The Influence of Diagnostic Bronchoscopy on Clinical Outcomes Comparing Adult Autologous and Allogeneic Bone Marrow Transplant Patients*

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Study objectives: **To review our experience with diagnostic bronchoscopy in the evaluation of pulmonary infiltrates in adult hematopoietic stem cell transplantation (HSCT) recipients in the era of Pneumocystis prophylaxis and cytomegalovirus antigen testing. The study focused on diagnostic yields and the influence of bronchoscopic findings on pharmacologic therapy and mortality, comparing allogeneic (allo) HSCT patients to autologous (auto) HSCT patients.**
Design: **Case series review.**
Setting: **Tertiary care academic urban medical centers.**
Patients: **All adult allo-HSCT and auto-HSCT patients undergoing bronchoscopy for the evaluation of pulmonary infiltrates from January 1997 to September 2001.**
Measurements and results: **The review identified 169 bronchoscopies that had been performed on HSCT patients, representing 12.5% of all HSCT patients (allo-HSCT patients, 125 bronchoscopies; auto-HSCT patients, 44 bronchoscopies). Bronchoscopy was requested more often in allo-HSCT patients (18.7%) compared to auto-HSCT patients (6.6%). Findings at bronchoscopy provided a specific diagnosis more frequently in allo-HSCT patients (50%) compared to auto-HSCT patients (34%). For both allo-HSCT and auto-HSCT patients, most diagnoses were obtained by BAL alone, whereas transbronchial biopsy (TBBx) provided additional specific information in < 10% of cases. For select patients (n = 27), surgical lung biopsy following bronchoscopy provided unique diagnoses in 47 to 50% of cases. Information from bronchoscopy influenced clinical decisions more often in allo-HSCT patients (50%) than in auto-HSCT patients (36%), and allowed for the discontinuation or addition of antimicrobial, corticosteroid, or antineoplastic agents to treatment. Complications from bronchoscopy occurred in 9% of all HSCT patients (n = 15), and were associated with higher in-hospital mortality rates in allo-HSCT patients (82%; n = 9) compared to auto-HSCT patients (50%; n = 2). The overall in-hospital mortality rates for allo-HSCT and auto-HSCT patients having bronchoscopy was similar (38% vs 27%, respectively; p = 0.25), and establishing a specific diagnosis by bronchoscopy did not improve the in-hospital mortality rate for allo-HSCT or auto-HSCT patients.**
Conclusions: **Bronchoscopy may provide clinically useful information in the evaluation of adult allo-HSCT and auto-HSCT recipients with pulmonary infiltrates. The results of testing BAL fluid samples alone suggested an etiology in most cases, whereas the findings of TBBx provided unique diagnoses infrequently. Further studies are warranted to improve the utility of diagnostic bronchoscopy in the evaluation of HSCT patients.** ***(CHEST 2005; 127:1388–1396)***

Key words: bone marrow transplantation; bronchoscopy; immunocompromised host

Abbreviations: allo = allogeneic; auto = autologous; CMV = cytomegalovirus; DAD = diffuse alveolar damage; DAH = diffuse alveolar hemorrhage; FIO_2 = fraction of inspired oxygen; HSCT = hematopoietic stem cell transplantation; PT = prothrombin time; SaO_2 = arterial oxygen saturation; SLB = surgical lung biopsy; TBBx = transbronchial biopsy

Hematopoietic stem cell transplantation (HSCT) has been used increasingly for a variety of medical indications since its inception in 1968.[1] The International Bone Marrow Transplant Registries[2] have estimated that 50,000 HSCTs are performed annually, including approximately 30,000 autologous (auto) HSCTs and approximately 17,000 allogeneic (allo) HSCTs. Pulmonary complications develop in 40 to 60% of HSCT recipients,[3–5] with an associated mortality rate of 32 to 61%.[4–6]

Bronchoscopy is often requested to evaluate HSCT patients with respiratory symptoms and chest

radiographic abnormalities. Bronchoscopy is generally considered a safe and minimally invasive procedure with which to establish the diagnosis in these patients. However, the reported diagnostic yield is highly variable, with prior studies[6–10] reporting diagnostic yields of 31 to 80% of patients. Diagnoses provided by bronchoscopy often influence decisions that are related to pharmacologic therapy, although the identification of a pathogen by bronchoscopy in these studies did not influence mortality, and the reported complication rates were reported as 0 to 27%.

The wide disparity in reported diagnostic yields, their influence on therapeutic decisions, and bronchoscopy-related complications may be multifactorial, and may in part reflect changes in the management of HSCT patients and the specific characteristics of the populations of HSCT recipients who were examined. Most prior studies were performed prior to the routine use of cytomegalovirus (CMV) antigen testing and Pneumocystis prophylaxis, and the clinical utility of bronchoscopy in this context has not been fully examined. With the routine use of prophylaxis, the spectrum of pulmonary complications may be evolving, and whether bronchoscopy remains helpful in the evaluation remains uncertain. Finally, prior studies have reported the experience of bronchoscopy in combined populations of allo-HSCT and auto-HSCT patients[6,8] or have focused on allo-HSCT patients only.[9,10] Recognizing differences in the spectrum of pulmonary complications for these two populations, prior studies did not directly compare allo-HSCT patients to auto-HSCT patients. The purpose of this study was to review our experience with diagnostic bronchoscopy in the evaluation of pulmonary infiltrates in adult HSCT recipients at urban tertiary care medical centers in the era of Pneumocystis prophylaxis and CMV antigen testing. Particular emphasis focused on diagnostic yields and the influence of bronchoscopic findings on clinical pharmacologic therapy and mortality, comparing allo-HSCT patients to auto-HSCT patients.

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Presented in part at the American Thoracic Society International Meeting, Atlanta, GA, May 17–22, 2002.
Manuscript received March 25, 2004; revision accepted September 15, 2004.

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Materials and Methods

Identification of Study Subjects

HSCT patients who underwent bronchoscopy during the period January 1997 to September 2001 were identified by a review of computerized hospital records. For patients who had undergone multiple bronchoscopies, each bronchoscopy was considered independently. The study included patients at the Brigham and Women's Hospital, a 635-bed tertiary care center, and the Beth Israel-Deaconess Medical Center, a 535-bed tertiary care center, each with active, accredited HSCT programs.

Clinical Characteristics

The medical records of each identified patient were reviewed, and the data were recorded on standardized forms. The collected data included the following: (1) general information (*ie*, age, gender, date of HSCT, and indication for HSCT); (2) information related to the time of bronchoscopy (*ie*, nature and duration of symptoms, number and duration of antimicrobial agents used, vital signs, routine blood testing results, chest radiographic results, and microbial culture data for sputum and blood); (3) findings related to bronchoscopy (*ie*, a description of visual findings, BAL culture, BAL cytology, and endobronchial and transbronchial biopsy (TBBx) pathology results; and (4) clinical outcomes (*ie*, changes in therapy related to bronchoscopy, complications related to bronchoscopy, and hospital mortality).

The vital signs recorded included heart rate, BP, respiratory rate, and an estimate of blood oxygenation. The variability in oxygen requirements were normalized by the use of an arterial oxygen saturation (Sa_{O_2})/fraction of inspired oxygen (F_{IO_2}) ratio. To determine the F_{IO_2} for patients receiving oxygen therapy by nasal cannula, each liter of supplemental oxygen was multiplied by 0.02 and was added to the room air F_{IO_2} (0.21). For intubated patients or patients requiring supplemental oxygen by face mask, the F_{IO_2} setting was considered to be the absolute F_{IO_2}. For example, for a patient with an Sa_{O_2} of 100% while breathing room air, the ratio was recorded as 1.0/0.21 = 4.76. For a patient with an Sa_{O_2} of 90% while breathing oxygen at 4 L/min by nasal cannula, the ratio was 0.90/0.29 = 3.1. Radiographic infiltrates were categorized as diffuse, focal, or nodular, according to the final report.

Bronchoscopic Findings

There was no standard protocol for the evaluation of pulmonary infiltrates in HSCT patients at either medical institution. Bronchoscopy in HSCT patients was performed at the discretion and direction of individual pulmonary consultants at each institution. The identification of potential pathogens was recorded from final microbiological laboratory reports. The reports included the results of routine microbiological cultures (bacterial, fungal, and viral), in addition to stains for acid-fast bacilli and special stains for organisms such as Pneumocystis sp. Reports for cytologic diagnosis were examined for the identification of nuclear inclusion bodies for CMV and hemosiderin-laden macrophages (for hemorrhage). The diagnosis of diffuse alveolar hemorrhage (DAH) was considered with the demonstration of a progressively bloody return of fluid at the time of BAL. For bronchoscopic biopsy specimens, pathologic diagnoses were obtained from the final pathology report. Medical records also were reviewed for surgical and/or autopsy lung pathology reports related to the same episode of illness.