

Esophageal Function and Reflux Evaluations in Lung Transplantation: A Nationwide Survey of UNOS-Accredited Transplant Centers in the United States

Ryan Leung^{1,2}, Wai-Kit Lo, MD, MPH^{1,3}, Nirmal S. Sharma, MD^{3,4}, Hilary J. Goldberg, MD, MPH^{3,4} and Walter W. Chan, MD, MPH^{1,3}

INTRODUCTION: Gastroesophageal reflux disease has been associated with worse lung transplant outcomes. We aimed to assess local practices for esophageal function testing (EFT) across transplant centers.

METHODS: This was a survey study of all United Network for Organ Sharing–accredited adult lung transplant centers regarding local EFT practice.

RESULTS: Among 39/63 (60%) responded centers, 38.5% required any EFT (35.9% esophageal manometry, 15.4% pH monitoring, and 28.2% pH impedance), while another 28.2% may consider EFT based on symptoms. Five-year transplant volume was higher among centers requiring EFT (253 vs 159, $P = 0.04$).

DISCUSSION: Only a minority of lung transplant centers routinely obtained EFT, supporting the need for guidelines for standardized reflux/esophageal assessment.

KEYWORDS: lung transplantation; reflux monitoring; pH-impedance; pH monitoring; esophageal manometry; barium esophagram

SUPPLEMENTARY MATERIAL accompanies this paper at <http://links.lww.com/CTG/B15>

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INTRODUCTION

Gastroesophageal reflux disease (GERD) and esophageal dysmotility have been associated with increased rejection and allograft failure in lung transplant patients (1–3). Prior studies demonstrated that early antireflux treatments for patients with evidence of GERD significantly reduce allograft injury and rejection risk (4,5). However, there is currently no established guideline for esophageal function and reflux evaluations for patients undergoing lung transplantation. This study aims to compare local practices for esophageal function testing (EFT) across US lung transplant centers.

METHODS

This was a survey study of all lung transplant centers in the United States accredited by the United Network for Organ Sharing (UNOS). A 10-item survey was distributed to the centers' directors regarding local practices of any pretransplant or posttransplant

EFT (ambulatory pH monitoring [APM], multichannel intraluminal impedance–pH study [MII-pH], and esophageal manometry [ESMO]) and other foregut studies (upper endoscopy [EGD], barium esophagram [BE], and gastric emptying scintigraphy [GES]). Survey questions addressed the role of any peri-transplant testing requirement, including timing and type of testing, patient selection, and management implication (see Supplementary Table 1, Supplementary Digital Content, <http://links.lww.com/CTG/B15>). In addition, the 5-year transplant data and patient characteristics for each site were obtained from the UNOS (see Supplementary Methods, Supplementary Digital Content, <http://links.lww.com/CTG/B15>).

RESULTS

Of 63 UNOS-listed adult lung transplant centers, 39 (60%) responded to the survey, with no missing data and high degree of response reliability in the questions with dichotomized (yes/no)

¹Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, Boston, Massachusetts, USA; ²LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China; ³Harvard Medical School, Boston, Massachusetts, USA; ⁴Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA. **Correspondence:** Walter W. Chan, MD, MPH. E-mail: wchan@bwh.harvard.edu.

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Table 1. Characteristics of lung transplant center respondents

	N = 39
5-yr transplant volume (mean ± SD)	171 ± 136
Female, % (mean ± SD)	40.1 ± 7.3
Race/ethnicity, % (mean ± SD)	
White	79.1 ± 13.5
Black	10.3 ± 7.8
Latinx	8.2 ± 9.9
Asian	1.8 ± 2.1
Age groups, % (mean ± SD)	
<50	22.0 ± 9.3
50–65	47.8 ± 8.8
>65	30.2 ± 11.0
Primary lung disease, % (mean ± SD)	
IPF	35.3 ± 12.1
COPD	21.2 ± 7.9
CF	11.0 ± 7.1
Alpha-1 antitrypsin	2.6 ± 2.1
Diabetes mellitus, % (mean ± SD)	22.5 ± 10.1

responses (Table 1). Overall, only 15 (38.5%) centers required any EFT during peritransplant management, including 14 (35.9%) ESMO, 6 (15.4%) APM, and 11 (28.2%) MII-pH. Another 11 (28.2%) centers would consider EFT based on symptoms/findings of other tests. Overall, EFT was not part of peritransplant management protocol in 12 (30.8%) centers (Figure 1a).

During pretransplant workup, BE (n = 23, 59%) was the most commonly obtained study. Only 11 (28.2%) programs required EFT, while 12 (30.8%) may consider EFT based on symptoms/findings of other tests. Specifically, 21 (53.9%) and 23 (59.0%) centers required/considered pretransplant ESMO or GERD testing (APM/MI-pH), respectively. Among those requiring EFT, 4/11 (36.4%) may exclude candidates from transplant based on testing results, specifically for scleroderma esophagus/absent contractility. Thirteen (33.3%) centers required/considered GES, while EGD was rarely obtained (n = 4, 10.2%). Among centers conditionally requiring EFT, common indications for testing include underlying connective tissue disorders, interstitial lung disease, cystic fibrosis, and esophageal symptoms (Figure 1b, Supplementary Table 2 [see Supplementary Digital Content, <http://links.lww.com/CTG/B15>]).

During the posttransplant period, EFT was routinely obtained in 10 (26.3%) centers (13.2% APM, 18.9% MII-pH, and 23.7% ESMO), all within 3–6 months posttransplant. Another 9 (23.7%) may consider post-transplant EFT depending on symptoms or clinical status, such as pulmonary function decline or acute

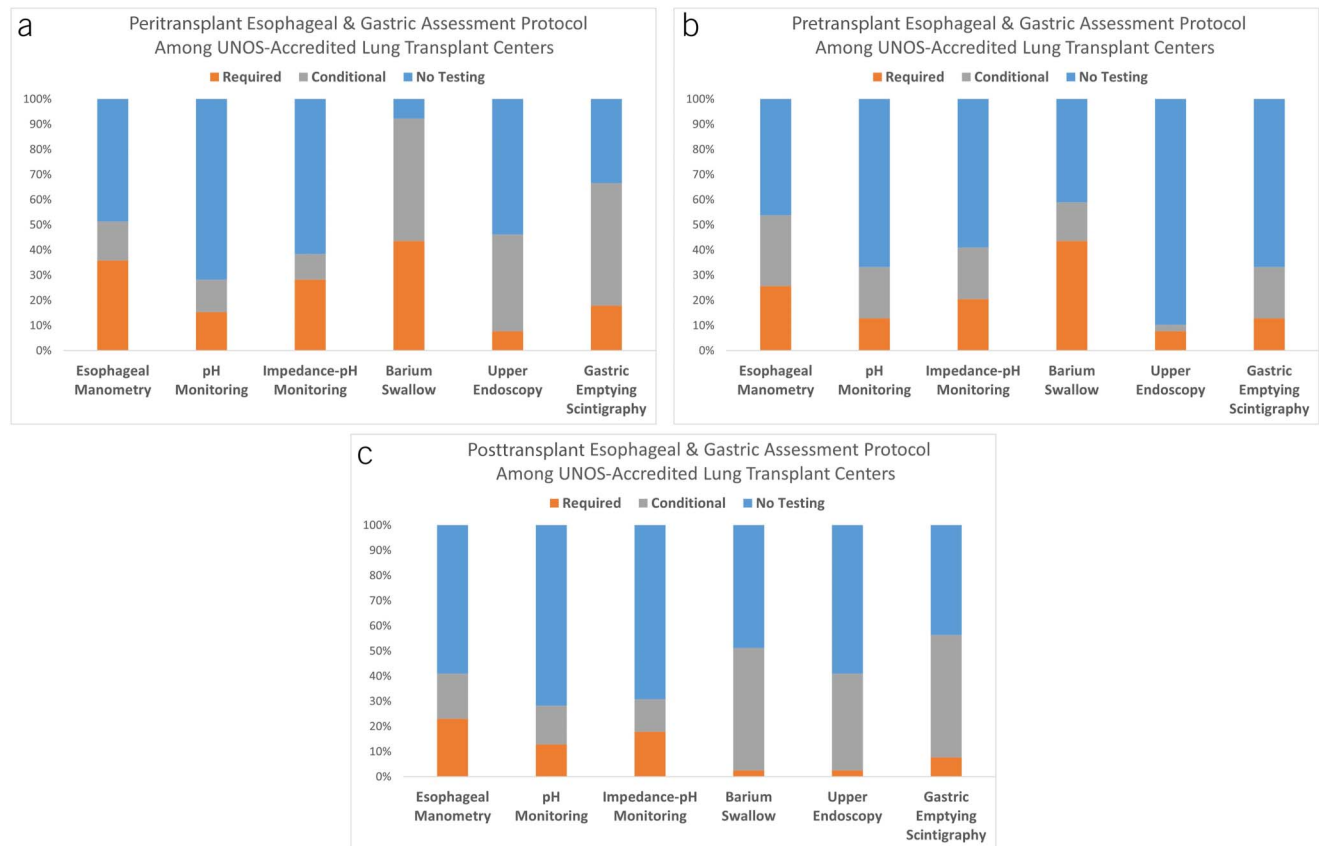


Figure 1. Esophageal, gastroesophageal reflux, and foregut assessments at lung transplant centers during (a) overall peritransplant period, (b) pretransplant assessment, and (c) posttransplant follow-up. Required: testing routinely obtained in all patients either prelung or postlung transplant, regardless of clinical symptoms. Conditional: testing obtained only if indicated by the presence of esophageal symptoms or abnormal findings on other studies. No testing: testing not obtained as part of lung transplant evaluation or management.

rejection (Figure 1c, Supplementary Table 2 [see Supplementary Digital Content, <http://links.lww.com/CTG/B15>]). Among centers routinely or conditionally obtaining posttransplant EFT, 1 (5.3%) would complete testing at <3 months, 12 (63.2%) at 3–6 months, and 3 (15.8%) at >6 months posttransplant, while 3 (15.8%) centers do not have specific time line.

In the assessment of transplant center characteristics, the mean 5-year transplant volume was higher among those requiring EFT (253 vs 159, $P = 0.04$). There was no significant association between EFT requirement and the centers' rate of restrictive lung disease (37% vs 34.1%, $P = 0.50$), age older than 65 years (31.6% vs 31.4%, $P = 0.94$), or diabetes mellitus (20.8% vs 21.9%, $P = 0.62$) among lung transplant recipients.

DISCUSSION

GERD is highly prevalent in patients with end-stage lung disease (6) and has been postulated to increase allograft rejection risk through nonallogeneic injury through aspiration of gastroduodenal contents (7). Esophageal dysmotility, particularly ineffective esophageal motility, has also been associated with increased allograft dysfunction and mortality (3). Through this national survey, we report for the first time the diverse practice patterns related to pretransplant/posttransplant esophageal testing among US lung transplant centers.

Despite established evidence in prior literature, more than half of respondents in this survey of UNOS-listed lung transplant centers do not routinely perform EFT either before or after lung transplantation. Specifically, only approximately 1 in 3 centers required EFT during the peritransplant period, while another 1 in 4 would consider EFT based on symptoms.

GERD and esophageal dysfunction may predispose to lung allograft injury through microaspiration, which may lead to immunomodulation through release of proinflammatory cytokines, acute rejection, and ultimately chronic rejection in the form of bronchiolitis obliterans syndrome and chronic lung allograft dysfunction (7,8). Of importance, such injury may begin during the early posttransplant period because pepsin has been detected in the bronchoalveolar lavage fluid within the first month, and pretransplant GERD has been associated with worse early posttransplant outcomes (9,10), which positions GERD as an early target for intervention.

Indeed, prior studies have demonstrated that medical therapy with acid suppression posttransplantation was associated with reduced time-to-allograft rejection (11), while antireflux surgery improved lung allograft function and stabilized posttransplant pulmonary status among those with GERD (12,13). In particular, early antireflux therapy within 6 months of transplantation was found to provide significant benefits over later treatment (4). More recently, a protocol for routine reflux testing among lung transplant candidates with early antireflux treatment as indicated has been shown to reduce acute/chronic rejection (5). Despite this evidence, we found that only a minority of lung transplant centers routinely incorporates EFT as part of the management algorithm, though some centers would consider EFT based on the presence of esophageal symptoms. However, many patients with chronic lung disease with GERD may not exhibit typical symptoms of reflux or dysmotility (14), so a symptom-based approach may not be sufficient.

Among centers routinely or conditionally obtaining EFT, the timing and modality of testing remain highly variable. Specifically,

a significant proportion of centers reported BE as the preferred modality of esophageal assessment, likely due to availability and ease of testing. However, the utility of studies such as BE, EGD, and GES in lung transplantation remains questioned, given their suboptimal sensitivity and specificity for GERD diagnosis (15). Oro-pharyngeal assessment with modalities such as modified barium swallow may also be considered, although clinical data in this population are similarly limited. The preferred time for testing relative to transplantation is also unclear, considering the benefits of early intervention with the risks and clinical complexity during the peritransplant period.

Limitations of this study include its response rate (60%) and potential for reporting bias toward centers with standard esophageal evaluation protocols in place, thereby affecting the generalizability of the survey findings. However, our responses were still representative of a majority of UNOS-listed transplant centers, and this potential bias would indicate that the esophageal testing rate is likely even lower, further strengthening our conclusion that only a minority of centers incorporates routine EFT. This brief survey primarily used questions with dichotomized (yes/no) responses, which may not fully capture the nuances of EFT practice. Another limitation is that allograft rejection and outcome data of the transplant centers were not readily available for further analysis. Finally, detailed aspects of EFT, such as acid suppression use during study and choice of study type and the underlying reasons or challenges in pursuing EFT were not assessed in this brief exploratory study. These represent areas for further investigations in future studies. Regardless of the limitations, we believe it is useful to assess and highlight the heterogeneous status of esophageal evaluation within lung transplantation protocols in centers across the country.

In conclusion, only a minority of lung transplant centers routinely obtained EFT in the perilung transplantation period despite evidence supporting more aggressive evaluation and management of GERD to improve outcomes. Guidelines should be established for an evidence-based approach to EFT in this high-risk population to encourage widespread adoption and standardization of practice.

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