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The economic costs to United States hospitals of invasive fungal infections in transplant patients

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Background: Patients with a solid organ transplant (SOTs) and hematopoietic stem cell or bone marrow transplants (HSC/BMTs) are at risk of contracting invasive fungal infections (IFIs). Data on the economic burden of IFIs in the United States are sparse.
Methods: We conducted a retrospective matched cohort study using the 2004-2005 Healthcare Cost and Utilization Project Nationwide Inpatient Sample. The IFI cohort included patients with ICD-9-CM codes indicating a transplant procedure and an IFI. Matched controls (transplant recipients without an IFI) were chosen based on age (10 year categories), sex, region, hospital type, year, and transplant type. Mortality, length of stay, and costs were reported overall, by transplant type, and by type of mycosis.
Results: Nine thousand eight hundred ninety-six patients underwent SOT, and 4661 underwent HSC/BMT. Of these, 80 (0.8%) SOT and 111 (2.4%) HSC/BMT patients had an IFI. Mean age was 41.8 years (SOT) and 37.8 years (HSC/BMT). Aspergillosis was the most common infection. Patients with an IFI had a 5-fold increase in mortality, an additional 19.2 hospital days, and $55,400 in excess costs compared with patients without an IFI. Excess mortality, length of stay, and costs varied by type of transplant and mycosis.
Conclusion: The clinical and economic burden of IFIs in transplant recipients may be high.
Key Words: Costs and cost analysis; length of stay; mycoses; transplants; mortality.

The number of solid organ transplant procedures has increased by over 40% in the last decade, with over 26,000 solid organ transplants (SOTs) and 8500 hematopoietic stem cell or bone marrow transplant (HSC/BMTs) procedures performed in the United States in 2006.[1,2] Whereas new immunosuppressive agents have increased survival by decreasing the likelihood of organ rejection,[3-6] they have also increased the risk of contracting bacterial, viral, and invasive fungal infections (IFIs).

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Several studies have evaluated the incidence and clinical burden of IFIs in selected transplant populations.[7-9] Abbott et al assessed hospitalizations for IFIs in a large group of renal transplant patients, documenting incidence, risk factors, and mortality, but no data were presented regarding excess costs.[7] Rabkin et al evaluated incidence, mortality, and lengths of stay among 96 liver transplant recipients for up to 120 days post-transplant and found an excess mortality of 19% and 12 additional hospital days related to fungal infections.[8] Rabkin et al also found that IFIs were significantly more prevalent in patients at high risk, such as those with renal insufficiency (34% in those with renal insufficiency vs 18% in those without). Patterson also found that the incidence of IFI in solid organ transplant patients varies by the type of transplantation performed and how immunosuppressed the patient would be based on the type of transplant, also noting that liver transplant recipients are more likely to have candidiasis infections, whereas heart and lung transplant patients are more likely to have aspergillosis infections.[10] Pugliese et al analyzed mortality and intensive care unit (ICU) lengths of stay among 278 solid organ transplant recipients in Italy.[9] They found that patients with IFIs had an excess mortality of 31% and spent an additional 25 days in the ICU.

There are limited data on the economic burden of IFIs in transplant patients. In a recent analysis using nationally representative data, Menzin et al studied the excess mortality, lengths of stay, and costs attributable to IFIs in high-risk patients in the United States.[11] They found that patients undergoing transplant procedures had the highest rate of excess mortality, lengths of stay, and costs compared with all other high-risk groups, although no data were available by specific transplant type. Wilson et al studied the excess costs of IFIs in the United States in a large nationally representative population and also found that transplant patients had the greatest cost burden compared with other high-risk populations. However, their study used data now more than a decade old, and no information regarding types of transplants and outcomes such as lengths of stay and mortality were reported for transplant patients.[12]

To understand better the clinical and economic burden of IFIs among transplant recipients, new data are needed that characterize key outcomes for various types of transplants and mycoses. The objective of this study was to assess the excess mortality, lengths of stay, and costs associated with IFIs during hospital stays for transplant procedures in the United States.

METHODS

Overview

This was a retrospective cohort study using data from the 2004 and 2005 Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS) (HCUP-NIS). Analyses of rates of infection, mortality, lengths of stay, and costs were performed for transplant patients with and without IFIs. Matching techniques were employed to estimate the excess burden for transplant patients with IFIs relative to similar transplant patients without IFIs. Costs were derived by converting charges for each hospital stay using hospital-specific cost-to-charge ratios.

Data source

HCUP-NIS is a database managed by the Agency for Healthcare Research and Quality (AHRQ) that contains discharge-level information on inpatient stays. Approximately 8 million hospitalizations (roughly 20% of all inpatient stays) from over 1000 US institutions are included in the database. A standard extraction from the database consists of 3 files: admission details, hospital characteristics, and disease severity. The admissions file contains information on patient demographics (such as age, sex, and race), ICD-9-CM diagnosis codes (up to 15), ICD-9-CM procedure codes (up to 15), lengths of stay, total charges, admission source, admission weight (to obtain national estimates), and discharge status. The hospital characteristics file contains details on hospital region, teaching status, number of beds, and location (urban or rural). The disease severity file contains details on severity of illness and comorbidities using the AHRQ categorization scheme.[13]

Patient selection

All patients with an ICD-9-CM procedure code indicating a transplant were included in this study. Those with an ICD-9-CM primary or secondary diagnosis code indicating an IFI were included in the IFI cohort, whereas those without a diagnosis code indicating an IFI were included in the comparison (non-IFI) cohort. Each patient from the IFI cohort was matched to 1 patient from the comparison cohort on the basis of age (within 10 years), sex, hospital region, hospital type, year in hospital (2004 or 2005), and type of transplant (heart, lung, kidney, liver, pancreas, allogeneic HSC/BMT, autologous HSC/BMT). Comparison patients were randomly selected when more than 1 match was possible.

Study measures

Study measures included the rate of IFIs as well as the excess burden of IFIs in terms of mortality, lengths of stay, and costs (in 2007 US dollars).

Data analyses

Patient demographics and AHRQ comorbidities were reported separately for SOT and HSC/BMT patients. Analyses of mortality, lengths of stay, and costs were reported by type of transplant (SOT, allogeneic HSC/BMT, and autologous HSC/BMT) and also by type of mycosis (candidiasis, aspergillosis, and other mycoses). Results were not stratified by the type of SOT because of sample size limitations. HCUP sample weights were used to calculate weighted means and standard errors that reflect the survey's complex sampling design. When using nationally representative health surveys, each record represents an observation from a sample that may not be a pure random sample. Applying sample weights is required to produce national totals as well as accurate estimate of means and standard errors. The excess mortality was estimated as the difference between the IFI and non-IFI cohorts in the proportion of patients who died in-hospital. Excess lengths of hospital stay and costs were assessed as the overall difference in means for each of the 2 cohorts. All outcomes were evaluated for statistical significance using P values derived from the SAS (SAS Institute, Cary, NC) procedure SURVEYREG, with statistical significance defined as $P < .05$. Multivariate