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Research Letters

A Comparison of COVID-19 and Influenza in Heart Transplant Recipients: A Nationwide Study in the United States



Previous studies have established the increased susceptibility of patients with cardiovascular comorbidities to COVID-19 and associated worse outcomes.^{1,2} Heart transplant (HT) recipients often have an increased burden of comorbidities and are also receiving chronic immunosuppressive therapies. Immunosuppression can increase susceptibility to infections but has also been hypothesized to blunt the cytokine storm in COVID-19 patients. Further, recipients of solid organ transplants have been proven to be at greater risk for complications from viral respiratory infections such as seasonal influenza than the general population. However, the effect of COVID-19 on HT recipients remains to be fully elucidated.

We aimed to evaluate the demographic and clinical characteristics, and effect of COVID-19 compared with influenza infection in HT recipients in a large, nationally representative database.

Methods

We queried the National Inpatient Sample from 2019 to 2020 for all adult (≥ 18 years) hospitalizations for COVID-19 or influenza in patients with a history of HT. The primary outcome of interest was in-hospital mortality. Secondary outcomes included respiratory failure, length of stay, and hospitalization costs. A 1:1 propensity score-matched analysis was performed to adjust for possible confounders. STATA 16.0 (StataCorp, College Station, TX) was used for analysis.

Results

We identified 34,930 hospitalizations (18,735 in 2019 and 16,195 in 2020) of patients with a history of HT. There was a total of 535 (1.5%) influenza-related hospitalizations and 1165 (3.3%) COVID-19-associated hospitalizations in patients with a history of HT from 2019 to 2020.

HT patients hospitalized with COVID-19 compared with influenza were more likely to be older (median age 62 vs 55 years; $P < 0.001$) and had a higher prevalence of comorbidities such as diabetes (53.0% vs 39.3%; $P = 0.01$), chronic kidney disease (70.5% vs 58.9%; $P = 0.04$), dementia (3.9% vs 0%; $P = 0.04$), and obesity (22.2% vs 9.3%; $P = 0.004$). There was no significant difference in chronic obstructive pulmonary disease among the 2 groups (18.7% vs 17.1%; $P = 0.72$).

After propensity score-matching, there were 390 hospitalizations in each group. The in-hospital mortality was

significantly higher among HT patients with COVID-19 infection compared with influenza infection (20 [5.1%] vs < 10 [0%]; $P = 0.02$). Respiratory failure requiring intubation > 24 hours was also more common in HT patients with COVID-19 (8.9% vs 1.3%; $P = 0.03$). Myocarditis was low and comparable in both groups (COVID-19, 5 [0.43%] vs influenza, 0 [0%]; $P = 0.50$; propensity matching could not be performed because of low number of participants), as was rejection (10 [2.5%] vs 0 [0%]; $P = 0.10$).

The median length of stay was significantly longer in HT patients with COVID-19 compared with those with influenza (5 [interquartile range {IQR}, 3-9] vs 3.5 [IQR, 2-5] days; $P = 0.01$), as was the median cost of hospitalization (\$12,620 [IQR, 6561-24,912] vs \$8208 [IQR, 5590-16,456]; $P = 0.01$).

The prevalence of HT patients with concomitant COVID-19 increased through the year in 2020 whereas a decrease in influenza infection in HT recipients was noted (Fig. 1). The highest mortality was noted in the initial phase of the pandemic with a significant decrease through the year.

Discussion

To the best of our knowledge, this is the first study to directly compare outcomes of COVID-19 and influenza infection in HT recipients.

HT recipients using chronic immunosuppressive medications might have greater viral burden, heightened infectivity, and worse outcomes. Elevated cytokine production and systemic inflammatory state play a critical role in COVID-19 infection whereas the interaction between immunomodulators and the inflammatory state is poorly understood.³ Previous reports have shown a worse mortality with COVID-19 in HT recipients—as high as 20%-30%.^{3,4} Compared with our study, most of these studies were done in the early phases of the pandemic and are comparable to mortality noted in the earlier phase of our study.^{3,4}

The American Society of Transplantation recommends annual influenza vaccination for HT recipients because of the higher mortality rate in this vulnerable population. Previous studies have reported worse mortality with COVID-19 compared with influenza in the general population.⁵ This was also evident in our study of HT recipients, in whom COVID-19 was associated with a significantly higher mortality rate after propensity score-matching for comorbidities.

In our study we used a national database, overcoming the biases with single-center studies, however, there might be misclassification errors and potential confounding. Further, the differential in the vaccination rates of both groups likely also affects outcomes because COVID-19 vaccination was not

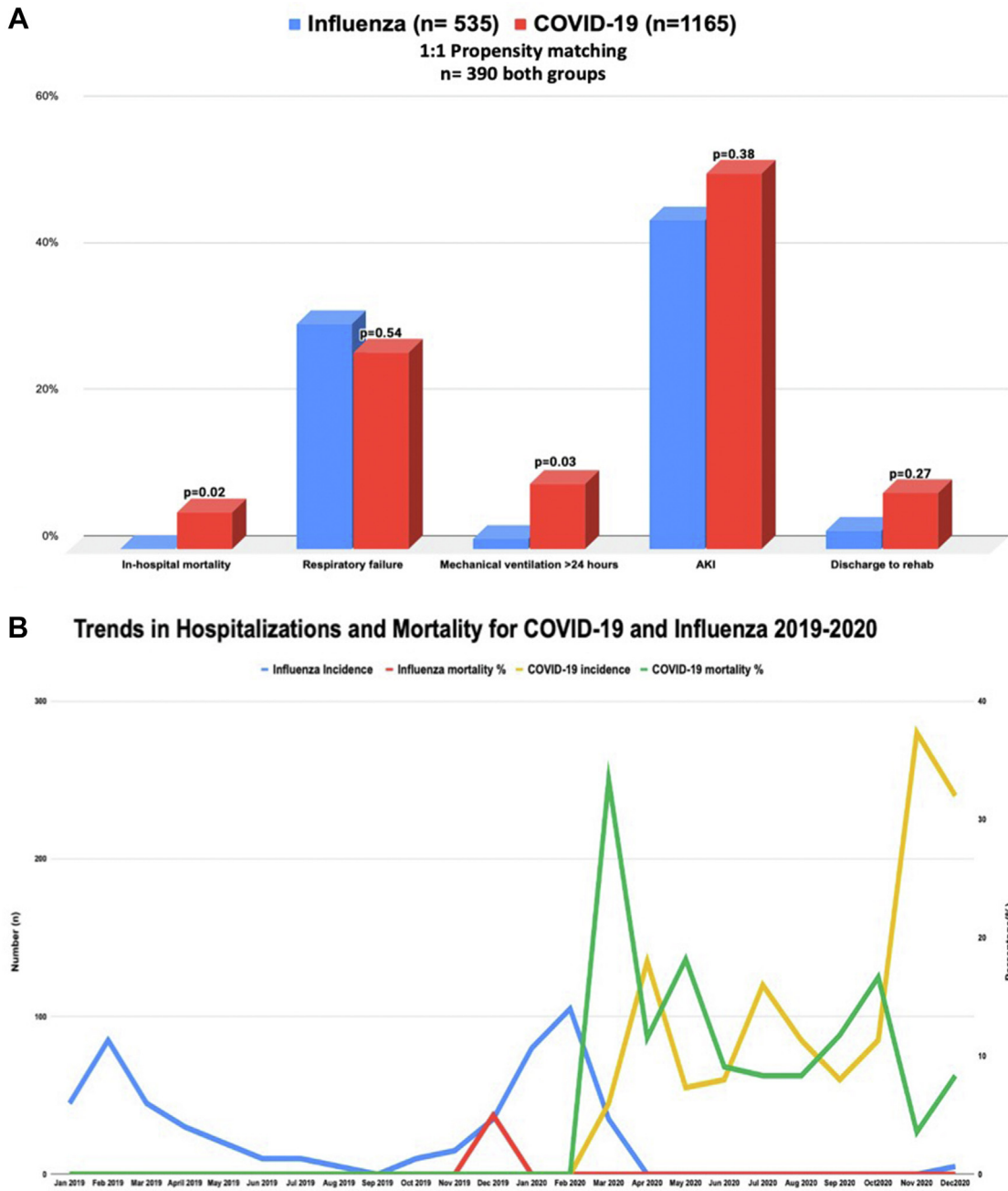


Figure 1. (A) Propensity score-matched outcomes of COVID-19 vs influenza in heart transplant recipients. (B) Trends in hospitalizations and mortality. **Left y axis:** number (n); **right y axis:** percentage (%).

available in 2020. In summary, among patients hospitalized with a history of HT, COVID-19 was associated with an increased risk of mortality and respiratory failure, and healthcare utilization compared with influenza infection.

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