Safety and efficacy of delaying lung transplant surgery to a morning start

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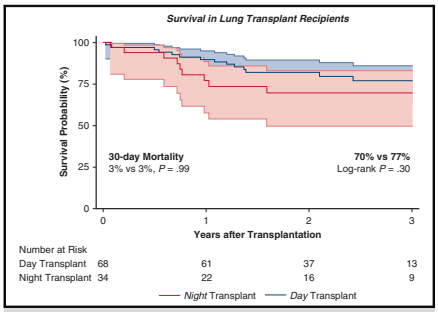
ABSTRACT

Objective: We aimed to evaluate the safety and efficacy of delaying lung transplantation until morning for donors with cross-clamp times occurring after 1:30 AM.

Methods: All consented adult lung transplant recipients between March 2018 and May 2022 with donor cross-clamp times between 1:30 AM and 5 AM were enrolled prospectively in this study. Skin incision for enrolled recipients was delayed until 6:30 AM (Night group). The control group was identified using a 1:2 logistic propensity score method and included recipients of donors with cross-clamp times occurring at any other time of day (Day group). Short- and medium-term outcomes were examined between groups. The primary endpoint was early mortality (30-day and in-hospital).

Results: Thirty-four patients were enrolled in the Night group, along with 68 well-matched patients in the Day group. As expected, donors in the Night group had longer cold ischemia times compared to the Day group (344 minutes vs 285 minutes; $P < .01$). Thirty-day mortality (3% vs 3%; $P = .99$), grade 3 primary graft dysfunction at 72 hours (8% vs 4%; $P = .40$), postoperative complications (26% vs 38%; $P = .28$), and hospital length of stay (15 days vs 14 days; $P = .91$) were similar in the 2 groups. No significant differences were noted between groups in 3-year survival (70% vs 77%; $P = .30$) or freedom from chronic lung allograft dysfunction (91% vs 95%; $P = .75$) at 3 years post-transplantation. The median follow-up was 752.5 days (interquartile range, 487-1048 days).

Conclusions: Lung transplant recipients with donor cross-clamp times scheduled after 1:30 AM may safely have their operations delayed until 6:30 AM with acceptable outcomes. Adoption of such a policy in clinically appropriate settings may lead to an alternative workflow and improved team well-being. (JTCVS Open 2023;16:1008-17)



Three-year survival among lung transplant recipients with nighttime donor cross-clamp times delayed until morning (Night transplant) vs. a daytime cohort (Day Transplant). *CLAD*, Chronic lung allograft dysfunction; *ICU*, intensive care unit, *LOS*, length of stay.

CENTRAL MESSAGE

Lung transplant recipients with nighttime donor cross-clamp times may safely have their operations delayed until the morning without compromising 30-day mortality or 3-year survival.

PERSPECTIVE

Lung transplantation is still routinely performed at night owing to the unpredictability of donor organ procurement. However, late start times for complex operations such as lung transplantation have been associated with adverse outcomes.

See Discussion on page 1018.

Nighttime procedures have been linked to adverse postoperative outcomes across many surgical disciplines.[1,2] This has been attributed to the fatigue and sleep deprivation associated with operating at night, which may decrease cognitive and psychomotor function and lead to higher rates of medical errors.[3,4] However, nighttime procedures are still widely accepted and practiced in solid organ transplantation, with procedural timing being

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Abbreviations and Acronyms

CLAD = Chronic lung allograft dysfunction
ECMO = extracorporeal membrane oxygenation
ICU = intensive care unit
IQR = interquartile range
LOS = length of stay
NPI = nonprolonged ischemia
OR = operating room
OPO = organ procurement organization
PI = prolonged ischemia
PGD = primary graft dysfunction
SMD = standardized mean difference

dictated almost uniformly by the availability of donor organs and a concerted effort to avoid prolonged organ cold ischemia times. Several variables may affect the timing of organ procurement, including the donor family's wishes, availability of donor hospital operating rooms and staff, availability of the organ procurement organization (OPO) staff, and coordination with multiple procurement teams and recipient hospitals.[5,6] Owing to such logistical issues, donor organ procurement often falls in the evenings and early morning hours, usually after regularly scheduled cases are completed. This in turn results in late evening or early morning start times for the recipient operation.

Several studies have examined the relationship between nighttime surgery and postoperative outcomes in organ transplantation.[1,2,7] In kidney transplantation, the incidences of operative complications and graft failure were higher in procedures performed at night.[8] Lonze and colleagues[9] observed a nearly doubled incidence of early death in nighttime liver transplant recipients compared to recipients undergoing operation during daytime. In lung transplantation, George and colleagues[7] examined the United Network for Organ Sharing database and found an association between 90-day mortality and transplantation at nighttime, though other outcome measures were not affected. More recently, Yang and colleagues[2] reviewed their large single-center cohort and found that nighttime lung transplantation was associated with a greater risk of major postoperative adverse events along with decreased 5-year survival and freedom from bronchiolitis obliterans syndrome.

Given this background literature and the ability of donor lungs to withstand longer ischemia time owing to inflation with oxygenated air,[10-12] we hypothesized that delaying the nighttime transplant procedures to a morning start would result in similar outcomes as daytime lung transplant procedures.

METHODS

Study Population

This study was approved by the Institutional Review Board at the University of California, Los Angeles (approval 17-001134; approved October 24, 2018). From March 2018 to May 2022, we approached all adult lung transplant recipients at our institution with donor cross-clamp times scheduled to occur after 1:30 AM but before 5 AM. This protocol was designed based on discussions with the Institutional Review Board at our institution and using a conservative time frame to limit harm to the recipients. Although 1 patient refused, the remaining 34 patients provided informed consent to participate in the study, serving as the main study cohort (Night group). Donor organs in the Night group underwent routine procurement, with donor lungs preserved using standard preservation techniques in an ice cooler at 4 °C until implantation. Donor clamp times were not delayed, and standard organ procurement protocols were not altered in any way for donors in the Night group. The recipient operation was subsequently coordinated such that the skin incision would occur at 6:30 AM. The control group included a contemporaneous cohort of lung transplant recipients who had donor cross-clamp times occurring at any other time of day.

Owing to the differences in the sample size and transplant year, the propensity score used for matching the 34 Night subjects to 68 corresponding Day subjects at a 1:2 match was computed by carrying out a logistic regression of the Night group or Day group on the 6 matching variables: age, diagnosis group (A, B, C, D), lung allocation score, extracorporeal membrane oxygenation (ECMO; no/yes), procedure type (double, single right, single left), and treatment date. Exact matches were required for ECMO and single versus double treatment. Each Night group subject was matched to 2 different Day subjects from the pool of 1286 Day subjects by taking the 2 subjects with the closest propensity score. An optimal (nongreedy) match was done, and no Day subject was used more than once. Matching was carried out using the R "MatchIt" library (R Foundation for Statistical Computing). Standardized mean differences (SMDs) before matching versus after matching are reported.

Baseline Characteristics

The following baseline characteristics of the 2 groups were compared: age, sex, race, height, weight, body mass index, year of transplant, lung allocation score, blood group, diagnosis group, diabetes, hyperlipidemia, hypertension, any smoking history, coronary artery disease, preoperative ECMO, mechanical ventilation, waitlist duration, and 6-minute walk test results. Preoperative lab values were compared between groups and included hemoglobin, albumin, bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and creatinine. Donor characteristics were also compared between the Night and Day groups and included donor age, sex, race, blood group, history of drug abuse, hypertension, any smoking status, P/F ratio (arterial partial pressure of O_2:fraction of inspired O_2), and use of steroids.

Operative characteristics included in the study were procedure type (double lung, left lung, right lung); cardiopulmonary bypass, cardiopulmonary bypass time among those requiring bypass; use of mechanical circulatory support, including ECMO and cardiopulmonary bypass, organ ischemic time, and percentage of patients requiring concomitant cardiac surgeries.

Outcomes

The primary study outcome was early mortality (30-day and in-hospital). Secondary study endpoints were primary graft dysfunction grade III (at 24, 48, and 72 hours), and a composite of postoperative complications (operative reexploration, postoperative ECMO, atrial fibrillation, tracheostomy, cerebrovascular accident, and wound dehiscence). Additional secondary endpoints analyzed included postoperative ventilation, intensive care unit (ICU) length of stay (LOS), and hospital LOS. We also compared

survival across the span of the first 3 years and freedom from chronic lung allograft dysfunction (CLAD) at 3 years post-transplantation. The Night group was further stratified into 2 groups based on donor cold ischemia time to compare postoperative outcomes: prolonged ischemia (PI), >6 hours, and nonprolonged ischemia (NPI), ≤6 hours.

Statistical Analysis

Categorical variables in the study are presented as frequency (proportion of cohort), and continuous variables are presented as mean ± standard deviation for normally distributed variables and median (interquartile range [IQR]) for skewed variables. Categorical variables were compared using the χ^2 test or Fisher exact test if >25% of the expected values were <5. Continuous variables were compared using the t test for normally distributed variables and the Wilcoxon rank-sum test for skewed distributions. Skewness for each continuous variable was assessed both visually and using skewness and kurtosis tests for normality. Kaplan-Meier survival estimates were used to assess 3-year survival. Nelson-Aalen cumulative hazard functions were calculated to visualize estimates of CLAD at 3 years post-transplantation.

Either a 2-tailed P value <.05 or an SMD >0.1 was considered significant for all analyses. All data were collated prospectively or otherwise acquired via prospective and retrospective chart review. Other than logistic propensity score matching, all statistical analyses were performed using Stata 15.1 (StataCorp).

RESULTS

Preoperative Characteristics of Lung Transplant Recipients

The year of transplantation was more recent in the Night group (median, 2020 [IQR, 2019-2020] vs 2013 [IQR, 2008-2017]; SMD = 1.73), whereas the rate of smoking history was higher in the Day group (52% vs 30%; SMD = 0.45) (Table E1). In addition, restrictive lung disease and pulmonary vascular disease were more common in the Night group (SMD = 0.50). After matching, the difference between the 2 groups was significant only in the diagnosis group (SMD = 0.19) out of the 6 matching variables (Table 1), suggesting that those variables are fairly balanced.

Baseline Characteristics of Lung Transplant Donors

Lung transplant donor characteristics are displayed in Table E2. Donors in the Day group were younger (mean, 36 ± 14 vs 40 ± 13; SMD = 0.28) and had a higher rate of smoking history (42% vs 26%; SMD = 0.33). On the other hand, there was a greater proportion of Black and Hispanic patients in the Night group (SMD = 0.35). The donor characteristics with propensity score matching are shown in Table 2. The SMDs were >0.20 for age (SMD = 0.28), race distribution (SMD = 0.24), and diabetes mellitus (SMD = 0.25).

Operative Characteristics

The majority of patients underwent double lung transplantation (71% vs 71%), with Night patients more often undergoing right lung transplantation (21% vs 9%) and less commonly left lung transplantation (9% vs 21%; P = .13 for all) compared to those in the Day group (Table 3). There were no significant differences in the rates of concomitant cardiac surgery (38% vs 37%; P = .89), mechanical circulatory support use (76% vs 97%; P = .76), cardiopulmonary bypass use (62% vs 76%; P = .12), cardiopulmonary bypass time (median, 159 minutes [IQR, 138-177 minutes] vs 175.5 minutes [IQR, 140-217.5 minutes]; P = .18) between the 2 groups. Night recipients had longer donor organ ischemic time (mean 344 ± 83 minutes vs 285 ± 93 minutes; P < .01), as expected.

Postoperative Outcomes

Postoperative outcomes in the Night and Day groups are shown in Table 4. Following transplantation, the Night group and Day group had similar rates of early mortality (in-hospital, 3% vs 4%; P = .99), 30-day mortality (3% vs 3%; P = .99), and primary graft dysfunction (PGD) at 24 hours (12% vs 10%; P = .99), 48 hours (18% vs 4%; P = .11), and 72 hours (8% vs 4%; P = .40). A composite of postoperative complications rates was also similar in the 2 groups (26% vs 38%; P = .24) and consisted of reexploration (3% vs 10%; P = .26), postoperative ECMO use (3% vs 4%; P = .99), atrial fibrillation (12% vs 22%; P = .28), need for tracheostomy (14.7% vs 17.7%; P = .71), incidence of CVA (0% vs 3%; P = .55), and wound dehiscence (0% vs 1%; P = .99). Both ICU LOS (median, 7 days [IQR, 4.2–12.1 days] vs 6 days [IQR, 4.2-11.7 days]; P = .51) and hospital LOS (median, 15 days [IQR, 10-24 days] vs 14 days [median, 10-20.5 days]; P = .91) were similar in the 2 groups.

Overall, 30-day, 90-day, 1-year, and 3-year survival were 97% (81%-100%), 94% (78%-98%), 77% (58%-88%), and 70% (50%-83%), respectively, in the Night group and 97% (89%-99%), 97% (89%-99%), 90% (80%-95%), and 77% (64%-86%) in the Day group (Figure 1). The median duration of follow-up for the study population was 752.5 days (IQR, 487-1048 days), with a similar duration in the Night and Day groups (689.5 [IQR, 272-1100 days] vs 765 days [IQR, 502.5-1045 days]; P = .27). The number of patients at risk at 3 years after the operation was 9 of 34 in the Night group and 13 of 68 in the Day group. Similar to the survival estimates, freedom from CLAD at 3 years was not statistically different between the two groups (91% vs 95%; P = .75) (Figure 2).

Postoperative outcomes for night subgroups. In the Night group, approximately 35% of the donors had a cold ischemia time >6 hours. The NPI group had a significantly greater ischemic time than the PI group (median, 310 minutes [IQR, 259-346 minutes] vs 413.5 minutes [IQR, 393-469 minutes]; P < .001). However, all postoperative outcomes were comparable in the 2 groups (Table E3).

TABLE 1. Preoperative characteristics of matched lung transplant recipients

Characteristic	Night (N = 34)	Day (N = 68)	SMD
Age, y, mean ± SD	58 ± 12	57 ± 12	0.08
Male sex, n (%)	22 (65)	34 (50)	0.31
Race, n (%)			0.19
White	21 (62)	33 (49)	
Black	4 (12)	3 (4)	
Hispanic	6 (18)	28 (41)	
Other	3 (9)	4 (6)	
Height, cm, mean ± SD	169 ± 9	168 ± 10	0.11
Weight, kg, mean ± SD	72 ± 16	71 ± 17	0.05
BMI, kg/m^2, mean ± SD	25 ± 4	25 ± 4	0.02
Year of transplantation, median (IQR)	2020 (2018-2020)	2020 (2019-2020)	0.01
Lung allocation score, median (IQR)	44 (37-65)	44 (38-58)	0.03
Blood group, n (%)			0.18
O	15 (44)	33 (49)	
A	14 (41)	20 (30)	
B	5 (15)	11 (16)	
AB	0 (0)	3 (4)	
Diagnosis group, n (%)			0.19
A	1 (3)	5 (7)	
B	2 (6)	3 (4)	
C	1 (3)	5 (7)	
D	30 (88)	55 (81)	
Diabetes, n (%)	9 (26)	15 (22)	0.09
Hyperlipidemia, n (%)	12 (35)	22 (32)	0.08
Hypertension, n (%)	13 (38)	21 (31)	0.17
Smoking history, n (%)	10 (29)	23 (34)	0.15
Coronary artery disease, n (%)	5 (15)	11 (16)	0.04
Preop ECMO, n (%)	1 (3)	2 (3)	0
Mechanical ventilation, n (%)	2 (6)	5 (7)	0.06
Waitlist duration, d, median (IQR)	60.5 (17-134)	32 (10-120)	0.13
6-min walk, ft, median (IQR)	443 (200-787)	394 (197-777)	0.09
Hemoglobin, g/dL, mean ± SD	12 ± 2	12 ± 2	0.10
Hematocrit, %, mean ± SD	38 ± 6	38 ± 7	0.07
Albumin, g/dL, mean ± SD	4.0 ± 0.6	4.1 ± 0.4	0.05
Bilirubin, mg/dL, median (IQR)	0.4 (0.3-0.6)	0.3 (0.2-0.5)	0.40
Aspartate aminotransferase, U/L, median (IQR)	23 (18-28)	22 (18.5-30)	0.20
Alanine aminotransferase, U/L, median (IQR)	20 (16-30)	18 (13-27)	0.27
Alkaline phosphatase, U/L, mean ± SD	85 ± 69	87 ± 32	0.03
Creatinine, mg/dL, median (IQR)	0.8 (0.7-0.9)	0.8 (0.6-1.0)	0.13

Night transplant: donor cross-clamp at 1:30-5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation performed at any other time of day. Diagnosis groups: A, obstructive lung disease; B, pulmonary vascular disease; C, cystic fibrosis; D, restrictive lung disease. *SMD*, Standardized mean difference (in absolute values); *SD*, standard deviation; *BMI*, body mass index; *IQR*, interquartile range; *ECMO*, extracorporeal membrane oxygenation.

DISCUSSION

The findings of this study provide evidence that lung transplants with donor cross-clamping occurring after 1:30 AM may have the subsequent recipient procedure safely delayed until 6:30 AM. Compared to a matched cohort of lung transplant recipients with donor cross-clamping occurring at any other time of day, the Night group experienced similar rates of early mortality, postoperative

TABLE 2. Baseline characteristics of matched lung transplant donors

Characteristic	Night (N = 34)	Day (N = 68)	SMD
Age, y, mean ± SD	40 ± 13	36 ± 12	0.28
Male sex, n (%)	23 (68)	41 (61)	0.13
Race, n (%)			0.24
White	10 (29)	29 (43)	
Black	6 (18)	5 (7)	
Hispanic	16 (47)	27 (40)	
Other	2 (6)	6 (9)	
Blood type, n (%)			0.15
O	16 (47)	36 (54)	
A	12 (35)	18 (27)	
B	6 (18)	11 (16)	
AB	0 (0)	2 (3)	
Hypertension, n (%)	6 (18)	13 (19)	0.04
Diabetes, n (%)	6 (18)	6 (9)	0.25
Smoking, n (%)	9 (26)	24 (35)	0.20
P/F ratio, median (IQR)	469.4 (405-516)	458 (404-496)	0.01
Steroid use, n (%)	31 (91)	63 (93)	0.04

Night transplant: donor cross-clamp at 1:30-5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation performed at any other time of day. *SMD*, Standardized mean difference (in absolute values); *SD*, standard deviation; *P/F ratio*, arterial partial pressure of O_2 to fractional inspired O_2; *IQR*, interquartile range.

complications, and PGD; similar ICU and hospital LOS; and similar survival and freedom from CLAD at 3 years post-transplantation.

Despite the known adverse events associated with nighttime operations and ICU handoffs, lung transplantation at night remains common at many transplant centers.[1,13] For lung transplantation, several studies have shown a higher risk of postoperative complications, PGD development, and mortality.[2,7] Given the accumulating evidence indicating that lung transplantation at night may pose a greater risk to the recipient, several strategies have been proposed. One option is to delay the donor operation such that the recipient operation can be performed during the daytime. Given the complexity of the donor operation timing (multiple team involvement, availability of the donor operating room [OR] time/staff, OPO staff availability, and family constraints), a delay in the donor OR time might not be feasible in all cases. Another proposed solution has been to transfer the donor to a dedicated procurement facility to decrease the logistic burden and enhance scheduling flexibility.[2] However, this practice might not always be feasible, as many OPOs do not have a dedicated procurement facility. A third solution, as explored in this study, is to delay the recipient operation until the morning at the expense of prolonging the allograft ischemia time. This report provides data on the safety and efficacy of such a strategy for all donors with an expected cross-clamping time past 1:30 AM.

The role of ischemia time in lung transplantation has been the subject of several studies. In a retrospective review of the United Network for Organ Sharing database, Grimm and colleagues[10] found no difference in the development of PGD or in 1- and 5-year survival between patients receiving

TABLE 3. Operative characteristics

Characteristic	Night (N = 34)	Day (N = 68)	*P* value
Double lung, n (%)	24 (71)	48 (71)	.13
Left lung, n (%)	3 (9)	14 (21)	
Right lung, n (%)	7 (21)	6 (9)	
CPB, n (%)	21 (62)	52 (76)	.12
CPB time*, min, median (IQR)	159 (138-177)	175.5 (140-217.5)	.18
Ischemia time, min, mean ± SD	344 ± 83	285 ± 93	<.01
MCS, n (%)	26 (76)	53 (79)	.76
Concomitant cardiac surgery, n (%)	13 (38)	25 (37)	.89

Night transplant: donor cross-clamp at 1:30-5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation performed at any other time of day. *CPB*, Cardiopulmonary bypass; *IQR*, interquartile range; *SD*, standard deviation; *MCS*, mechanical circulatory support. *Only for transplants requiring CPB.

TABLE 4. Postoperative outcomes

Outcome	Night (N = 34)	Day (N = 68)	*P* value
Primary graft dysfunction (grade 3), n (%)			
24 h	4 (12)	7 (10)	.99
48 h	6 (18)	3 (4)	.11
72 h	3 (8)	3 (4)	.40
Postoperative complications, n (%)	9 (26)	26 (38)	.24
Re-exploration	1 (3)	7 (10)	.26
ECMO	1 (3)	3 (4)	.99
Atrial fibrillation	4 (12)	15 (22)	.28
Tracheostomy	5 (14.7)	12 (17.7)	.71
CVA	0 (0)	2 (3)	.55
Dehiscence	0 (0)	1 (1)	.99
ICU LOS, d, median (IQR)	7 (4.2-12.1)	6 (4.2-11.7)	.51
Hospital LOS, d, median (IQR)	15 (10-24)	14 (10-20.5)	.91
In-hospital mortality, n (%)	1 (3)	3 (4)	.99
30-d mortality, n (%)	1 (3)	2 (3)	.99

Night transplant: donor cross-clamp at 1:30-5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation performed at any other time of day. *ECMO*, Extracorporeal membrane oxygenation; *CVA*, cerebrovascular accident; *ICU*, intensive care unit; *LOS*, length of stay; *IQR*, interquartile range.

lung grafts with ischemia times <6 hours versus >6 hours. Other studies have reported conflicting results on the role of cold ischemia time on lung transplantation outcomes.[12,14] In contrast to other solid organs, insufflation of the lung allografts with oxygenated air during preservation allows for ongoing aerobic metabolism and greater resistance to ischemic changes.[10,15,16] One interpretation of this study is that prolongation of the cold ischemia time by nearly 1 hour at our center does not appear to adversely affect the clinical outcomes. The equivalence in outcomes may be because the duration of cold ischemia in both groups in the present study were not extreme by national standards.[17,18] A critical threshold of extended ischemia time, which leads to poorer outcomes, might not have been reached. Alternatively, it may be that any impact of the modest increase in cold ischemia time was offset by improved performance of a well-rested surgical team at the time of implantation.

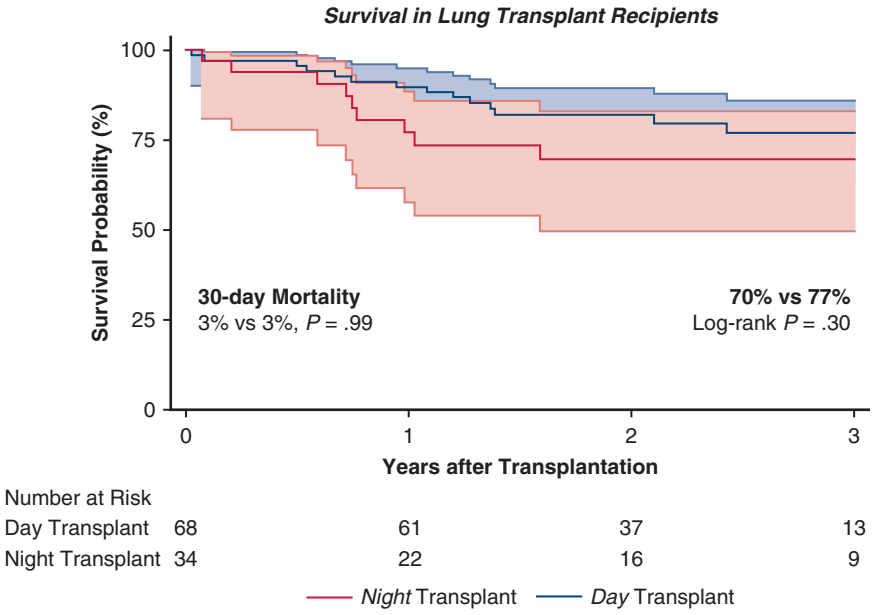

FIGURE 1. Kaplan-Meier 3-year survival in lung transplant recipients by time of donor organ procurement. Night transplant: donor cross-clamping between 1:30 and 5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation occurring at any other time of day. *The colored areas around the solid lines* represent 95% confidence limits, with 3-year survival estimates displayed as percentages. *Numbers below the horizontal axis* represent patients remaining at risk.

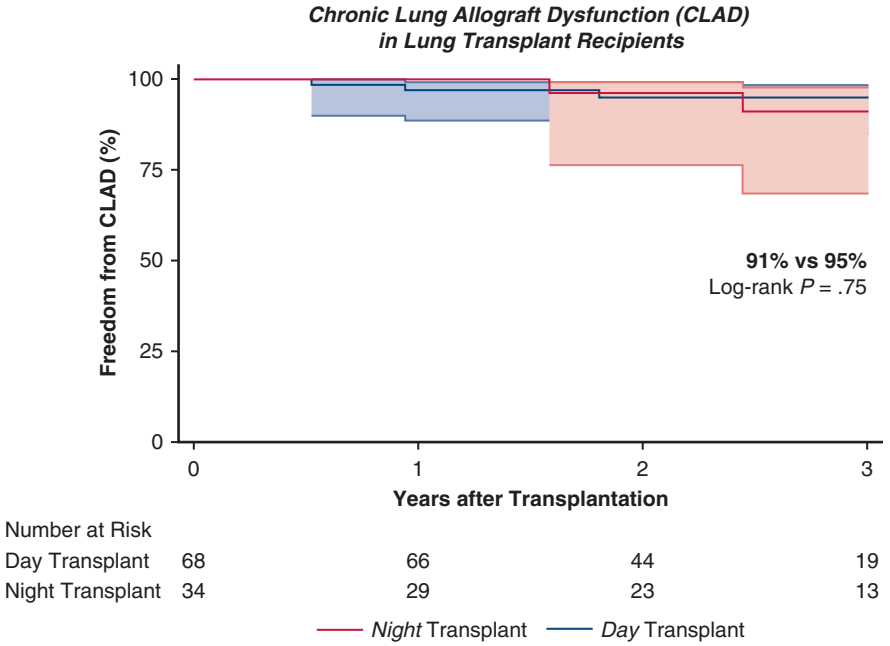

FIGURE 2. Freedom from 3-year chronic lung allograft dysfunction (CLAD) in lung transplant recipients by time of donor organ procurement. Night transplant: donor cross-clamping between 1:30 to 5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation occurring at any other time of day. *The colored areas around the solid lines* represent 95% confidence limits, with the freedom from CLAD estimates at 3-years displayed as percentages. *Numbers below the horizontal axis* represent patients remaining at risk.

Delaying the nighttime lung transplant procedures to a morning start also may reduce team "burnout" and enhance morale. Given the recent national emphasis on physician wellness, system-based changes such as a morning start may enhance transplant surgeons/team wellness and retention.[4,19,20] An additional advantage of a morning start is better resource management and less overtime personnel utilization/cost savings. The detrimental impact of delaying transplant procedures to a morning start on regularly scheduled cases in busy transplant centers and on possible surgical caseload overcrowding should be considered. However, significantly more resources are available during peak operating hours to create efficient logistical solutions for these issues.

In this study, a standard ice cooler (~4 °C) was used to preserve the donor lungs after procurement. Despite its cost-effectiveness and universality, the method allows for a maximum preservation time of only roughly 6 to 8 hours. However, Ali and colleagues[21] explored the use of 10 °C static lung storage to push the upper limit up to 10 to 12 hours. By maintaining the temperature at 10 °C, key metabolites involved in the mitochondrial mechanism and antioxidative system were better preserved than at 4 °C. In addition, recent studies examined the effectiveness of LUNGguard (LG) technology, a lung storage device that provides a controlled environment, to determine that the LG storage system can be used as an alternative for lung preservation.[22,23] Such advances in preservation techniques also may safely prolong donor lung ischemic time such that the recipient OR time may be delayed until the morning with equivalent outcomes. Given our noninferior findings with standard preservation techniques, the use of newer technology may augment the findings of our prospective study and represents an exciting new direction to further extend recipient start times outside the time frame (1:30 AM to 5:00 AM) explored in our study.

Several limitations of this study warrant acknowledgment. This trial is a single-center study with all of its limitations and inherent issues related to the small number of subjects. The noninferior outcomes between the study groups could be the result of a type II error. In addition, the trial was conducted at a large-volume lung transplant center and might not be reproducible at other centers. Furthermore, despite the statistical difference in cold ischemia time between the 2 groups, the average difference was only 59 minutes. Many of our donors were from our local OPO, and prolongation of the cold ischemia time in this trial might not have reached a critical threshold, which may explain the similar survival rates in the Night and Day groups. Other studies are needed to define the "upper limit" of safe ischemia time. However, the primary aim of this study was not to prolong organ ischemic time, but rather to determine the feasibility and safety of delaying nighttime lung transplantation to a morning start time. Furthermore, there was limited follow-up in both study groups, given that most transplant operations were performed after 2018. Future studies with larger sample sizes, longer

follow-up, and data on admission status may further elucidate the findings of this study.

In conclusion, the findings of this study suggest that at selected centers, late night lung transplant procedures can be safely delayed until the morning with acceptable short- and medium-term outcomes. Further studies are needed to better define the limits of cold ischemia times and safe duration of delays. However, such changes in workflow may allow for overall enhanced transplant surgeon/team well-being and improved resource utilization while ensuring optimal patient outcomes.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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TABLE E1. Preoperative characteristics of lung transplant recipients

Characteristic	Night (N = 34)	Day (N = 1286)	SMD
Age, y, mean ± SD	58 ± 12	58 ± 12	.04
Male sex, n (%)	22 (65)	758 (59)	.11
Race, n (%)			.05
White	21 (62)	872 (68)	
Black	4 (12)	73 (6)	
Hispanic	6 (18)	261 (20)	
Other	2 (6)	72 (6)	
Height, cm, mean ± SD	169 ± 9	168 ± 11	.01
Weight, kg, mean ± SD	72 ± 16	72 ± 17	.07
BMI, kg/m^2, mean ± SD	25 ± 4	27 ± 4	.04
Year of transplantation, median (IQR)	2020 (2018-2020)	2013 (2008-2017)	1.73
Lung allocation score, median (IQR)	44 (37-65)	43 (36-53)	.21
Blood group, n (%)			.09
O	15 (44)	617 (48)	
A	14 (41)	446 (35)	
B	5 (15)	149 (12)	
AB	0 (0)	73 (6)	
Diagnosis group, n (%)			.50
A	1 (3)	260 (20)	
B	2 (6)	44 (3)	
C	1 (3)	65 (5)	
D	30 (88)	915 (71)	
Diabetes history, n (%)	9 (26)	291 (23)	.09
Hyperlipidemia, n (%)	12 (35)	459 (36)	.01
Hypertension, n (%)	13 (38)	471 (37)	.03
Smoking history, n (%)	10 (30)	673 (52)	.45
Coronary artery disease, n (%)	5 (15)	132 (11)	.12
Preoperative ECMO, n (%)	1 (3)	58 (5)	.09
Mechanical ventilation, n (%)	2 (6)	116 (9)	.12
Waitlist duration, d, median (IQR)	60.5 (17-134)	57 (19-164)	.05
6-min walk test, ft, median (IQR)	443 (200-787)	356 (186-689)	.23
Hemoglobin, g/dL, mean ± SD	12 ± 2	13 ± 4	.12
Hematocrit, %, mean ± SD	38 ± 7	39 ± 8	.10
Albumin, g/dL, mean ± SD	4.0 ± 0.6	4.0 ± 0.5	.04
Bilirubin, mg/dL, median (IQR)	0.4 (0.3-0.6)	0.4 (0.3-0.6)	.08
Aspartate aminotransferase, U/L, median (IQR)	23 (18-28)	22 (18-28)	.15
Alanine aminotransferase, U/L, median (IQR)	20 (16-30)	17 (13-25)	.27
Alkaline phosphatase, U/L, mean ± SD	85 ± 69	78 ± 44	.11
Creatinine, mg/dL, median (IQR)	0.8 (0.7-0.9)	0.8 (0.7-1.0)	.13

Night transplant: donor cross-clamp at 1:30-5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation performed at any other time of day. Diagnosis groups: A, obstructive lung disease; B, pulmonary vascular disease; C, cystic fibrosis; D, restrictive lung disease. *SMD*, Standardized mean difference (in absolute values); *SD*, standard deviation; *BMI*, body mass index; *IQR*, interquartile range; *ECMO*, extracorporeal membrane oxygenation.

TABLE E2. Baseline characteristics of lung transplant donors

Variable	Night (N = 34)	Day (N = 1286)	SMD
Age, y, mean ± SD	40 ± 13	36 ± 14	.28
Male sex, n (%)	23 (68)	813 (65)	.06
Race, n (%)			.35
White	10 (29)	566 (44)	
Black	6 (18)	90 (7)	
Hispanic	16 (47)	514 (40)	
Other	2 (6)	116 (9)	
Blood type, n (%)			.14
O	16 (47)	694 (54)	
A	12 (35)	347 (27)	
B	6 (18)	205 (16)	
AB	0 (0)	38 (3)	
Hypertension, n (%)	6 (18)	263 (22)	.11
Diabetes, n (%)	6 (18)	176 (14)	.09
Smoking, n (%)	9 (26)	477 (42)	.33
P/F ratio, median (IQR)	467.5 (401.8-516)	458 (404-496)	<.01
Steroids, n (%)	31 (91)	1131 (88)	.10

Night transplant: donor cross-clamp at 1:30-5:00 AM, recipient operation delayed until 6:30 AM. Day transplant: routine lung transplantation performed at any other time of day. *SMD*, Standardized mean difference (in absolute values); *SD*, standard deviation; *P/F ratio*, arterial partial pressure of O_2 to fractional inspired O_2; *IQR*, interquartile range.

TABLE E3. Postoperative outcomes of Night subgroups

Outcome	NPI (N = 22)	PI (N = 12)	*P* value
Cold ischemia time, min, median (IQR)	310 (259-346)	413.5 (393-469)	<.001
Primary graft dysfunction (grade 3), n (%)			
24 h	3 (14)	1 (8)	.65
48 h	3 (14)	3 (25)	.41
72 h	1 (5)	2 (17)	.25
Postoperative complications, n (%)	5 (23)	4 (33)	.50
Re-exploration	0 (0)	1 (8)	.17
ECMO	1 (5)	0 (0)	.45
Atrial fibrillation	2 (9)	2 (17)	.51
Tracheostomy	3 (14)	2 (17)	.81
CVA	0 (0)	0 (0)	
Dehiscence	0 (0)	0 (0)	
ICU LOS, d, median (IQR)	7 (4.2-12.1)	7 (4.25-15.5)	.84
Hospital LOS, d, median (IQR)	14 (10-17)	16.5 (10-30)	.29
In-hospital mortality, n (%)	0 (0)	1 (8)	.17
30-d mortality, n (%)	0 (0)	1 (8)	.17

NPI, Nonprolonged ischemia (graft cold ischemic time ≤6 hours); *PI*, prolonged ischemia (graft cold ischemic time >6 hours); *IQR*, interquartile range; *ECMO*, extracorporeal membrane oxygenation; *CVA*, cerebrovascular accident; *ICU*, intensive care unit; *LOS*, length of stay.