin B was not inferior to and was less expensive than conventional therapy with amphotericin B deoxycholate. (Clinical Trials.gov number, NCT00628719.)

An Algorithm for Tuberculosis Screening and Diagnosis in People with HIV

Kevin P. Cain, Kimberly D. McCarthy, Charles M. Heilig, Patama Monkongdee, Theerawit Tasaneeyapan, Nong Kanara, Michael E. Kimerling, Phalkun Chheng, Sopheak Thai, Borann Sar, Praphan Phanuphak, Nipat Teeratakulpisarn, Nittaya Phanuphak, Nguyen Huy Dung, Hoang Thi Quy, Le Hung Thai, and Jay K. Varma

The New England Journal of Medicine 2010;362:707-16

Background. Tuberculosis screening is recommended for people with human immunodeficiency virus (HIV) infection to facilitate early diagnosis and safe initiation of antiretroviral therapy and isoniazid preventive therapy. No internationally accepted, evidence-based guideline addresses the optimal means of conducting such screening, although screening for chronic cough is common.

Methods. We consecutively enrolled people with HIV infection from eight outpatient clinics in Cambodia, Thailand, and Vietnam. For each patient, three samples of sputum and one each of urine, stool, blood, and lymph-node aspirate (for patients with lymphadenopathy) were obtained for mycobacterial culture. We compared the characteristics of patients who received a diagnosis of tuberculosis (on the basis of having one or more specimens that were culture-positive) with those of patients who did not have tuberculosis to derive an algorithm for screening and diagnosis.

Results. Tuberculosis was diagnosed in 267 (15%) of 1748 patients (median CD4+ T-lymphocyte count, 242 per cubic millimeter; interquartile range, 82 to 396). The presence of a cough for 2 or 3 weeks or more during the preceding 4 weeks had a sensitivity of 22 to 33% for detecting tuberculosis. The presence of cough of any duration, fever of any duration, or night sweats lasting 3 or more weeks in the preceding 4 weeks was 93% sensitive and 36% specific for tuberculosis. In the 1199 patients with any of these symptoms, a combination of two negative sputum smears, a normal chest radiograph, and a CD4+ cell count of 350 or more per cubic millimeter helped to rule out a diagnosis of tuberculosis, whereas a positive diagnosis could be made only for the 113 patients (9%) with one or more positive sputum smears; mycobacterial culture was required for most other patients.

Conclusions. In persons with HIV infection, screening for tuberculosis should include asking questions about a combination of symptoms rather than only about chronic cough. It is likely that antiretroviral therapy and isoniazid preventive therapy can be started safely in people whose screening for all three symptoms is negative, whereas diagnosis in most others will require mycobacterial culture.

Timing of Initiation of Antiretroviral Drugs during Tuberculosis Therapy

Salim S. Abdool Karim, Kogieleum Naidoo, Anneke Grobler, Nesri Padayatchi, Cheryl Baxter, Andrew Gray, Tanuja Gengiah, Gonasagrie Nair, Sheila Bamber, Aarthi Singh, Munira Khan, Jacqueline Pienaar, Wafaa El-Sadr, Gerald Friedland and Quarraisha Abdool Karim

The New England Journal of Medicine 2010;362:697-706

Background. The rates of death are high among patients with coinfection with tuberculosis and the human immunodeficiency virus (HIV). The optimal timing for the initiation of antiretroviral therapy in relation to tuberculosis therapy remains controversial.

Methods. In an open-label, randomized, controlled trial in Durban, South Africa, we assigned 642 patients with both tuberculosis and HIV infection to start antiretroviral therapy either during tuberculosis therapy (in two integrated-therapy groups) or after the completion of such treatment (in one sequential-therapy group). The diagnosis of tuberculosis was based on a positive sputum smear for acid-fast bacilli. Only patients with HIV infection and a CD4+ cell count less than 500 per cubic millimeter were included. All patients received standard tuberculosis therapy, prophylaxis with trimethoprim-sulfamethoxazole, and a once-daily antiretroviral regimen of didanosine, lamivudine, and efavirenz. The primary end point was death from any cause.

Results. This analysis compares data from the sequential-therapy group and the combined integrated-therapy groups up to September 1, 2008, when the data and safety monitoring committee

recommended that all patients receive integrated antiretroviral therapy. There was a reduction in the rate of death among the 429 patients in the combined integrated-therapy groups (5.4 deaths per 100 person-years, or 25 deaths), as compared with the 213 patients in the sequential-therapy group (12.1 per 100 person-years, or 27 deaths); a relative reduction of 56% (hazard ratio in the combined integrated-therapy groups, 0.44; 95% confidence interval, 0.25 to 0.79; P = 0.003). Mortality was lower in the combined integrated-therapy groups in all CD4+ count strata. Rates of adverse events during follow-up were similar in the two study groups.

Conclusions. The initiation of antiretroviral therapy during tuberculosis therapy significantly improved survival and provides further impetus for the integration of tuberculosis and HIV services. (ClinicalTrials.govnumber, NCT00398996.)

Step-up Therapy for Children with Uncontrolled Asthma Receiving Inhaled Corticosteroids

Robert F. Lemanske, Jr, David T. Mauger, Christine A. Sorkness, Daniel J. Jackson, Susan J. Boehmer, Fernando D. Martinez, Robert C. Strunk, Stanley J. Szefler, Robert S. Zeiger, Leonard B. Bacharier, Ronina A. Covar, Theresa W. Guilbert, Gary Larsen, Wayne J. Morgan, Mark H. Moss, Joseph D. Spahn and Lynn M. Taussig, for the Childhood Asthma Research and Education (CARE) Network of the National Heart, Lung, and Blood Institute

The New England Journal of Medicine 2010;362:975-85

Background. For children who have uncontrolled asthma despite the use of low-dose inhaled corticosteroids (ICS), evidence to guide step-up therapy is lacking.

Methods. We randomly assigned 182 children (6 to 17 years of age), who had uncontrolled asthma while receiving 100 µg of fluticasone twice daily, to receive each of three blinded step-up therapies in random order for 16 weeks: 250 µg of fluticasone twice daily (ICS step-up), 100 µg of fluticasone plus 50 µg of a long-acting beta-agonist twice daily (LABA step-up), or 100 µg of fluticasone twice daily plus 5 or 10 mg of a leukotriene-receptor antagonist daily (LTRA step-up). We used a triple-cross-over design and a composite of three outcomes (exacerbations, asthma-control days, and the forced expiratory volume in 1 second) to determine whether the frequency of a differential response to the step-up regimens was more then 25%.

Results. A differential response occurred in 161 of 165 patients who were evaluated (P<0.001). The response to LABA step-up therapy was most likely to be the best response, as compared with responses to LTRA step-up (relative probability, 1.6; 95% confidence interval [CI], 1.1 to 2.3; P=0.004) and ICS step-up (relative probability, 1.7; 95% CI, 1.2 to 2.4; P=0.002). Higher scores on the Asthma Control Test before randomization (indicating better control at baseline) predicted a better response to LABA step-up (P=0.009). White race predicted a better response to LABA step-up, whereas black patients were least likely to have a best response to LTRA step-up (P=0.005).

Conclusions. Nearly all the children had a differential response to each step-up therapy. LABA step-up was significantly more likely to provide the best response than either ICS or LTRA step-up. However, many children had a best response to ICS or LTRA step-up therapy, highlighting the need to regularly monitor and appropriately adjust each child's asthma therapy. (ClinicalTrials.govnumber, NCT 00395304.)