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Short Communication

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Impact of Gastroesophageal Reflux Disease on Patients Undergoing Lung Transplantation for COVID-19: A Single Institution Retrospective Study

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Abstract

Background: Patients with coronavirus disease 2019 (COVID-19)-associated respiratory failure undergoing lung transplantation is an emerging subset of transplant patients in which gastroesophageal reflux disease (GERD) pre- or post-transplant is not well characterized.

Methods: We retrospectively evaluated patients undergoing lung transplant for COVID-19, with attention to pre- and post-operative physiological testing for GERD.

Results: Seventeen patients were identified who had undergone lung transplant for COVID-19. No patient underwent pre-transplant GERD testing. Post-transplant, 70.5% (12/17) patients reported reflux symptoms confirmed with additional testing. Three patients underwent anti-reflux surgery (ARS) based on results of testing, and none had complications or symptom-based recurrence of reflux.

Conclusion: Our study depicts a unique cohort of patients who were unable to undergo pre-transplant testing for GERD in the setting of a global pandemic, and who were routinely assessed and managed post-transplant.

Keywords: Gastroesophageal reflux disease; Lung transplant; COVID-19 infection

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Introduction

Gastroesophageal reflux disease (GERD) symptoms are prevalent in up to 40% of the population, and this can increase in patients after lung transplantation [1]. The incidence is estimated to be up to 65% of patients who have undergone lung transplant [2]. The exact mechanisms for post-transplant GERD are unclear; proposed mechanisms include intra-operative vagal nerve damage, esophageal and gastric dysmotility, and underlying structural compromise with the presence of a hiatal hernia [3]. Optimizing management of GERD is important to preserve graft function after lung transplantation as patients with GERD are at higher risk of rejection [4]. With the recent coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an increasing number of patients presented with COVID-19-associated respiratory failure with lung transplantation explored for this unique cohort of patients. As such, lung transplantation is an emerging subset of transplant patients in which GERD pre- or post-transplant is not well characterized.

Materials and Methods

A retrospective review was conducted at a single academic medical center with a large multi-organ transplant program, with the aim of evaluating the prevalence of GERD pre-transplant and the incidence of GERD post-transplant in patients undergoing lung transplantation for COVID-19-associated respiratory failure. The research was conducted ethically in accordance with the Health Insurance Portability and Accountability Act and the World Medical Association Declaration of Helsinki. The analysis received approval from the Institutional Review Board (IRB) through the Houston Methodist Research Institute (ID: MOD00005383). All patients undergoing lung transplant due to COVID-19 from 2020 to 2021 were included in the study, with attention to pre- and post-operative physiological testing for GERD. Data collected included the following: age at transplant, body mass index (BMI), gender, ethnicity, time from documented COVID-19 to date of transplant, requirement of veno-venous extracorporeal membrane oxygenation (VV ECMO), reflux symptoms or GERD diagnosis

Table 1. Clinical Characteristics in Patients Who Underwent Lung Transplant for COVID-19 Prior to Transplantation

	Patients who underwent lung transplant for COVID-19 (n = 17)
Gender	
Male	17/17
Female	0/17
Ethnicity	
Caucasian	6/17
Hispanic	9/17
Black	2/17
Median age at transplant	50
Mean age at transplant	48
Range of age at transplant	24 - 70
Median BMI	28.9
Mean BMI	31.5
Median time from documented COVID-19 infection to transplant	131 days
Mean time from documented COVID-19 infection to transplant	163 days
Requirement of VV ECMO	13/17
GI symptoms reported prior to transplant	5/17
Reflux	5/5
Comorbidities	
Obesity (BMI > 30)	8/17
Hiatal hernia	2/17
Pre-transplant testing/workup for reflux disease	
Yes	3/17
No	14/17
Testing/workup performed	
Upper endoscopy	3/3
Reason for pre-transplant testing	
Gastrointestinal bleed	3/3
PEG tube placement	1/3
On PPI prior to transplant	2/17
On PPI post-transplant	17/17

VV ECMO: veno-venous extracorporeal membrane oxygenation; BMI: body mass index; PEG: percutaneous endoscopic gastrostomy; PPI: proton pump inhibitor.

reported prior to transplant, comorbidities prior to transplant (i.e., diabetes, obesity, and hiatal hernia), any completed pre-transplant reflux testing, whether the patient was on acid suppression therapy before and/or after transplant, single versus dual organ transplant, post-transplant reflux symptoms, reflux studies completed post-transplant (i.e., gastric emptying, pH-impedance, barium esophagram, and esophagogastroduodenoscopy (EGD)), and evaluation for anti-reflux surgery (ARS).

Results

Seventeen patients were identified who had undergone lung transplant for COVID-19. All patients were male, with the following demographics: 52.9% (9/17) Hispanic, 35.3% (6/17) Caucasian and 11.8% (2/17) Black (Table 1). The median age was 50 (24 - 70 years), with median time to transplant from documented infection of 131 days. A pre-hospitalization GERD diagnosis was found in 29.4% (5/17) patients, and two of these patients (11.8%) were taking prescribed proton pump inhibitor (PPI) prior to their COVID-19-associated hospitalization. No patient underwent pre-transplant GERD testing, although three patients did undergo upper endoscopy for gastrointestinal (GI) bleeding prior to transplant. Post-transplant, all patients were immediately treated with a PPI per institutional protocol. Seventy point five percent (12/17) patients reported post-transplant

Table 2. Clinical Characteristics in Patients Who Underwent Lung Transplant for COVID-19 After Transplantation

	Patients who underwent lung transplant for COVID-19 (n=17)
Post-operative foregut symptoms	12/17
Cough	7/12
Early satiety	1/12
Abdominal bloating	4/12
Abdominal pain	2/12
Nausea and/or vomiting	5/12
Dysphagia	1/12
Reflux symptoms (heartburn or regurgitation)	1/12
Post-operative foregut studies completed	17/17
Gastric emptying study	14/17
Normal	6/14
Delayed gastric emptying at 4 h	6/14
Incomplete studies	2/14
Barium esophagram	7/17
Normal	5/7
Abnormal	2/7
EGD	2/17
Normal	1/3
Abnormal	1/3
pH study (capsule or impedance manometry)	6/17
Normal	2/6
Abnormal	1/6
Incomplete studies	3/6
Non-adherence to study	2/3
Unable to tolerate study	1/3
Esophageal manometry	3/17
Normal	1/3
EGJOO	1/3
IEM	1/3
Bronchoscopy	3/3
Positive cultures	2/3
Referral for ARS	3/17
Toupet fundoplication completed	3/3
Hiatal hernia repair completed	2/3
Median time from transplant to ARS	240 days
Mean time from transplant to ARS	189 days
Range of time from transplant to ARS	73 - 255 days

EGD: esophagogastroduodenoscopy; EGJOO: esophagogastric junction outlet obstruction; IEM: ineffective esophageal motility; ARS: anti-reflux surgery.

foregut symptoms including heartburn, regurgitation, dysphagia, early satiety, abdominal bloating/cramping, nausea, and vomiting (Table 2). All 17 patients had at least one symptom-driven foregut study such as a barium esophagram, upper endoscopy, gastric emptying study, esophageal manometry or pH testing. Three patients were referred for ARS based on results of testing, including delayed gastric emptying, abnormal pH testing and bronchoscopy findings concerning for aspiration

pneumonia. All three underwent Toupet fundoplication with or without hiatal hernia repair; one was performed early (< 3 months) post-transplant, two occurred late (> 6 months), and none had complications or symptom-based recurrence of reflux at 12 months post-transplant.

Discussion

In this retrospective single-center descriptive study on patients with COVID-19-associated respiratory failure and undergoing lung transplant, pre-operative reflux testing could not be performed in the unique setting of a global pandemic with acutely critically ill patients. Nevertheless, GERD symptoms were still routinely assessed and evaluated post-transplant prompting medical and surgical management with acid suppression therapy and ARS, respectively, in a small subset of patients. This was seen in both early (< 6 months) and late (> 6 months) post-transplant, with resolution of GERD symptoms reported.

Notably, the incidence of post-transplant GERD was 70.5% in our cohort, which is around the reported incidence based on prior studies [2]. The prevalence of GERD prior to transplant was seen in 29.4% of our cohort, comparable to prior reported studies [1, 2, 4]. Thus, the underlying insult causing the respiratory failure, which in our cohort was infectious and a more acute process, does not appear to affect the overall incidence of GERD post-transplant. However, this postulation is clearly limited given the retrospective nature of the study, the small number of patients in the cohort, and the fact that pre-transplant testing for GERD was unable to be pursued in this critically ill group of patients.

While this is not the largest cohort of lung transplantation for COVID-19 published, it is the largest and only cohort of such patients where an attention to GERD and therapy has been described [5]. Management of GERD has been shown to reduce the risk of rejection and improve overall transplantation outcomes [6, 7]. Evidence for the role of medical anti-reflux therapy has been limited; however, exposure to acid suppression after transplantation has been associated with reduced risk of allograft rejection [8, 9]. ARS has been suggested to better prevent allograft injury and improve survival, as acid suppression, while altering the acidity of refluxate, does not necessarily prevent volume reflux and aspiration, and therefore may only play an adjunctive role, especially when ARS cannot be immediately performed [10, 11]. However, none of these studies included a subset of patients where transplantation occurred for severe acute lung injury such as COVID-19.

The retrospective and descriptive nature of this study and the inability to evaluate the role of GERD pre-operatively restricts the assessment of the impact of GERD on allograft dysfunction. However, even in this smaller group of respiratory failure due to COVID-19, a pragmatic post-operative approach to GERD driven by either symptoms or deterioration of lung function, suggests that testing may be foregone in select cases and performed post-operatively without change in 3- or 6-month survival. Ultimately, the unique nature of this group, with acute lung injury leading to transplantation, merits further investigation in assessing the impact of GERD on allograft dysfunction and mortality.

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Financial Disclosure

None to declare.

Conflict of Interest

The authors have no conflict of interest to declare.

Informed Consent

All subjects provided informed consents.

Author Contributions

CK wrote the paper and performed analysis on the collected data; CK, DB, EC and GE conceived the study and helped write the paper; HH, RC, AG, SY, JY, TM, ES and PC contributed to the study design and analysis and critically reviewed the manuscript. All authors approved the final version of the article, including the authorship list.

Data Availability

The data underlying this article are available in the article, and will also be shared on reasonable request to the corresponding author.

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