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Staging of Bilateral Lung Transplantation For High-Risk Patients with Interstitial Lung Disease: One lung at a time

MG Hartwig¹, AM Ganapathi¹, AA Osho¹, SJ Hirji¹, BR Englum¹, PJ Speicher¹, SM Palmer², RD Davis¹, and LD Snyder²

¹Department of Surgery, Duke University Medical Center, Durham, NC, USA

²Department of Medicine, Duke University Medical Center, Durham, NC, USA

Abstract

The choice of single or bilateral lung transplant for interstitial lung disease (ILD) is controversial as surgical risk, long term survival and organ allocation are competing factors. In an effort to balance risk and benefit, our center adopted a staged bilateral lung transplant approach for higher surgical risk ILD patients where the patient has a single lung transplant followed by a second single transplant at a later date. We sought to understand the surgical risk, organ allocation and early outcomes of these staged bilateral recipients as a group and in comparison to matched single and bilateral recipients. Our analysis demonstrates staged bilateral lung transplant recipients (n=12) have a higher LAS, lower pulmonary function tests and lower glomerular filtration rate prior to the first transplant compared to the second (p<0.01). There was a shorter length of hospital stay for the second transplant (p=0.02). The staged bilateral compared to single and bilateral case matched controls had comparable short-term survival (p=0.20) and pulmonary function tests at one year. There was a higher incidence of renal injury in the conventional bilateral group compared to the single and staged bilateral groups. The staged bilateral procedure is a viable option in select ILD patients.

Introduction

As the indication for the first successful lung transplant by Joel Cooper in 1983,¹ idiopathic pulmonary fibrosis (IPF) is a leading cause for the need for lung transplantation.² Based on early experience, single orthotopic lung transplantation (SOLT) was the treatment for end-stage IPF, however as more recent data has demonstrated the benefits of bilateral orthotopic lung transplantation (BOLT),^{3, 4} patients are more commonly receiving a BOLT.⁵ However, this practice has been controversial as some authors have described equivalent overall outcomes for both SOLT and BOLT in IPF.^{6, 7} Recently a study that considered conditional 1-year survival noted a long-term survival advantage for BOLT in IPF candidates.⁶

Corresponding Author: Matthew G. Hartwig, MD, Duke University Medical Center, Durham, North Carolina 27710, Phone: 919-613-5635, Fax: 919-613-5654, matthew.hartwig@duke.edu.

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Directly linked to the question of survival benefit is the perioperative morbidity and mortality risk of a SOLT versus a BOLT. A SOLT is associated with decreased operative times, less hemodynamic perturbations, and subsequently lower perioperative mortality in high-risk lung recipients.⁸ In contrast, a BOLT requires a larger incision with associated worse pulmonary mechanics.^{9, 10} This, coupled with the increased need for cardiopulmonary bypass and other operative factors leads to increased perioperative mortality in selected BOLT recipients.

Given that both SOLT and BOLT have theoretical drawbacks, a therapeutic option that could combine the decreased perioperative risk of SOLT with the long-term benefit of BOLT would be ideal for some patients. We hypothesized that a potential solution would be a staged BOLT procedure where the patient would undergo a SOLT and then if the recipient is felt to be suitable for relisting, the recipient would be considered for subsequent contralateral SOLT (i.e., staged BOLT). Herein, we describe our institutional experience with this novel approach along with its safety profile and potential compared with conventional SOLT and BOLT recipients.

Materials and Methods

Study Cohort and Data Sources

This is a retrospective review of early outcomes in a cohort of lung transplant recipients at our center following a change in clinical protocols. All lung transplants for ILD at a single institution between January 1, 2009 to August 31, 2013 were eligible as we introduced the change in clinical protocol in 2009. Pediatric recipients, those who underwent redo or multi-organ transplantation, and patients with a diagnosis other than ILD were excluded. Donor and waitlist characteristics were obtained from the United Network for Organ Sharing (UNOS) file specific to Duke University recipients. Additional data was obtained from the patient's electronic medical record. Follow-up was complete and patients alive were censored on August 31, 2014, allowing for a minimum of 12 months follow-up. This study was approved by the Duke University IRB, Pro00061146. All patients underwent separate informed consent prior to all lung transplant procedures after a thorough discussion regarding the risks and benefits of lung transplantation was performed.

Protocol for Staged Bilateral Lung Transplantation

Our institutional approach to patients with end-stage ILD requiring transplant is detailed in Figure 1. Briefly, when ILD patients are evaluated for lung transplantation, a perioperative risk assessment is done. Patients who are considered low or average risk or those with severe secondary pulmonary hypertension (PH) are preferentially listed for a BOLT. However patients who are considered to be at higher surgical risk were listed for a SOLT. Specifically, patients over the age of 65, those with significant concomitant coronary artery disease (CAD), and patients demonstrating diminished functional status were considered higher perioperative risk and preferentially underwent an initial SOLT procedure. All SOLT recipients are then reviewed for a second SOLT (i.e. a staged BOLT). SOLT recipients who had no significant perioperative complications and independent functional status following the initial transplant were then offered a contralateral second SOLT. Listing for a

contralateral procedure is offered as soon as clinically appropriate (i.e. no active infection or rejection, recovery of functional status). Listing could be delayed based on patient preference. All variables relevant to the LAS were updated for the second transplant listing to reflect the current status of the patient. The diagnosis for the second lung transplant was listed as the native lung disease. Immunosuppression regimens for the two stages of a Staged BOLT were the same with induction Basiliximab and solumedrol. Maintenance immunosuppression included prednisone, mycophenolate mofetil and tacrolimus.

Study design

The first part of the study was to understand the clinical variables of the first and second stages focusing just on the staged BOLT recipients. The second part of the study employed a case control analysis matching the staged BOLT recipients to conventional SOLT and conventional BOLT recipients in a 1:2:2 fashion. Controls were randomly selected out of all possible matches to other ILD transplant recipients from our center. Matching criteria included age within 3 years and lung allocation score (LAS) within 10 points. If a match was not able to meet these criteria, then the matched age control was extended to 8 years.

The primary outcome of the case control part of the study was cumulative survival following lung transplantation. The cumulative survival for staged BOLT recipients was determined from the time of the first-stage transplant. Secondary outcomes included postoperative length of stay (LOS), days in the intensive care unit (ICU), days on the ventilator, PaO₂:FiO₂ ratio at 72 hours, and perioperative morbidity, as measured by atrial fibrillation, acute renal failure (ARF), need for dialysis, and stroke. Additionally, a combined morbidity score was created with 1 point being assigned for each of the following: length of stay > 25 day, ICU stay > 4 days, days on the ventilator > 2, incidence of atrial fibrillation, post-operative stroke, Risk, Injury, Failure, Loss, and End-stage (RIFLE) kidney injury or kidney failure event (maximum score of 7). In cases of LOS, ICU, and ventilator days, for the staged BOLTs, the morbidity event was considered to have happened if the combined number of days for both stages of the transplant were greater than defined above. For all other events, one point was assigned if it occurred in either the first or second stage.

Statistical Analysis

Descriptive statistics were used for the first part of the study to evaluate clinical characteristics and perioperative outcomes before the first and the second stages of the staged BOLT recipients. These comparisons were done with a paired t-test or McNemar's test for continuous and categorical variables. For the primary outcome of cumulative survival, an unadjusted Kaplan-Meier survival model considered the survival among SOLT, BOLT and staged BOLT recipients. For secondary endpoints, the one way analysis of variance or the Kruskal-Wallis analysis of variance test was utilized as appropriate.

A p-value of <0.05 was considered statistically significant, and type I error was controlled at the level of the comparison. Analyses were performed using R version 3.0.2, R Foundation for Statistical Computing, Vienna, Austria and SAS 9.4, Cary, NC.

Results

Study cohort

From January 1, 2009 to August 31, 2013, there were 192 lung transplant patients with ILD that met inclusion and exclusion criteria. Of these, 12 (6.3%) patients had a staged BOLT procedure, n=106 (55.2%) had a conventional SOLT, and n=74 (38.5%) had a conventional BOLT. Following matching, there were n=24 control SOLTs and n=24 control BOLTs identified. Overall, comparison of recipient and donor characteristics amongst the three groups revealed no significant differences (Table 1).

Comparison of first and second stages of the staged BOLT procedure

Median time between the two transplants was 167.5 days (range: 70–765 days). No significant differences were noted in donor characteristics, although there was a trend towards the donors for the second stage procedure being older (35 vs. 49 years for first and second stage, respectively; $p=0.22$) (Table 2). As all the LAS was updated to reflect current status prior to the second transplant, the median LAS was significantly lower prior to transplant in the second stage (48.6 vs. 34.5 in the first and second stage respectively; $p<0.01$). Despite the lower LAS, there was no significant difference in median waitlist time for the second stage transplant (11.5 days vs. 5.5 days for the first and second stage respectively, $p=0.69$). Notably, there was a trend to a higher recipient sequence match number for the second stage (6 vs. 53; $p=0.06$).

There was a significant improvement prior to the second transplant in percent predicted FEV₁ (median of 44.5% vs. 62% for the first and second stage respectively; $p<0.01$) and FVC (median of 42% vs. 63% for the first and second stage respectively; $p<0.01$). Notably, the incidence of diabetes was higher prior to the second stage compared to the first (16.7% vs. 41.7% in the first and second stage respectively; $p=0.25$) and the median baseline glomerular filtration rate (GFR) at the time of listing was lower prior to the first (92.7 ml/min/1.73m² vs. 53.0 ml/min/1.73m²; $p<0.01$). The minimum functional requirements to be listed for transplant included a 20 minute walk test of at least ½ mile and a 6 minute walk distance of at least 1000 feet, regardless of oxygen use.

There was a significant reduction in median postoperative length of stay (LOS) for the second transplant (10 vs. 6 days for the first and second stage, respectively) as well as days in the ICU (4 vs. 2 days, $p=0.02$ in both cases). No significant differences were seen regarding days on the ventilator, incidence of postoperative stroke or dialysis. The incidence of postoperative renal injury or worse as defined by the RIFLE kidney classification¹¹ was 25% (n=3) in the first stage with no renal injury in the second stage ($p=0.25$). Interestingly, there was only one instance (8.3%) of postoperative atrial fibrillation in the second stage, compared to 5 instances (41.7%) ($p=0.22$) for the same patients after the first stage. There was a trend to higher PaO₂ to FiO₂ ratio at 72 hours following the second stage (Table 3).

Survival after lung transplant

The median follow up time for the survival analysis was 1036 (IQR 700,1491) days posttransplant for all the groups. Median SOLT follow up time was 929 days (IQR 559,

1472), median BOLT follow up time was 1171 days (IQR 588, 1697) and median staged BOLT follow up time was 1011 (IQR 901, 1185). During this period, there were 9 SOLT deaths and 10 BOLT deaths. There was one death in the staged BOLT cohort due to lung cancer that occurred 965 days after the first lung transplant. As noted above, the staged BOLT survival time was calculated at the time from first transplant. In an unadjusted analysis, there were no statistically significant differences in survival between the staged BOLT, conventional SOLT and conventional BOLT ($p=0.20$ by log rank test) (Figure 2).

Secondary outcome measurements

Comparison of the staged BOLT, conventional SOLT and conventional BOLT groups revealed no significant differences in length of stay, with the combined length of stay for both stages of the staged BOLT procedures being almost identical to that of the control BOLT patients (16 vs. 15 days respectively). Moreover, no differences were noted for the total number of days in the ICU ($p=0.38$) or postoperative days on the ventilator ($p=0.36$). There was no difference in the max FEV1 ($p=0.33$), max FVC ($p=0.14$), percent predicted FEV1 ($p=0.40$), and percent predicted FVC ($p=0.10$) at one year between the 3 groups. There was a lower rate of RIFLE kidney injury or worse in the staged BOLT and control SOLT patients as compared to the control BOLT patients ($p=0.03$), however, no other significant differences were noted in individual measures of morbidity (stroke, atrial fibrillation, or dialysis). Finally, the calculation of the combined morbidity score did not differ amongst the three groups ($p=0.75$) (Table 4).

Discussion

In the current era of balancing perioperative risk and long-term outcomes, the staged BOLT approach offers a viable alternative that capitalizes on the short-term advantages of a SOLT as well as the potential long-term advantages of a BOLT. Our study demonstrates that the process of a staged BOLT is a viable option for patients with ILD. Furthermore, we found that the cumulative LOS, ICU days and ventilator days for the staged BOLT recipients is comparable to a conventional BOLT. Similarly, the risk of postoperative comorbidities was comparable between the three groups, which underscores the safety of the staged BOLT approach. The risk of renal dysfunction after staged BOLT was notably less than that for the control BOLT recipients.

The ideal transplant procedure for ILD is controversial. Our center has a strong preference for BOLT given data for superior pulmonary function as well as a survival advantage for various diseases.^{4, 12, 13} Despite the shift towards an increased use of BOLT for patients with IPF in recent years⁵, a practice supported by several studies^{14, 15}, multiple groups have demonstrated that there is no significant difference in long-term survival after adjustment for numerous covariates when comparing SOLT and BOLT in all patients with IPF.^{6, 7, 16} In the most extensive analysis of this issue, Thabut et al. examined the UNOS registry of all patients with a diagnosis of IPF and found no overall survival difference between SOLT and BOLT. However, the analysis suggested a short-term benefit for SOLT and a potential long-term benefit for patients receiving BOLT. Based on these findings, individual patient's risk profiles may indicate the optimal choice of transplant procedure.⁷ Force et al. found similar

results when utilizing the same dataset; however they also examined conditional 1-year survival and found that for patients living at least 1-year after transplant, there was a significant survival advantage for BOLT.⁶

Since these analyses were done, there has been a general transplant community shift in accepting older patients for lung transplant and these older recipients predominantly have ILD. With increasing age, these patients may have additional comorbid disease burden, such as concomitant coronary artery disease requiring intervention.¹⁷ Notably, a recent analysis confirmed that older IPF recipients with the higher functional status were more likely to benefit from receiving a BOLT but older IPF recipients with a reduced pre-operative functional status do not appear to derive similar benefit from BOLT.¹⁸ Another report indicated that patients with IPF who are only listed for BOLT are less likely to receive a suitable organ and more likely to die on the waitlist.¹⁹ At our center, rather than declining transplant entirely due to operative risk, we adopted the staged BOLT approach, offering first the SOLT with the option later to complete the staged BOLT if the patient appeared to be an appropriate candidate. This staged approach was implemented by the clinical transplant team and represented a shift in our clinical protocol that previously stated all patients would be preferentially provided a standard BOLT.

One of the main concerns with staging a BOLT is that a patient is subject to two operations and the perioperative risk inherent to each one. This increased risk is particularly problematic when considering that the potential recipient may be ambulatory, off supplemental oxygen, and without significant complications from the first transplant. We believed an early analysis of this approach was important because of this risk. In this initial cohort, the second stage SOLT had no perioperative mortality, recipients had no perioperative renal injury or failure as defined by the RIFLE criteria, short LOS and ICU days as well as a low incidence of postoperative atrial fibrillation. These lower events are notable in the setting of lower GFR and a trend to an increased incidence of diabetes prior to the second transplant. Because these patients were clinically well, the second stage for these patients was likely similar to an elective operation and the perioperative experiences reflect this.

An important observation is the low mortality in the staged BOLT group from the index transplant. It must be acknowledged that these patients represent a selection bias as they were considered to have done well with the first transplant and willing to undergo a second transplant. The staged BOLT approach was not offered to SOLT recipients who demonstrated significant postoperative complications or co-morbidities. This selection process is an inherent limitation of this analysis.

Another unknown is the immunologic effect and response to a second lung from a separate donor. There is scant literature regarding this topic, however patients who have undergone redo contralateral single lung transplantation may provide a useful comparison regarding subsequent immunologic phenomenon. Perhaps the most important question is the incidence of developing chronic lung allograft dysfunction (CLAD) in a staged BOLT approach. Due to our follow up time, we are unable to draw any conclusions about the development of CLAD and more long-term data is necessary to determine any association.

The concept of a staged BOLT will likely be controversial at many centers because it raises the question of limited resource utilization. At first glance, one could argue that the second allograft could be used for alternative patients who have not been transplanted. This is an important consideration in light of waitlist deaths. However, our center has a short waitlist time and rare waitlist deaths, thus a selective staged BOLT policy can enhance societal utilization of a limited resource by prioritizing an additional allograft to those most likely to benefit (i.e., those with expected 1-year survival) rather than offering a BOLT initially. Our center updated the LAS to reflect the current status of the patient after their first transplant as reflected in the lower LAS for the second transplant.

There are some limitations to the study that should be noted when interpreting the results. First, this is relatively small sample size with regards to the staged BOLT patients. However, since this approach might offer an option to recipients that would otherwise be declined for a BOLT, we believe reporting our initial experience using a staged BOLT approach is important. Second, although we employed a case control match with relatively strict criteria to compare the staged BOLT patients to control BOLT and SOLT patients, ultimately these were different patient populations as reflected by the choice of procedure they underwent. Third, our center has a short waitlist time and few waitlist deaths which led us to consider this type of a staged BOLT approach. This approach may not be appropriate at centers with donor limitations. Fourth, the economic implications of a staged approach are unclear given the unknown longer term survival benefit. Finally, our follow up time is relatively short so the long term implications of this approach on acute and chronic rejection is unknown.

In conclusion, the concept of a staged BOLT is a novel technique that to date has provided comparable short term survival and acceptable perioperative results. While the sample size is still limited, this procedure may help to provide an additional long-term survival benefit for a small subset of patients who would have otherwise undergone an isolated SOLT. Further study is necessary to determine the true long-term effectiveness, immunologic sequelae, and efficacy of this procedure.

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Abbreviations

BOLT	Bilateral Orthotopic Lung Transplant
BOS	Bronchiolitis Obliterans Syndrome
CAD	Coronary Artery Disease
IPF	Idiopathic Pulmonary Fibrosis
ICU	Intensive Care Unit
ILD	Interstitial Lung Disease
LAS	Lung Allocation Score

LOS	Length of Stay
SOLT	Single Orthotopic Lung Transplant
UNOS	United Network for Organ Sharing

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Figure 1.
Institutional algorithmic approach to patients with idiopathic pulmonary fibrosis

Figure 2.

Kaplan-Meier Analysis of Survival of First Stage of Staged BOLT, Conventional BOLT and Conventional SOLT. Number at risk is presented at the bottom of the graph.

Table 1

Case Control Comparison-Recipient, Transplant, and Donor Characteristics

Variable	Control BOLT (n=24)	Control SOLT (n=24)	Staged Bilateral- First Stage (n=12)	P-Value
Pretransplant Recipient				
Age	63.5 (60.8, 66)	65 (61, 67)	64 (61.5, 65)	0.593
Male sex	6 (25%)	5 (20.8%)	3 (25%)	0.999
BMI	25.6 (23.3, 26.9)	25.6 (24.5, 27.4)	25.7 (24.7, 26.6)	0.954
White Race	24 (100%)	22 (91.7%)	12 (100%)	0.541
Waitlist time (days)	8.5 (3.8, 14.2)	8 (3.8, 19)	11.5 (5.2, 17.8)	0.709
Lung allocation score	47.3 (43.2, 53.7)	49.4 (45.3, 55.5)	48.6 (44.2, 55.6)	0.838
FEV1 percent predicted	57 (42, 63)	49.5 (43, 59.2)	44.5 (37.8, 54.5)	0.367
FVC percent predicted	57.5 (42.2, 72)	45.5 (40, 58.5)	42 (35, 50)	0.14
Transplant type				
Bilateral Sequential	24 (100%)	0 (0%)	0 (0%)	
Single Left	0 (0%)	15 (62.5%)	8 (66.7%)	
Single Right	0 (0%)	9 (37.5%)	4 (33.3%)	
Medical condition				0.489
Not Hospitalized	21 (87.5%)	23 (95.8%)	11 (91.7%)	
Hospitalized	2 (8.3%)	0 (0%)	0 (0%)	
In ICU	1 (4.2%)	1 (4.2%)	1 (8.3%)	
Ventilator/Life Support Pre-Transplant	0 (0%)	0 (0%)	0 (0%)	
Diabetes	5 (20.8%)	3 (12.5%)	2 (16.7%)	0.901
GFR (ml/min/1.73 m ²)	83.4 (75.7, 93.4)	83.5 (75.2, 95.1)	92.7 (76.9, 96.6)	0.571
PA pressure	22 (19,30)	21 (17, 27)	20 (17, 24)	0.39
Transplant				
Distance Organ Travelled (miles)	335 (176, 572)	375.9 (209.8, 435.6)	281 (188.3, 428.7)	0.674
Ischemia time	7.8 (6.7, 9.2)	5.2 (4.8, 6.3)	5.7 (5, 5.9)	< 0.001
Donor				
Age	31.5 (25.5, 49.5)	36 (27.5, 48)	35 (26.8, 43.2)	0.93
Male sex	8 (33.3%)	10 (41.7%)	6 (50%)	0.615
BMI	26.5 (23.3, 29.3)	27.9 (22.8, 31)	24.2 (21.2, 29.6)	0.562
Cigarette smoker	2 (8.3%)	1 (4.2%)	1 (8.3%)	0.866
Diabetes	3 (12.5%)	2 (8.3%)	1 (8.3%)	0.999
GFR (ml/min/1.73 m ²)	72.3 (34.6, 101.3)	100.1 (66, 112.8)	72.3 (46.9, 87.7)	0.184
PaO2	422.4 (352, 515.2)	421 (191.4, 511.2)	426.5 (402.5, 498)	0.836

All statistics displayed as median (interquartile range) or number (percent). BMI, Body Mass Index; FEV1, Forced Expiratory Volume in 1 second; FVC, Forced Vital Capacity; ICU, Intensive Care Unit; GFR, Glomerular Filtration Rate; PaO2, Partial Pressure of O2 on 100% inspired oxygen

Table 2

Staged BOLT Comparison of Recipient, Transplant and Donor Characteristics

Variable	1st Stage (n=12)	2nd Stage (n=12)	P-Value
Recipient			
Age	64 (61.5, 65)	64 (62.5, 65)	0.66
Male sex	3 (25%)	3 (25%)	NA
BMI	25.7 (24.7, 26.6)	25.2 (23.5, 26.2)	0.77
White Race	12 (100%)	12 (100%)	NA
Waitlist time (days)	11.5 (5.2, 17.8)	5.5 (4, 10)	0.69
Lung allocation score	48.6 (44.2, 55.6)	34.5 (34.1, 36.7)	< 0.01
Sequence Number	6 (2.8, 36.2)	53 (23.8, 101.2)	0.06
FEV1	44.5 (37.8, 54.5)	62 (52.8, 70.8)	< 0.01
FVC	42 (35, 50)	63 (48, 75.5)	< 0.01
Medical condition			0.99
Not Hospitalized	11 (91.7%)	12 (100%)	
In ICU	1 (8.3%)	0 (0%)	
Ventilator/Life Support Pre-Transplant	0 (0%)	0 (0%)	NA
Diabetes	2 (16.7%)	5 (41.7%)	0.25
GFR (ml/min/1.73m ²)	92.7 (76.9, 96.6)	53 (44.2, 63.5)	<0.01
Transplant			
Distance Organ Travelled (Miles)	281 (188.3, 428.7)	317.2 (224.9, 445.2)	0.51
Ischemia time (Hours)	5.7 (5, 5.9)	5.5 (5, 6.3)	0.26
Time to Second Transplant, days	NA	167.5 (112.8, 216.5)	NA
Donor			
Age	35 (26.8, 43.2)	49 (35, 54.8)	0.22
Male sex	6 (50%)	6 (50%)	0.99
BMI	24.2 (21.2, 29.6)	25.1 (21.1, 29.4)	0.94
Cigarette smoker	1 (8.3%)	1 (8.3%)	0.99
Diabetes	1 (8.3%)	1 (8.3%)	0.99
GFR (ml/min/1.73m ²)	72.3 (46.9, 87.7)	81 (58.7, 97.3)	0.63
PaO2	426.5 (402.5, 498)	367 (291.2, 500.5)	0.48

All statistics displayed as median (interquartile range) or number (percent). BMI, Body Mass Index; FEV1, Forced Expiratory Volume in 1 second; FVC, Forced Vital Capacity; ICU, Intensive Care Unit; GFR, Glomerular Filtration Rate; PaO2, Partial Pressure of O2 on 100% inspired oxygen

Table 3

Stage Comparison-Outcomes

Variable	1st Stage (n=12)	2nd Stage (n=12)	P-Value
Length of Stay (Days)	10 (9, 13.2)	6 (4, 9)	0.02
Days in the ICU	4 (3, 4.2)	2 (1, 2.2)	0.02
Days on the Ventilator	1 (1, 2)	1 (1, 1)	0.08
Acute Rejection Score of Lung	3 (1, 4.2)	1 (0.8, 2)	0.09
PaO ₂ /FiO ₂ at 72H	296.1 (264.2, 307.7)	335.7 (298.8, 357.4)	0.02
Atrial Fibrillation	5 (41.7%)	1 (8.3%)	0.22
RIFLE Kidney Injury or Worse	3 (25%)	0 (0%)	0.25
RIFLE Kidney Failure or Worse	0 (0%)	0 (0%)	NA
Dialysis	0 (0%)	0 (0%)	NA
Stroke	0 (0%)	0 (0%)	NA

All statistics displayed as median (interquartile range) or number (percent). ICU, Intensive Care Unit; PaO₂/FiO₂, Partial Pressure of O₂/Fractional Content of Inspired Oxygen; RIFLE, Risk, Injury, Failure, Loss, and End-Stage Kidney Classification

Table 4Case Control Comparison-Outcomes (1st and 2nd Stages Combined)

Outcome	Control BOLT (n=24)	Control SOLT (n=24)	Staged BOLT (Combined) (n=24)*	P-Value
Length of Stay (Days)	15 (11, 25)	11 (7, 47.2)	16 (14, 21)	0.378
Days in the ICU	4 (2.8, 9.5)	2.5 (1.8, 14.5)	5.5 (5, 6)	0.379
Days on the Ventilator	1 (1, 5.2)	1 (1, 9.5)	2 (2, 3)	0.358
Atrial Fibrillation	12 (50%)	12 (50%)	6 (25%)	0.118
Dialysis	2 (8.3%)	1 (4.2%)	0 (0%)	0.798
Stroke	1 (4.2%)	1 (4.2%)	0 (0%)	0.933
RIFLE Kidney Injury or Worse	11 (45.8%)	5 (20.8%)	3 (12.5%)	0.025
RIFLE Kidney Failure or Worse	4 (16.7%)	3 (12.5%)	0 (0%)	0.50
PaO ₂ /FiO ₂ at 72H**	358.9 (336.9, 425)	325.9 (267.7, 352.4)	NA	NA
Combined Morbidity***	2 (0, 3.2)	1 (0, 3.2)	2 (1, 3)	0.745

All statistics displayed as median (interquartile range) or number (percent). ICU, Intensive Care Unit; RIFLE, Risk, Injury, Failure, Loss, and End-Stage Kidney Classification.

* Represents outcomes as combination of first and second stage.

** As the PaO₂/FiO₂ ratio for each stage are not able to be combined these values are not displayed for the staged BOLT patients.

*** Represents composite morbidity with 1 point assigned for each incidence of morbidity, maximum of 7 (length of stay > 25 days, ICU stay > 4 days, ventilator days > 2 days, atrial fibrillation, stroke, RIFLE Kidney Injury, and RIFLE Kidney Failure).