CHEST

Understanding the Concept of Health Care-Associated Pneumonia in Lung Transplant Recipients

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BACKGROUND: Limited data are available regarding the etiologic impact of health care-associated pneumonia (HCAP) in lung transplant recipients. Therefore, our aim was to evaluate the microbiologic differences between HCAP and hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) in lung transplant recipients with a radiographically confirmed diagnosis of pneumonia.

METHODS: We performed a retrospective cohort study of lung transplant recipients with pneumonia at one transplant center over a 7-year period. Eligible patients included lung transplant recipients who developed a first episode of radiographically confirmed pneumonia ≥ 48 h following transplantation. HCAP, HAP, and VAP were classified according to the American Thoracic Society/Infectious Diseases Society of America 2005 guidelines. χ^2 and Student *t* tests were used to compare categorical and continuous variables, respectively.

RESULTS: Sixty-eight lung transplant recipients developed at least one episode of pneumonia. HCAP (n = 42; 62%) was most common, followed by HAP/VAP (n = 26; 38%) stratified in HAP (n = 20; 77%) and VAP (n = 6; 23%). *Pseudomonas aeruginosa* was the predominantly isolated organism (n = 22; 32%), whereas invasive aspergillosis was uncommon (< 10%). Multiple-drug resistant (MDR) pathogens were less frequently isolated in patients with HCAP compared with HAP/VAP (5% vs 27%; *P* = .009). Opportunistic pathogens were less frequently identified in lung transplant recipients with HCAP than in those with HAP/VAP (7% vs 27%; *P* = .02). Lung transplant recipients with HCAP had a similar mortality at 90 days (n = 9 [21%] vs n = 4 [15%]; *P* = .3) compared with patients with HAP/VAP.

CONCLUSIONS: HCAP was the most frequent infection in lung transplant recipients. MDR pathogens and opportunistic pathogens were more frequently isolated in HAP/VAP. There were no differences in 30- and 90-day mortality between lung transplant recipients with HCAP and those with HAP/VAP.

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ABBREVIATIONS: HAP = hospital-acquired pneumonia; HCAP = health care-associated pneumonia; IQR = interquartile range; LOS = length of stay; LT = lung transplant; MDR = multidrug resistant; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus*; VAP = ventilator-associated pneumonia

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Development of new immunosuppressive agents and advances in surgical technology in solid organ transplantations have significantly improved outcomes in lung transplantation.[1] Survival rates have improved from 70% in 1990 to 81% in 2012, but complications, especially infections, remain common.[1,2] Infections in lung transplant (LT) recipients are one of the major causes of early and late morbidity and mortality, accounting for > 50% of deaths.[3-5] Pneumonia is the most frequent infection seen in LT recipients, reportedly accounting for 35% to 82.7% of all infections in this setting.[1,4,6] In addition, pneumonia following lung transplantation bears a high risk for multidrug-resistant (MDR) pathogens, including *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Acinetobacter* species.[6]

Clinical practice guidelines from the Infectious Diseases Society and American Thoracic Society classify pneumonia as either health care-associated (HCAP), hospital-acquired pneumonia (HAP), or ventilator-associated pneumonia (VAP), with HCAP introduced due to similarities in MDR pathogens observed in patients with HAP or VAP.[7,8]

HCAP as a subtype of pneumonia is defined as a respiratory infection associated with specific health-care risk factors that include hospitalization for ≥ 2 days in the preceding 90 days, residence in a nursing home or extended care facility, home infusion therapy (including antibiotics), chronic dialysis within 30 days, home wound care, and family member(s) with an MDR pathogen.[7,9] By virtue of this, all LT recipients, who are immunosuppressed, are considered at risk for MDR pathogens. However, data regarding the association of MDR pathogens with pneumonia in LT recipients are lacking, which limits appropriate antimicrobial therapy and assessment of clinical outcomes of HCAP in LT recipients. Therefore, our aim was to evaluate the microbiologic differences between HCAP compared with HAP/VAP in LT recipients with a radiographically confirmed diagnosis of pneumonia.

Materials and Methods

This was a retrospective cohort study of patients hospitalized with HCAP, HAP, and VAP at one academic tertiary care hospital in San Antonio, Texas. The institutional review board of the University Health Science Center at San Antonio classified this project as an exempt study.

Study Sites and Inclusion and Exclusion Criteria

We identified all patients admitted to the study hospitals with a primary discharge diagnosis of pneumonia (*International Classification of Diseases-9* codes 480.0-483.99 or 485-487.0) or secondary discharge diagnosis of pneumonia with a primary diagnosis of respiratory failure (code 518.81) over a 7-year period (January 1, 2001, to December 31, 2008). In addition, we reviewed all positive microbiology cultures from respiratory and blood samples.

Subjects were included if (1) they were older than 18 years; (2) had received a LT; (3) their first episode of pneumonia after transplantation was classified as HCAP, HAP, or VAP, with symptoms of lower respiratory tract infection (at least one of the following: fever, cough, sputum production, dyspnea, chest pain); and (4) had radiographically confirmed opacities or other findings consistent with pneumonia on chest radiographs or CT scans of the chest obtained during the hospitalization. For HCAP, radiographic diagnosis of pneumonia was done within 48 h of admission. We excluded patients who received "comfort measures" at the time of admission. In subjects admitted more than once during the study period, only the first pneumonia event was abstracted. MDR pathogens included proven resistance on the susceptibility patterns for MRSA, *P aeruginosa*, and *Acinetobacter* species resistant to at least two classes of antibiotics, and extended spectrum β-lactamase phenotype *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Citrobacter* species, *Achromobacter xyloxosidans*, and *Burkholderia* species.

Outcomes

Primary outcome was the incidence of MDR pathogens. Secondary outcomes included mortality at 30 and 90 days and length of hospital stay (LOS).

Diagnostic Criteria

Microbiologic data were reviewed, and a microbiologic cause was assigned independently by one of the investigators (F. P.). Microbiologic diagnosis was made if one of the following conditions was met: (1) positive blood cultures for bacterial pathogens (in the absence of extrapulmonary source of infection), (2) pleural fluid cultures yielding a bacterial pathogen, (3) endotracheal aspirates with moderate or heavy growth of bacterial pathogens, (4) significant quantitative culture growth from bronchoscopic respiratory samples (protected specimen brush cultures of at least 10^3 colony-forming unit (CFU)/mL, or BAL of at least 10^4 CFU/mL), and (5) positive *Legionella* urinary antigen. When two or more microbiologic causes were present, the patient was considered to have a polymicrobial infection. A patient was considered to have HCAP, HAP, or VAP of unknown cause if microbiologic studies were not performed or were inconclusive. As part of the local policies, every LT recipient who presents with symptoms suggestive of a lower respiratory tract infection will have a comprehensive microbiology evaluation that includes invasive bronchoscopy or, if unavailable, sputum collection, but this was not standardized during the study.

Statistical Analyses

The data collected in this project were descriptive. All analyses were performed using SPSS, version 20 (IBM Corp). Data were presented as frequencies, proportions (with 95% CIs), or median with interquartile range (IQR). ORs and their 95% CIs were calculated. Significance was defined as $P < .05$. A propensity score technique was used to balance covariates associated with HCAP diagnosis between groups.[10] Use of the propensity score technique in this nonrandomized study allowed for control of pretreatment differences by defining sets of comparable patients. The propensity score was derived from a logistic regression model. A dichotomous indicator variable indexing whether a patient had a diagnosis of HCAP was used as our response variable. The covariates used in the propensity score model were pulmonary hypertension, guideline concordant antibiotic therapy, ICU admission, need for mechanical ventilation, and acute rejection. We then created an ordered categorical variable based on a quintile stratification of the propensity score to include in the regression models.