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Impact of donor, recipient, and matching on survival after high-emergency lung transplantation in France

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Take-home message

The results of this first exhaustive multicenter French national study suggest that the adverse outcome associated with the high emergency lung transplantation procedure is mainly related to the severity of the recipients rather than donor or matching characteristics.

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Abstract

Introduction

Since July 2007, the French High Emergency Lung Transplantation (HELT) allocation procedure prioritizes available lung grafts to waiting patients with imminent risk of death. The relative impacts of donor, recipient, and matching on the outcome following HELT remain unknown.

We aimed at deciphering the relative impacts of donor, recipient, and matching on the outcome following HELT in an exhaustive administrative database.

Methods

All lung transplantations (LT) performed in France were prospectively registered in an administrative database. We retrospectively reviewed the procedures performed between July 2007 and December 2015 and analyzed the impact of donor, recipient, and matching on overall survival after the HELT procedure by fitting marginal Cox models.

Results

During the study period, 2335 patients underwent LT in 11 French centers. After exclusion of patients with chronic obstructive pulmonary disease/emphysema, 1544 patients were included: 503 HELT and 1041 regular allocations. HELT was associated with a hazard ratio (HR) for death of 1.41 (95% confidence interval [CI], [1.22 to 1.64], $p < 0.0001$) in univariate analysis, decreasing to 1.32 [1.10; 1.60] after inclusion of recipient characteristics in a multivariate model. A donor score computed to predict long term survival was significantly different between HELT and non-HELT groups ($p = 0.014$). However, the addition of donor characteristics to recipient characteristics in the multivariate model did not change the HR associated with HELT.

Conclusion

This exhaustive French national study suggests that High Emergency Lung Transplantation is associated with an adverse outcome as compared with regular allocation. This adverse outcome is mainly related to the severity of the recipients rather than donor or matching characteristics.

Introduction

The development of lung transplantation (LT) is currently limited by the availability of acceptable donor lungs. The imbalance between recipient demand and graft supply is still associated with a significant mortality on the waiting list (1, 2). To increase the donor pool, many strategies have been developed and include progressive extension of donor criteria, *ex vivo* assessment of marginal grafts, and development of donation after circulatory death (3). These strategies have permitted a substantial increase of available grafts without worsening recipient outcome (4, 5). Concomitantly, prioritization systems have been developed to improve graft allocation to the sickest recipients. Prioritization can be based on a recipient severity score applied to all patients such as the Lung Allocation Score (LAS) used in the United States and Germany (6-8), or on an emergency procedure to rescue only the sickest patients such as the urgent procedures used in Italy and France (9, 10).

Specifically, the French procedure of High Emergency Lung Transplantation (HELT) was implemented in 2007 to extract from the rotation list among centers and prioritize for graft allocation those patients whose life expectancy falls under 2 weeks. After an external assessment of recipient eligibility, the HELT procedure prioritizes the allocation of any adult graft available on the national territory for one week, which can be extended to a second week. Over the past 10 years, the crude analysis of the French lung transplant registry showed a decrease in waiting list mortality but also a decrease in post-transplant survival in HELT as compared with non-HELT patients (11). Concomitantly, many retrospective series focusing on recipients yield conflicting results regarding the impact of HELT on post transplant survival.

Aside from recipient severity, the prognostic impact of HELT could be ascribed to the more frequent use of marginal or mismatched donors in the specific context of an urgent procedure. We aimed at deciphering the relative impacts of donor, recipient, and matching on the outcome following HELT in an exhaustive administrative database.

Methods

Study design

We performed a retrospective study of a prospectively maintained national administrative database. We included recipients older than 12 years, who received a LT between July 2007 and December 2015 in one of the 11 French LT centers. Data were prospectively recorded in the nationwide administrative database *Cristal* maintained by the French organ procurement organization (OPO) *Agence de la Biomédecine* and retrospectively analyzed. The study was approved by the Institutional Review Board (IRB) of the French Thoracic and Cardiovascular Surgery Society, which waived the need for study-specific informed consent (IRB #No. CERC-SFCTCV-2016-3-23-16-35-3-MoPi), and by the French OPO *Agence de la Biomédecine* that provided the data. Study-specific authorization was obtained from the coordinating physician of each of the 11 French LT centers. In each center patients' consent to electronic record and scientific analysis of anonymous data was obtained at the time of listing.

Data collection

Recipient-related variables included age, sex, underlying disease, preoperative use of mechanical ventilation and extracorporeal assistance, systolic and mean pulmonary artery pressure, and body mass index (BMI). Donor-related variables included age, sex, smoking history and intensity, cause of death, PaO_2/fraction of inspired oxygen (FiO_2) ratio at the time of proposal (measured with FiO_2: 1 and positive expiratory pressure of 5 cmH_20), ischemic

time, and length of mechanical ventilation. Procedure-related variables included type of transplantation, intra-operative use of extracorporeal assistance, ABO blood group mismatch, cytomegalovirus (CMV) mismatch, and size mismatch. Graft size was defined as the predicted total lung capacity (pTLC), and size mismatch was defined as oversizing if the donor-to-recipient pTLC ratio was >1.2 and undersizing if the donor-to-recipient pTLC ratio was <0.8 (12).

Allocation procedure

Regular allocation is based on a rotation list among centers, with a priority based on administrative regions. The organ is allocated to a center in which the team selects the most adequate recipient on the waiting list. For patients whose access to LT is expected to be restricted due to uncommon blood group or anatomical considerations, derogation may be issued by the French OPO *Agence de la Biomédecine* allowing the use of ABO-compatible donors.

HELT allocation was defined in July 2007, and combined clinical and biological criteria are listed in ***Table 1***. Theoretically, only patients with pulmonary fibrosis (PF), cystic fibrosis (CF), or pulmonary hypertension (PH) are eligible for HELT; patients with Chronic Obstructive Pulmonary Disease (COPD)/emphysema are not. To be listed on the HELT list, patients have to be already listed on the regular LT list. Patients requiring mechanical ventilation or extracorporeal assistance are automatically listed on the HELT list. The request is evaluated and validated by two external experts. The HELT procedure gives a national priority for lung allocation for 8 days, with one renewal. Unlimited derogation can be allowed in selected cases.

For patients who do not fulfil the above mentioned criteria but are deemed critically ill by a transplantation team, a derogation can be allowed after examination by external experts, and

few patients with redo transplantation (included) and COPD/emphysema (excluded) might have beneficiated from the HELT procedure.

Table 1 Inclusion and exclusion criteria for high emergency lung transplantation registration

Inclusion criteria	Cystic fibrosis	Pulmonary fibrosis	Pulmonary hypertension
	Invasive MV*	Invasive MV*	Invasive MV*
Or	ECMO†	ECMO†	ECMO†
Or	PaCO2 > 80 mmHg and NIV‡ > 18/24h for 72h	SaO2 < 90% despite high concentration O2 therapy and medical maximal treatment	NYHA IV and cardiac index < 2L/min and PVR§ > 1200 dyn.s/cm^3 and maximal medical treatment for 72h
Exclusion criteria	Clinical statement not compatible with surgery : hemodynamic or multiorgan failure or uncontrolled sepsis		
	Etiology: COPDll, emphysema, retransplantation		

*MV = mechanical ventilation; † ECMO = Extracorporeal Membrane Oxygenation; ‡NIV = non-invasive ventilation; §PVR = pulmonary vascular resistance; llCOPD = chronic obstructive pulmonary disease

Statistical methods

Categorical data were expressed as number and percentage and compared using χ^2 test. Continuous variables were expressed as mean ± standard deviation and compared with Student's t-test. Missing covariate values were imputed using the multiple imputations by chained equations method, which resulted in 5 imputed data sets. Missing data were assumed to be data missing at random or missing completely at random. Each of the 5 data sets was analyzed independently. Estimates of the variables were averaged according to the Rubin rules.

The primary outcome was overall survival time following transplantation, defined as the time interval between the date of operation and the date of death or the last follow-up visit for censored patients. The follow-up was complete for all patients. Median follow-up was 39.3 months (interquartile range [IQR], 19.8–64.3). Overall survival was estimated by the Kaplan-Meier estimator and compared with the Log-Rank test.

We used Cox proportional hazards regression models to assess variables associated with overall survival following LT. All variables with a p value less than 0.2 in univariate analysis as well as variables known to be associated with the outcomes in the literature were included in the models. Because HELT is available only for patients in the most severe health status, only recipient characteristics not part of the criteria for HELT were included in the multivariable models. Within-center correlations were accounted for using the marginal Cox model, in which the variance is estimated by a grouped jackknife procedure (13).

To assess whether the effect of HELT was constant over time (proportional hazards assumption), we used a smoothing of the scaled Schoenfeld residuals plots (14). The relationships between recipient and donor characteristics (continuous variables) with the relative risk of death and the scale of the continuous covariates were estimated by fitting regression splines.

To explore the sensitivity of our results, we repeated the analyses across a range of different models. We restricted the analysis by adjusting only on covariates with less than 10% of missing data. We also modeled center using mixed-effect Cox model, which assumes that the center effect follows a normal distribution with a mean of 0. The random effect for a given center represents the deviation of this center from the overall underlying baseline risk.

Analyses were performed using R version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria). The marginal Cox model for survival involved use of the coxph function

(survival package) with the cluster option, while the mixed-effect model involved the use of the coxph function with the frailty option.

Results

Study group

During the study period, 2328 patients underwent a LT in France, including 784 (34%) patients with COPD/emphysema who were excluded from the analysis. Their characteristics and outcomes are summarized in ***Tables 1 and 2 and Figure 1*** *in the online data supplement*. The remaining 1544 patients were included in the analysis and accounted for the study group. The number of patients undergoing LT in each centre ranged between 102 and 412. Five hundred and three transplantations (33%) were performed following a high-emergency allocation of the lung graft and accounted for the HELT group. The evolution of the number of patients undergoing a LT during the study period and the number of HELT procedures are shown in ***Figure 1***. The main characteristics of donors, recipients, and procedures are summarized in ***Table 2 and Table 4*** *in the online data supplement*. The overall mean waiting time was 23 ± 39 months. The mean waiting time was 6.4 ± 5.4 days and 24 ± 36 months in the HELT and standard groups respectively.

Table 2 Comparison of characteristics of donors, recipients and surgical procedure according to the type of procedure: high emergency and standard lung transplantation

Characteristics	Patients (n= 1544)	HELT‡ (n=503)	Standard LT§ (n=1041)	P
Donor				
Age (years)	43.7 ± 15.5	44.3 ± 15.1	43.5 ± 15.7	0.35
Sex (male)	843 (55)	267 (53)	576 (55)	0.41
Smoking history	599 (39)	187 (37)	412 (40)	0.36
Smoking intensity (packs/year)	6.4 ± 11.8	5.9 ± 11.2	6.6 ± 12.1	0.26
Body mass index ($kg.m^{-2}$)	24.0 ± 4.1	24.1 ± 4.1	24.0 ± 4.1	0.70
Cause of death				0.87
Vascular	843 (55)	278 (55)	565 (54)	
Traumatic	450 (29)	149 (30)	301 (29)	
Anoxia	185 (12)	56 (11)	129 (13)	
Other**	66 (4)	20 (4)	46 (4)	

Length of MV* (days)	2.56 ± 2.46	2.55 ± 2.69	2.57 ± 2.33	0.93
PaO_2 before harvest (mmHg)	409.1 ± 92.0	416.4 ± 89.7	405.6 ± 93.0	0.031
PaO_2 before harvest according to two groups (mmHg)				0.086
≥ 350	1171 (76)	395 (79)	776 (75)	
< 350	373 (24)	108 (21)	265 (25)	
Predicted TLC† (l)	6.04 ± 1.11	6.01 ± 1.08	6.06 ± 1.13	0.36
Recipient				
Age (years)	40.2 ± 15.5	37.4 ± 15.2	41.6 ± 15.5	< 0.0001
Sex (male)	843 (55)	265 (53)	578 (56)	0.29
Body mass index ($kg.m^{-2}$)	21.4 ± 4.9	20.7 ± 4.6	21.7 ± 5.0	0.00012
Diabetes	423 (27)	139 (29)	284 (29)	0.82
Systolic pulmonary artery pressure (mmHg)	46.4 ± 23.2	52.3 ± 26.0	44.1 ± 21.6	0.00036
Mean pulmonary artery pressure (mmHg)	25.4 ± 15.2	29.7 ± 17.5	23.6 ± 13.8	< 0.0001
Mean pulmonary artery pressure according to two groups (mmHg)				0.017
> 25 mmHg	201 (13)	72 (45)	129 (34)	
≤ 25 mmHg	341 (22)	89 (55)	252 (66)	
Actual TLC† (% of predicted TLC†)	83 ± 33	77.7 ± 31.7	85.3 ± 33.0	0.0068
Predicted TLC† (l)	5.79 ± 1.12	5.71 ± 1.15	5.83 ± 1.11	0.060
Mismatch size	471 (31)	176 (35)	295 (28)	0.0078
Oversized	327 (70)	121 (69)	206 (70)	
Undersized	144 (30)	55 (31)	89 (30)	
Underlying disease				< 0.0001
Bronchiectasis/cystic fibrosis	745 (48)	235 (47)	510 (49)	
Fibrosis	499 (32)	166 (33)	333 (32)	
Pulmonary hypertension	119 (8)	61 (12)	58 (6)	
Redo transplantation	34 (2)	12 (2)	22 (2)	
Other††	147 (10)	29 (6)	118 (11)	
Support before lung transplantation				< 0.0001
No support	787 (51)	146 (49)	641 (62)	
MV* only	506 (33)	115 (39)	391 (38)	
Cardiopulmonary only	12 (1)	12 (4)	0 (0)	
MV* & cardiopulmonary	25 (2)	25 (8)	0 (0)	
Preoperative cardiopulmonary support	38 (2)	38 (13)	0 (0)	< 0.0001
Surgical procedure				
Type of transplantation				0.034
Double lung transplantation	1147 (74)	379 (75)	768 (74)	
Single lung transplantation	304 (20)	85 (17)	219 (21)	
Other (lobar, bilobar, bipartition)	93 (6)	39 (8)	54 (5)	
Intraoperative cardiopulmonary support	762 (49)	354 (72)	408 (40)	< 0.0001

Ischemic time (min)	371.7 ± 108.6	358.9 ± 88.7	378.2 ± 116.8	0.015
Blood group mismatch	139 (9)	121 (24)	18 (2)	< 0.0001
CMVll mismatch	343 (22)	118 (24)	225 (22)	0.36
Postoperative cardiopulmonary support	301 (19)	127 (39)	174 (26)	< 0.0001

*MV = mechanical ventilation; †TLC = total lung capacity; ‡HELT = high emergency lung transplantation; §LT = lung transplantation; llCMV = cytomegalovirus. Data are given as n (%) or mean ± SD.
**Other causes of death include intoxication, meningitis, tumor.
††Other underlying diseases include Eisenmenger syndrome, Langherans' cell histiocytosis, other congenital disease, toxic cause, sarcoidosis.

Comparison of baseline characteristics of HELT and non-HELT groups

Comparison between HELT and non-HELT groups for donor, recipients and surgery characteristics are summarized in ***Table 2***. Recipient characteristics differed significantly between groups, with a younger age (37.4 ± 15.2 vs 41.6 ±1 5.5, $p < 0.0001$), a higher mean pulmonary artery pressure (29.7 ± 17.5 vs 23.6 ± 13.8, $p < 0.0001$), and a higher proportion of PH (12% vs 6%, $p < 0.0001$) in the HELT group as compared with the non-HELT group. Interestingly, donor characteristics did not differ significantly between groups, except for PaO_2 before harvest with a slightly higher mean PaO_2 in the HELT group (416.4 ± 89.7 vs 405.6 ± 93.0, $p = 0.031$).

Blood group mismatch (24% vs 2%, $p < 0.0001$) and size mismatch (35% vs 28%, $p = 0.0078$) were more frequent in the HELT group than in the non-HELT group. A subgroup analysis of the 653 patients (42% of the study group) with actual TLC (aTLC) non-missing data was performed. The mean recipient aTLC was 4.82 ± 2.0 liters and the mean donor pTLC was 5.97 ± 1.1 liters resulting in 413 (63% of available aTLC) size mismatches, 35% in the HELT group vs 28% in the non-HELT group ($p = 0.0078$). Size mismatch characteristics according to the underlying diseases and allocation procedure are summarized in ***Table 3***.

Table 3. Size mismatch characteristics according to the underlying diseases and allocation procedure.

Size mismatch characteristics	Cystic fibrosis (n = 260)		Fibrosis (n = 247)		Pulmonary hypertension (n = 59)		Other* (n = 87)	
	HELT‡ (n = 71)	Standard LT§ (n = 189)	HELT (n = 82)	Standard LT (n = 165)	HELT (n = 26)	Standard LT (n = 33)	HELT (n = 13)	Standard LT (n = 74)
No mismatch	154 (59)		24 (10)		32 (54)		30 (34)	
	44	110	6	18	11	21	3	27
Oversizing	67 (26)		220 (89)		20 (34)		44 (51)	
	19	48	76	144	12	8	8	36
Undersizing	39 (15)		3 (1)		7 (12)		13 (15)	
	8	31	0	3	3	4	2	11

* Other underlying diseases include Eisenmenger syndrome, Langherans' cell histiocytosis, other congenital disease, toxic cause, sarcoidosis and redo transplantation.
Data are given as n (%).
‡HELT = high emergency lung transplantation; §LT = lung transplantation

Comparison of donor, recipient and matching characteristics was also performed in a subgroup analysis according to the underlying diagnosis, as shown in ***Tables 4-6*** *in the online data supplement*. In the CF subgroup, HELT patients underwent more lobar and split LTs and less regular double lung transplant (DLT) than non-HELT patients (9% lobar and split lung and 89% regular DLT in HELT vs 6% lobar and split lung and 93% regular DLT in non-HELT, p = 0.057). In the PF subgroup, HELT patients underwent more DLT and less single

lung transplant (SLT) than non-HELT patients (51% DLT and 40% SLT in HELT vs 41% DLT and 53% SLT in non-HELT, p = 0.031).

Impact of HELT on overall survival

The median survival was 76.0 months for the study group, with a significant difference between the HELT and non-HELT group (53.2 vs 79.0 months, respectively, p < 0.0001, ***Figure 2***). In univariate analysis accounting for within-center correlations, HELT was associated with a hazard ratio (HR) for death of 1.41 (95% confidence interval [CI], [1.22 to 1.64], p < 0.0001). The same increase in the instantaneous risk of death was found whatever the indication for LT, with an HR of 1.47 [95% CI, 1.12 to 1.92], 1.46 [95% CI, 1.19 to 1.79], and 1.62 [95% IC, 1.08 to 2.46] in the CF, PF, and PH groups, respectively, and no significant interaction between HELT and underlying diagnosis. Tests of the analyses' proportional hazards assumptions with residual plots suggest an increased relative risk of death in the HELT group during the early post-operative period, which vanishes over the first 3 years. We confirmed these findings with a separate analysis of HRs according to 4 post-operative periods, as shown in ***Figure 3 and Table 7*** *in the online data supplement*. In PH patients, the increase in the instantaneous risk of death associated with HELT was not statistically significant when postoperative periods were considered separately.

Other factors associated with long-term survival (univariate analysis)

In univariate analysis, among donor-related variables, age and smoking intensity were significantly associated with long-term survival. Among recipient-related variables, age, BMI, type of transplantation, and intra-operative cardiopulmonary support were significantly associated with long-term survival. Mismatches in the blood group and CMV were significantly associated with long-term survival. Relationships between continuous recipient and donor characteristics and the relative risk of death estimated by fitting regression splines are displayed in the ***Figures 2-3*** *in the online data supplement.* These models suggest non-

linear relationships between recipient age, recipient BMI, size mismatch, TLC mismatch, and log hazard for death.

Factors associated with long-term survival (multivariate analysis)

Inclusion of recipient characteristics in a Cox model reduces the HR for HELT from 1.47 to 1.32 [1.10; 1.59]. Inclusion of recipient and donor characteristics in the model did not change the HR associated with HELT in comparison with the model including the recipient characteristics only (HR = 1.32 [1.10; 1.60]). To further assess the impact of donor characteristics on postoperative survival, we computed a donor score based on the linear combination of variables pertaining to the donors from these models. Variables included in the donor score were donor characteristics (age, sex, smoking history, smoking intensity, BMI, PaO2 before harvest, and length of mechanical ventilation) and matching characteristics (size mismatch, blood group mismatch, and cytomegalovirus mismatch). Higher donor scores indicate lower expected survival after LT, with individual scores ranging from - 0.21 to 1.31. The mean donor scores significantly differed between the HELT and non-HELT group (0.27 ± 0.17 vs 0.24 ± 0.17, p = 0.014), indicating that patients undergoing HELT were given donors with a slightly higher hazard of death. This difference reflects an increase of the instantaneous risk of death of 4.2%. The donor scores according to centers and HELT using one of the 5 imputed data sets are shown in ***Figure 4***.

Sensitivity analyses

To explore the sensitivity of our findings to different assumptions, we repeated the analyses across a range of model specifications. The results remained unchanged by using a mixed-effect Cox model or adjusting on a different set of covariates by removing those with more than 10% of missing data.

Discussion

Main results reminder.

Studying the impact of donor, recipient, and matching on long-term outcome following HELT in France, we found that (i) HELT procedure was associated with an increased instantaneous risk of death whatever the underlying diagnosis; (ii) donor PaO2, ABO mismatch, and size mismatch differed between the HELT and non-HELT groups; and (iii) the adverse outcome associated with the HELT procedure was mainly related to the severity of the recipients rather than donor or matching.

Waiting list and post transplant outcome.

The French lung allocation system is based on a rotational list that was historically associated with significant mortality during the waiting period, especially for idiopathic pulmonary fibrosis patients (15). Introduced in 2007, the French HELT procedure has been designed to minimize mortality on the waiting list by rescuing the sickest patients through the allocation of any graft available on the national territory for 2 weeks, but its implication on graft utilization and long-term outcome has not been anticipated. The French HELT allocation is indeed an effective strategy to reduce mortality on the waiting list as demonstrated in previous studies (16-18). Waiting list data were not available for this study, but the 2017 annual report of the French OPO *Agence de la Biomédecine* showed a decrease of the cumulative incidence of death on the waiting list by taking into account the competing risk of transplantation from 1995 to 2017 (from 12% to 3% at 3-month post-registration, and from 22% to 5% at 1-year post-registration). Yet, this cumulative incidence of death on the waiting list by taking into account the competing risk of transplantation was still higher in HELT patients than in

standard patients (7% *vs* 3% at 3-month and 9% *vs* 6% at 1-year post registration respectively between 2012 and 2017) (19).

Since the implementation of HELT in France, two multicentric studies showed a significantly lower survival in HELT as compared with non-HELT patients, even though survival rates after HELT were improving over time, from 51% at 2 years in 2012 (n = 32 patients) to 59% at 3 years in 2014 (n = 95 patients) (9, 16). Unfortunately, these studies were based on retrospective questionnaires and were not exhaustive. Two unicentric studies focusing on certain diagnoses and a longer time span found no significant difference between HELT and non-HELT patients in CF, with 2-year survival of 73% and 75%, respectively (n = 201, p = 0.128), nor in PH, with 5-year survival of 50% and 72%, respectively (n = 234, p = 0.053) (17, 18). These studies were exhaustive but might have lacked statistical power to allow adequate comparisons. Conversely, we found the HELT procedure to be associated with an increased instantaneous risk of death and a high rate of prolonged ECMO post transplant, whatever the indication for LT. This adverse outcome is of particular concern given the relatively low proportion of mechanical ventilation/ECMO patients. Recent simulation works suggested that HELT should maintain a limited impact on the regular waiting list given that the graft supply is adequate (20). Albeit beneficial to the sickest patients, the impact of HELT on long-term outcome is detrimental, and its impact on lung utilization should be assessed carefully.

Donor and matching.

Whether the national priority could affect the quality of allocated grafts and matching was unclear before this study (18), with two hypotheses. On one hand, as the lung pool is divided between 11 centers without HELT and directed toward 1 patient with HELT, the national priority could bias graft allocation toward offering better grafts to HELT as compared with

non-HELT patients (i.e., matching the best grafts to the sickest patients). On the other hand, the emergency situation might lead transplant physicians to decrease the threshold to accept a graft, because of the fear that no other graft will be available in the following days (i.e., matching the worst grafts to the sickest patients). Interestingly, we found that lung grafts accepted through the HELT procedure were similar to that accepted through the regular allocation procedure, except for a small difference in the mean PaO_2 before harvest. Donor PaO_2/FiO_2 ratio is known to be associated with early gas exchange and mortality after LT, and although it is debated, the threshold of 350 mmHg is commonly accepted (21). The difference between HELT and non-HELT grafts has therefore limited clinical implications, as the proportion of patients with PaO2 < 350mmHg remains similar between groups. Even if the donor score was significantly different between HELT and non-HELT groups, its prognostic impact remains limited.

There were more ABO mismatches in the HELT than in the non-HELT group. However, ABO-compatible and ABO-identical LT have been reported to be associated with a similar prognosis in a large study of 6655 LTs included in the United Network for Organ Sharing (UNOS) database between 2005 and 2011 (22). The prognostic impact of size mismatches between donor and recipient is more difficult to analyze, as definition and indication varied across studies. Eberlein *et al* studied the Lung Transplant Outcome Group database, defined oversizing as a donor-to-recipient predicted TLC ratio >1.0, and found that patients undergoing bilateral LT with oversized lungs experienced improved survival, an effect that appears most apparent in non-COPD patients (23). Conversely, a recent analysis of the UNOS database focusing on restrictive lung disease found that moderate oversizing, defined as a donor-to-recipient predicted TLC ratio between 1.1 and 1.2, was associated with an adverse prognosis (24). Similarly, recipients of undersized allografts defined by Eberlein *et al* as a donor-to-recipient predicted TLC ratio ≤1 were more likely to experience primary graft

dysfunction, tracheostomy and had higher resource utilization (25). Following ISHLT guidelines, we defined size mismatch as oversizing if the donor-to-recipient predicted TLC ratio was >1.2 and as undersizing if the donor-to-recipient predicted TLC ratio was <0.8 and found it did not affect overall survival in the frame of the HELT procedure. Altogether, our data suggest that the adverse outcome associated with HELT is associated with recipient severity but not with donor or matching.

Allocation policy.

Transplantation is the only medical therapy in which there is a life-sustaining therapy that is in short supply relative to the need (26), making allocation policy a critical point from both the individual and the population perspective. The main ethical principles associated with organ allocation include equity to eliminate bias or discrimination, justice to render each individual what is due to him or her, beneficence to expect a greater good over harm for the patient, but also utility to make the best use of a limited resource (26, 27). The relative weights of theses principles are different from one country to another. In particular, the principle of utility implies scaling up from the patient-physician relationship to a population level and might be difficult to balance with the first three principles from a physician perspective. The lung allocation system is a direct reflection of the public investment into ethical considerations.

Beside France, other countries have chosen to prioritize patients based on their gravity only and therefore to allocate lungs based on urgency and not transplant benefit. The Scandiatransplant (Denmark, Estonia, Finland, Iceland, Norway, Sweden) urgent lung allocation system (ScULAS) was implemented in 2009, giving supranational priority to patients considered urgent (28). No pre-defined criteria for listing a patient as urgent are required, but Priority 0 includes patients on extracorporeal support or mechanical ventilation,

and Priority 1 includes patients not on life support but with a rapid progression of lung failure and poor short-prognosis as defined by the responsible centre. Yet, only 3 urgent calls per year are granted for each centre. Therefore, patients on life support might not beneficiated from an urgent status. Since the implementation of the ScULAS, 30-day graft survival and 90-day graft survival were significantly lower among patients listed as urgent but there was no difference in 1-year graft survival. However, 81 patients were on life support and among them, only 39 patients were listed as urgent and 15 patients (19%) died on the waiting list (5 patients listed as urgent status and 10 patients listed as regular status). Moreover, graft survival was found significantly lower in patients on life support compared with other patients (28). The Italian urgent lung transplant program was introduced in November 2010, giving national priority to patients $\leq$ 50 year-old requiring mechanical ventilation and/or extracorporeal lung support. Results of the first 14 months showed a 30-day, 6-month, and 1-year survival rates of 82%, 76%, and 71% respectively and a mortality rate on the urgent waiting list of 11%, while another 11% of the patients was excluded because of worsening conditions (10). The super-urgent and urgent lung allocation schemes were introduced in the United Kingdom (UK) in 2017, in order to give a national priority to patients who are at most risk of dying on the waiting list (29). Criteria for super-urgent lung allocation scheme registration include extra-corporeal life support with ECMO or Novalung while criteria for urgent lung allocation scheme registration depend on the underlying disease (30). The 2018 annual report on cardiothoracic organ transplantation in the UK showed that there were 33 urgent lung registrations and 7 super-urgent lung registrations between April 2017 and March 2018 (31). Results after the implementation of this new allocation system in the UK have not been reported yet. All together, these data suggest that HELT and other gravity-based urgent allocation systems are associated with suboptimal outcome. Given that the whole allocation

system is not destabilized, this might be an acceptable trade-off for minimizing waiting-list mortality.

Conversely, the Lung Allocation Score has been designed to maximize the benefits of transplantation and therefore allocates lungs based on both urgency and transplant benefit. The implementation of LAS in the United States has been reported to be associated with fewer waitlist deaths, more transplants performed, a change in the distribution of recipient diagnoses to patients more likely to die on the waiting list, and an improvement in 1-year survival (32). Yet, the LAS has been designed in the US and does not take into account two urgent status parameters, extracorporeal support and mechanical ventilation. Its applicability to other transplant population and to the most severe patients was therefore questionable. The impact of LAS in urgent and highly urgent LT candidates was assessed in 2011 in Eurotransplant (Austria, Belgium, Croatia, Germany, Hungary, Netherlands, Luxembourg, Slovenia). Smits *et al* showed that the LAS and the *LASplus* (encompassing extracorporeal support and non-invasive ventilation) were significantly associated with 1-year post-transplant mortality and overall mortality (27). Since then, Germany was the first European country to adopt the LAS in 2011, followed by the Netherlands in 2014. As patients on mechanical ventilation or extracorporeal support were not accounted for in the LAS, specific allocation rules were introduced in Eurotransplant as well as proposing an exceptional LAS when the calculated LAS does not reflect the transplant benefit for a particular patient (33). Since the introduction of the LAS, the German experience reported a 26% decrease in waiting list mortality and an improved 1-year survival rate from 76% (2009-2011) to 81% (2012-2014) (34), suggesting that the benefits associated with the LAS could be applicable outside the US and in very severe patients.

Limitations.

Our study has several limitations. The number of covariates (mean pulmonary artery pressure, preoperative cardiopulmonary support, and graft ischemic time) with more than 10% of missing data could bias the results. We tried to take these into account by using a multiple imputation method by chain equations. We also included recipient, donor, and surgical characteristics as potential cofounding factors in the multivariate analysis. Still, we cannot exclude that other factors not studied in our analysis or unidentified may have bias our results. Our survival rates are somewhat lower than those reported in the International Registry but represent the real-life data as depicted in an exhaustive administrative database that does not include COPD patients.

Conclusion

This exhaustive French national study suggests that the adverse outcome associated with the HELT procedure is related to the severity of the recipients rather than donor or matching characteristics.

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Figures

Figure 1: Evolution of the number of patients undergoing a lung transplantation and the number of high emergency lung transplantations between July 2007 and December 2015 in France (COPD excluded). LT = lung transplantation; HELT = high emergency lung transplantation; COPD = chronic obstructive pulmonary disease.

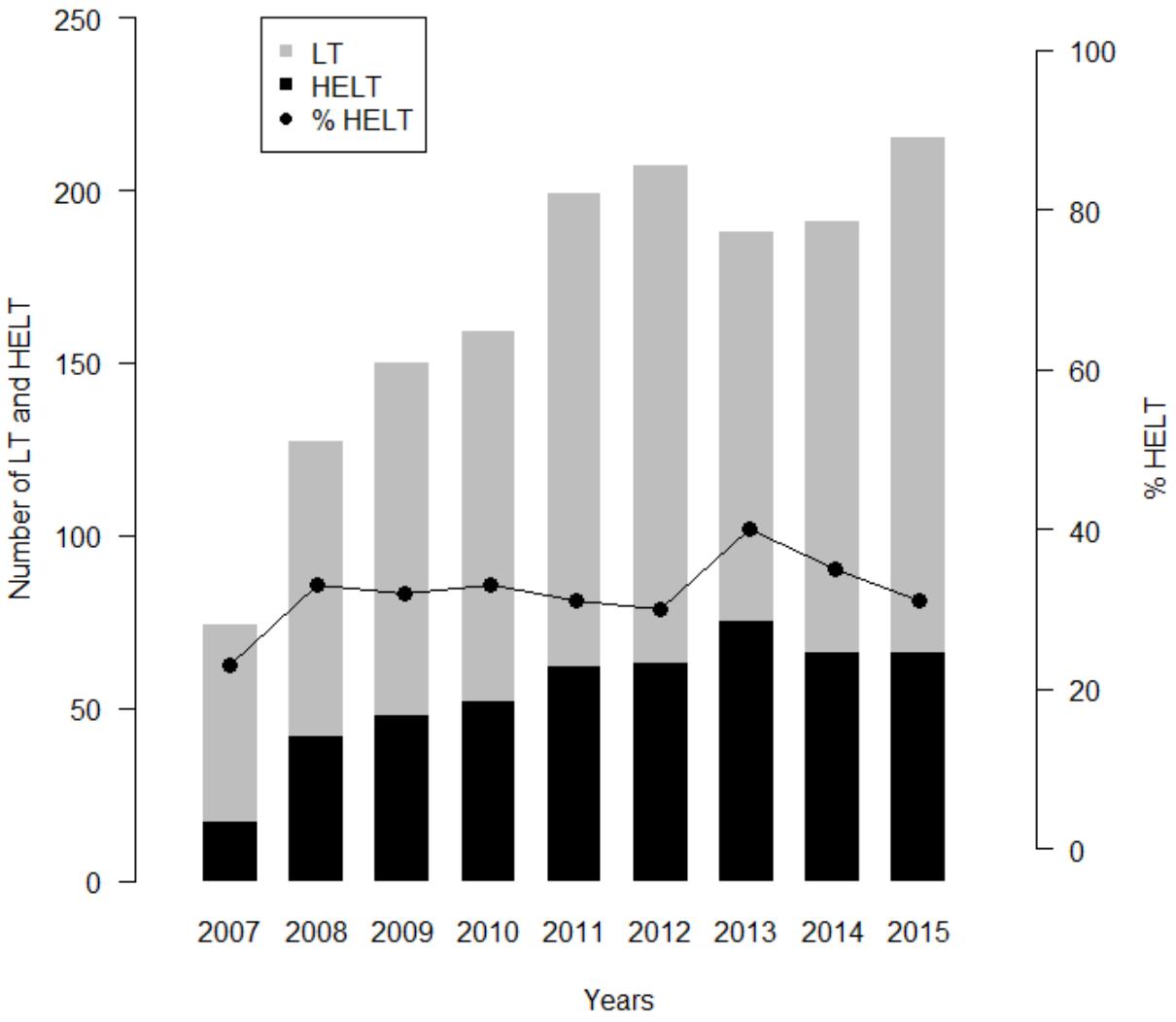


Figure 2: Kaplan-Meier estimates for survival after lung transplantation according to the type of procedure: high emergency and standard lung transplantation. HELT = high emergency lung transplantation.

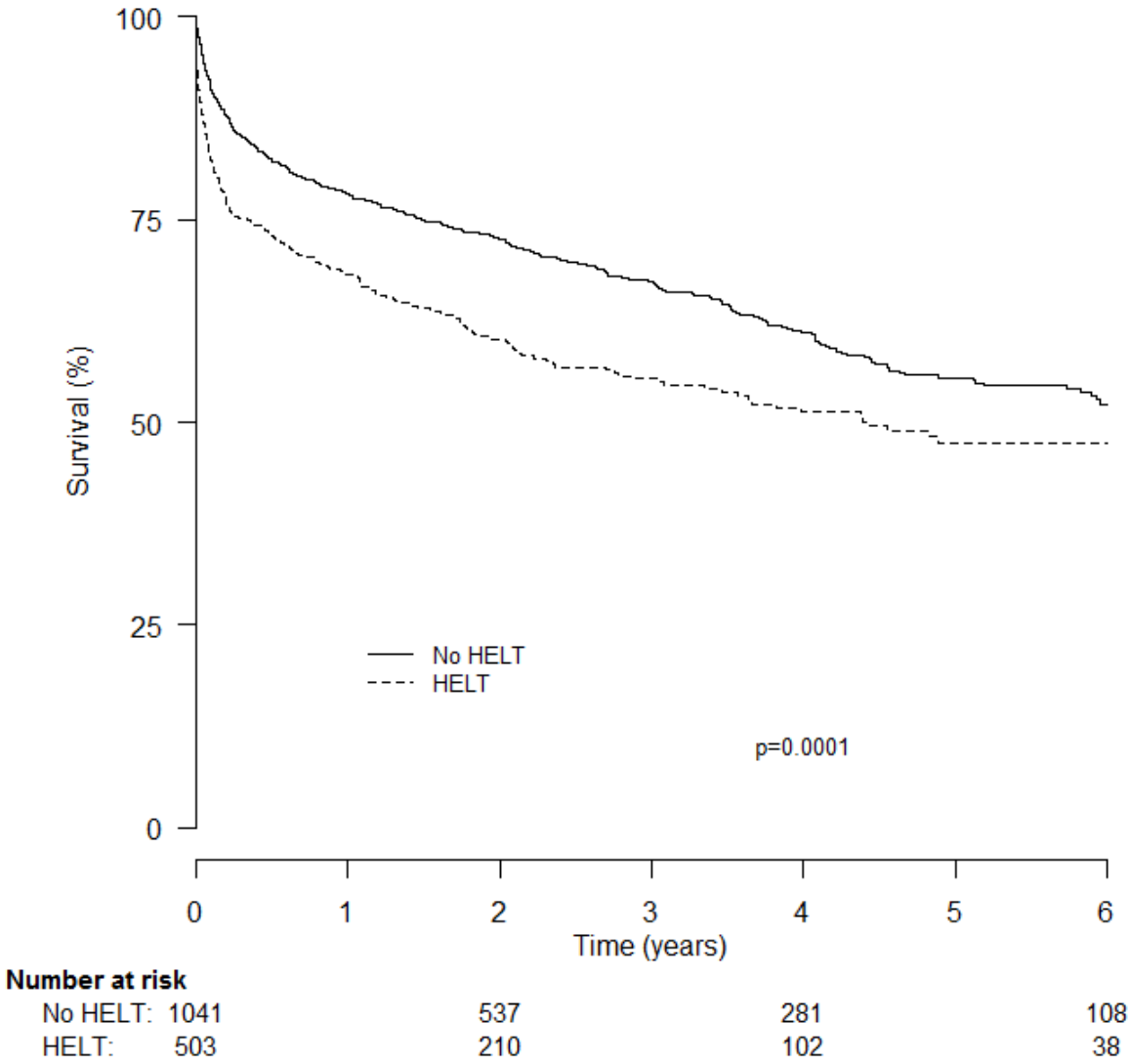


Figure 3: Hazard ratios according to 4 post-operative periods and indications. Error bars indicate 95% confidence intervals

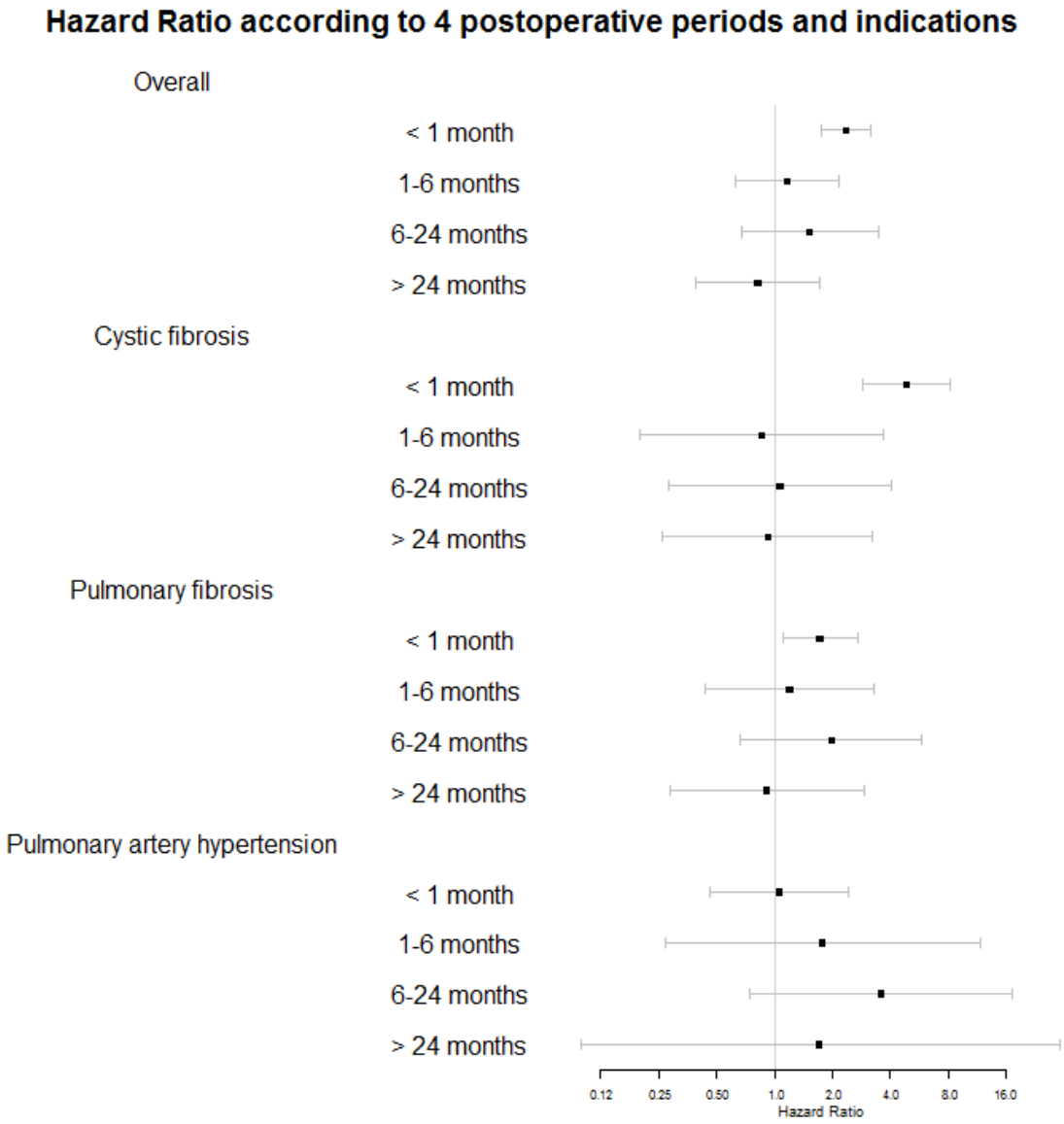
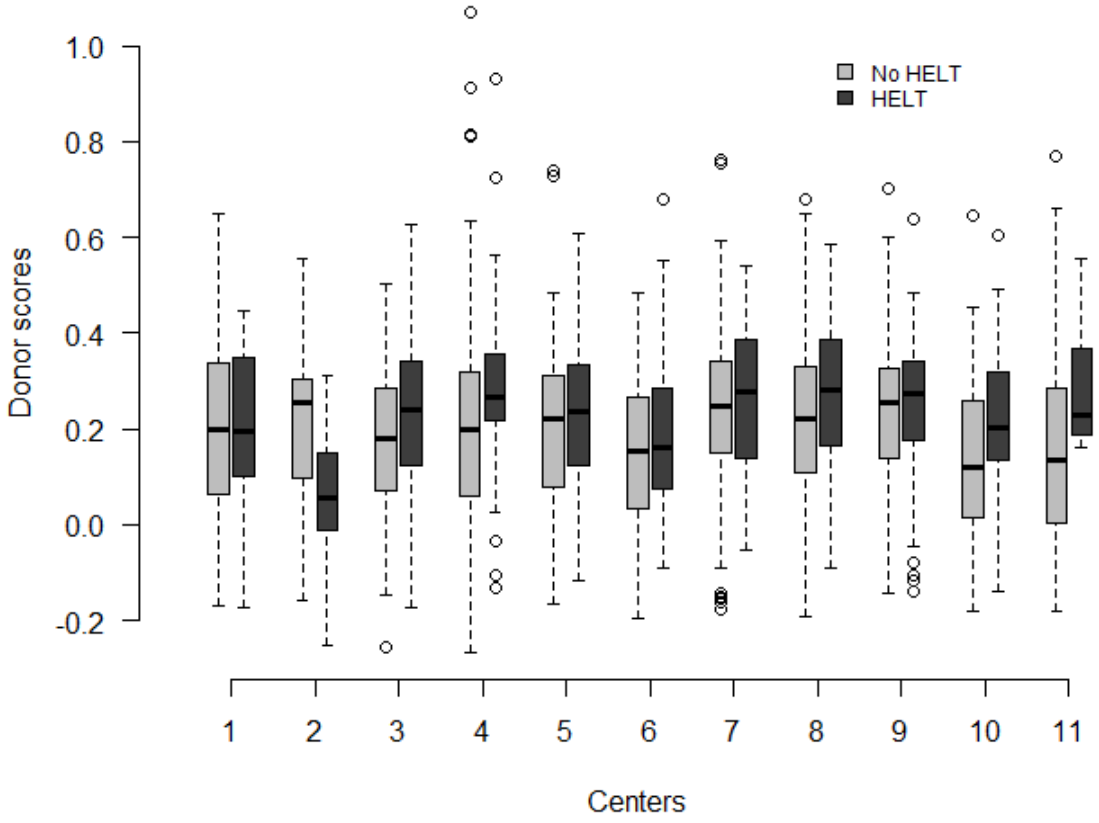


Figure 4: Donor scores according to centers and type of procedure: high emergency and standard lung transplantation using one imputed data set. HELT = high emergency lung transplantation.



Tables and Legends Online Data Supplement

Table 1

Characteristics	Patients (n=784)	HELT‡ (n=45)	Standard LT§ (n=739)
Donor			
Age (years)	46.3 ± 15	44.8 ± 14.4	46.4 ± 15.0
Sex (male)	500 (64)	29 (64)	471 (64)
Smoking history	303 (39)	18 (40)	285 (39)
Smoking intensity (packs/year)	6.6 ± 12	5.8 ± 8.8	6.6 ± 12.2
Body mass index ($kg.m^{-2}$)	24.4 ± 3.8	24.8 ± 4.5	24.3 ± 3.7
Cause of death			
Vascular	404 (52)	25 (56)	379 (51)
Traumatic	258 (33)	13 (29)	245 (33)
Anoxia	100 (13)	7 (16)	93 (13)
Other**	22 (3)	0 (0)	22 (3)
Length of MV* (days)	2.58 ± 2.29	2.22 ± 1.38	2.6 ± 2.34
PaO_2 before harvest (mmHg)	411.6 ± 87.4	429 ± 84.3	410.6 ± 87.5
PaO_2 before harvest according to two groups (mmHg)			
≥ 350	604 (77)	39 (87)	565 (76)
< 350	189 (23)	6 (13)	174 (24)
Predicted TLC† (l)	6.32 ± 1.11	6.22 ± 1.13	6.32 ± 1.11
Recipient			
Age (years)	53.3 ± 9.4	45.8 ± 12.8	53.8 ± 8.9
Sex (male)	447 (57)	24 (53)	423 (57)
Body mass index ($kg.m^{-2}$)	22 ± 4.2	20.1 ± 3.8	22.1 ± 4.2
Diabetes	62 (8)	10 (24)	52 (8)
Systolic pulmonary artery pressure (mmHg)	36.5 ± 9.5	37.4 ± 13.3	36.5 ± 9.3
Mean pulmonary artery pressure (mmHg)	20 ± 7.3	20.3 ± 9.7	19.9 ± 7.3
Mean pulmonary artery pressure according to two groups (mmHg)			
> 25 mmHg	89 (11)	1 (2)	88 (12)
≤ 25 mmHg	352 (45)	14 (31)	338 (46)
Actual TLC† (% of predicted TLC†)	131.1 ± 28.3	111.3 ± 37.2	132 ± 27.7
Predicted TLC† (l)	5.9 ± 1.07	5.8 ± 1.04	5.93 ± 1.07
Mismatch size	206 (26)	14 (31)	192 (26)
Oversized	165 (80)	12 (86)	153 (80)
Undersized	41 (20)	2 (14)	39 (20)
Support before lung transplantation			
No support	487 (62)	9 (20)	478 (65)
MV* only	272 (35)	15 (33)	257 (35)
Cardiopulmonary only	0 (0)	0 (0)	0 (0)

MV* & cardiopulmonary	0 (0)	0 (0)	0 (0)
Surgical procedure			
Type of transplantation Double lung transplantation Single lung transplantation Other (lobar, bilobar, bipartition)	 603 (77) 173 (22) 8 (1)	 33 (73) 11 (25) 1 (2)	 570 (77) 162 (22) 7 (1)
Intraoperative cardiopulmonary support	216 (28)	23 (51)	193 (26)
Ischemic time (min)	364.3 ± 101.8	361.7 ± 68	364.5 ± 103.6
Blood group mismatch	35 (4)	15 (33)	20 (3)
CMVll mismatch	117 (15)	14 (32)	103 (14)
Postoperative cardiopulmonary support	110 (14)	3 (11)	107 (21)

*MV = mechanical ventilation; †TLC = total lung capacity; ‡HELT = high emergency lung transplantation; §LT = lung transplantation; llCMV = cytomegalovirus. Data are given as n (%) or mean ± SD.

**Other causes of death include intoxication, meningitis, tumor.

Table 2

Period (months)	COPD*/emphysema
≤ 1	1.85 [0.92; 3.73]
1 - 6	1.67 [0.25; 11.3]
6 - 24	1.08 [0.14; 8.36]
> 24	1.04 [0.16; 6.72]

*COPD = chronic obstructive pulmonary disease

Table 3

Characteristics	Not available (%)
Donor	
Age (years)	0
Sex (male)	0
Smoking history	0
Smoking intensity (packs/year)	7
Body mass index ($kg.m^{-2}$)	0
Cause of death Vascular Traumatic Anoxia Other**	0
Length of MV* (days)	0
PaO_2 before harvest (mmHg)	0
PaO_2 before harvest according to two groups (mmHg) ≥ 350 < 350	0
Predicted TLC† (l)	0
Recipient	
Age (years)	0
Sex (male)	0
Body mass index ($kg.m^{-2}$)	0
Diabetes	5
Systolic pulmonary artery pressure (mmHg)	68
Mean pulmonary artery pressure (mmHg)	65
Mean pulmonary artery pressure according to two groups (mmHg) > 25 mmHg ≤ 25 mmHg	65
Actual TLC† (% of predicted TLC†)	58
Predicted TLC† (l)	0
Mismatch size Oversized Undersized	0
Underlying disease Bronchiectasis/cystic fibrosis Fibrosis Pulmonary hypertension Redo transplantation Other††	0
Mechanical ventilatory support before lung transplantation No Non invasive	1

Invasive	
Preoperative cardiopulmonary support	13
Surgical procedure	
High emergency LT§	0
Type of transplantation Double lung transplantation Single lung transplantation Other (lobar, bilobar, bipartition)	0
Intraoperative cardiopulmonary support	2
Ischemic time (min)	46
Blood group mismatch	0
CMVll mismatch	1
Postoperative cardiopulmonary support	36

*MV = mechanical ventilation; †TLC = total lung capacity; §LT = lung transplantation; llCMV = cytomegalovirus. Data are given as n (%) or mean ± SD.

**Other causes of death include intoxication, meningitis, tumor.

††Other underlying diseases include Eisenmenger syndrome, Langherans' cell histiocytosis, other congenital disease, toxic cause, sarcoidosis.

Table 4

Characteristics	High emergency LT† (n=235)	Standard LT† (n=510)	P
Donor			
Age (years)	43.5 ± 15.1	40.6 ± 15.7	0.021
Sex (male)	125 (53)	291 (57)	0.32
Smoking history	98 (42)	201 (39)	0.55
Smoking intensity (packs/year)	6.3 ± 11.2	5.7 ± 10.5	0.55
Body mass index ($kg.m^{-2}$)	24.2 ± 4.3	23.7 ± 4.2	0.15
Cause of death			0.29
Vascular	134 (57)	260 (51)	
Traumatic	70 (30)	156 (31)	
Anoxia	22 (9)	67 (13)	
Other**	9 (4)	27 (5)	
Length of MV‡ (days)	2.4 ± 2.6	2.7 ± 2.6	0.21
PaO_2 before harvest (mmHg)	418 ± 94	412 ± 95	0.37
PaO_2 before harvest according to two groups (mmHg)			0.55
≥ 350	183 (78)	387 (76)	
< 350	52 (22)	123 (24)	
Predicted TLC* (l)	6.02 ± 1.06	6.13 ± 1.14	0.23
Recipient			
Age (years)	27.4 ± 9.7	30.9 ± 11.7	0.00010
Sex (male)	107 (46)	265 (52)	0.10
Body mass index ($kg.m^{-2}$)	17.8 ± 2.3	18.6 ± 2.6	< 0.0001
Diabetes	108 (47)	207 (42)	0.18
Systolic pulmonary artery pressure (mmHg)	42.2 ± 20.1	39.1 ± 13.7	0.40
Mean pulmonary artery pressure (mmHg)	23.6 ± 17.2	20.6 ± 8.3	0.24
Mean pulmonary artery pressure according to two groups (mmHg)			0.72
> 25 mmHg	5 (23)	23 (26)	
≤ 25 mmHg	17 (77)	64 (74)	
Actual TLC† (% of predicted TLC†)	103.7 ± 22.2	107.3 ± 21.5	0.23
Predicted TLC† (l)	5.45 ± 1.12	5.65 ± 1.06	0.025
Size mismatch	89 (38)	151 (30)	0.025
Oversized	74 (83)	128 (85)	
Undersized	15 (17)	23 (15)	
Support before lung transplantation			< 0.0001
No support	25 (21)	165 (33)	
MV* only	80 (67)	340 (67)	
Cardiopulmonary only	2 (2)	0 (0)	
MV* & cardiopulmonary	13 (13)	0 (0)	
vSurgical procedure			
Type of transplantation			0.057
Double lung transplantation	209 (89)	476 (93)	

Single lung transplantation Other (lobar, bilobar, bipartition)	6 (3) 20 (9)	4 (1) 30 (6)	
Intraoperative cardiopulmonary support	170 (73)	190 (38)	< 0.0001
Ischemic time (min)	357.2 ± 104.1	399.3 ± 118.5	0.00045
Blood group mismatch	63 (27)	7 (1)	< 0.0001
CMV§ mismatch	74 (32)	143 (28)	0.30
Postoperative cardiopulmonary support	35 (26)	60 (18)	0.072

*TLC = total lung capacity; †LT = lung transplantation; ‡MV = mechanical ventilation; §CMV = cytomegalovirus. Data are given as n (%) or mean ± SD.

**Other causes of death include intoxication, meningitis, tumor.

Table 5

Characteristics	High emergency LT† (n=166)	Standard LT† (n=333)	P
Donor			
Age (years)	46.0 ± 14.8	47.0 ± 15.1	0.48
Sex (male)	90 (54)	187 (56)	0.68
Smoking history	54 (33)	115 (35)	0.66
Smoking intensity (packs/year)	6.0 ± 11.7	6.2 ± 12.8	0.92
Body mass index ($kg.m^{-2}$)	24.0 ± 3.7	24.6 ± 4.2	0.18
Cause of death			0.33
Vascular	79 (48)	187 (56)	
Traumatic	56 (34)	92 (28)	
Anoxia	23 (14)	42 (13)	
Other**	8 (5)	12 (4)	
Length of MV‡ (days)	2.7 ± 2.7	2.5 ± 2.1	0.41
PaO_2 before harvest (mmHg)	413.2 ± 84.6	394.5 ± 88.5	0.024
PaO_2 before harvest according to two groups (mmHg)			0.034
≥ 350	135 (81)	242 (73)	
< 350	31 (19)	91 (27)	
Predicted TLC* (l)	6.0 ± 1.1	6.1 ± 1.1	0.74
Recipient			
Age (years)	49.4 ± 13.1	55.5 ± 8.7	< 0.0001
Sex (male)	109 (66)	229 (69)	0.48
Body mass index ($kg.m^{-2}$)	24.2 ± 4.8	25.7 ± 4.5	0.00060
Diabetes	23 (15)	58 (18)	0.39
Systolic pulmonary artery pressure (mmHg)	43.7 ± 19	39.4 ± 16.7	0.070
Mean pulmonary artery pressure (mmHg)	22.5 ± 12.5	19.8 ± 11.6	0.078
Mean pulmonary artery pressure according to two groups (mmHg)			0.36
> 25 mmHg	25 (30)	45 (24)	
≤ 25 mmHg	59 (70)	139 (76)	
Actual TLC† (% of predicted TLC†)	52.3 ± 17.3	56.1 ± 19.9	0.14
Predicted TLC† (l)	6.02 ± 1.12	6.14 ± 1.08	0.26
Size mismatch	62 (37)	99 (30)	0.086
Oversized	34 (55)	46 (46)	
Undersized	28 (45)	53 (54)	
Support before lung transplantation			< 0.0001
No support	70 (65)	300 (91)	
MV* only	25 (23)	30 (9)	
Cardiopulmonary only	5 (5)	0 (0)	
MV* & cardiopulmonary	8 (7)	0 (0)	
Surgical procedure			
Type of transplantation			0.031
Double lung transplantation	84 (51)	138 (41)	

Single lung transplantation Other (lobar, bilobar, bipartition)	67 (40) 15 (9)	175 (53) 20 (6)	
Intraoperative cardiopulmonary support	110 (68)	107 (33)	< 0.0001
Ischemic time (min)	359.5 ± 74.5	353 ± 120.5	0.65
Blood group mismatch	42 (25)	8 (2)	< 0.0001
CMV§ mismatch	23 (14)	54 (16)	0.49
Postoperative cardiopulmonary support	58 (50)	72 (35)	0.0082

*TLC = total lung capacity; †LT = lung transplantation; ‡MV = mechanical ventilation; §CMV = cytomegalovirus. Data are given as n (%) or mean ± SD.

**Other causes of death include intoxication, meningitis, tumor.

Table 6

Characteristics	High emergency LT† (n=61)	Standard LT† (n=58)	P
Donor			
Age (years)	43.4 ± 15.1	42.9 ± 14.5	0.85
Sex (male)	29 (48)	25 (43)	0.63
Smoking history	19 (31)	28 (48)	0.056
Smoking intensity (packs/year)	5.1 ± 11.5	6.7 ± 10.4	0.46
Body mass index ($kg.m^{-2}$)	24.3 ± 4.7	23.1 ± 3.6	0.12
Cause of death			0.46
Vascular	43 (70)	34 (59)	
Traumatic	10 (16)	15 (26)	
Anoxia	6 (10)	8 (14)	
Other**	2 (3)	1 (2)	
Length of MV‡ (days)	2.7 ± 3.4	2.4 ± 2.3	0.55
PaO_2 before harvest (mmHg)	428.7 ± 86.1	422.1 ± 79.1	0.66
PaO_2 before harvest according to two groups (mmHg)			0.28
≥ 350	48 (79)	50 (86)	
< 350	13 (21)	8 (14)	
Predicted TLC* (l)	5.8 ± 1.1	5.9 ± 1.2	0.78
Recipient			
Age (years)	40.3 ± 13.8	44.1 ± 13	0.13
Sex (male)	23 (38)	22 (38)	0.98
Body mass index ($kg.m^{-2}$)	22.3 ± 3.7	23 ± 4.2	0.29
Diabetes	2 (3)	3 (5)	0.59
Systolic pulmonary artery pressure (mmHg)	85.7 ± 22.4	84.7 ± 29.2	0.89
Mean pulmonary artery pressure (mmHg)	50 ± 12	46.8 ± 14.8	0.29
Mean pulmonary artery pressure according to two groups (mmHg)			0.93
> 25 mmHg	37 (95)	34 (94)	
≤ 25 mmHg	2 (5)	2 (6)	
Actual TLC† (% of predicted TLC†)	89.6 ± 26.5	96.5 ± 21.9	0.28
Predicted TLC† (l)	5.57 ± 1.1	5.65 ± 1.25	0.70
Size mismatch	17 (28)	12 (21)	0.36
Oversized	10 (59)	8 (67)	
Undersized	7 (41)	4 (33)	
Support before lung transplantation			0.018
No support	38 (81)	57 (98)	
MV* only	2 (4)	1 (2é)	
Cardiopulmonary only	3 (6)	0 (0)	
MV* & cardiopulmonary	4 (9)	0 (0)	
Surgical procedure			
Type of transplantation			0.21
Double lung transplantation	56 (92)	55 (95)	

Single lung transplantation Other (lobar, bilobar, bipartition)	2 (3) 3 (5)	3 (5) 0 (0)	
Intraoperative cardiopulmonary support	51 (89)	51 (89)	1
Ischemic time (min)	370.5 ± 60.6	351.1 ± 66.4	0.20
Blood group mismatch	9 (15)	0 (0)	0.0023
CMV§ mismatch	11 (19)	7 (12)	0.32
Postoperative cardiopulmonary support	26 (55)	14 (38)	0.11

*TLC = total lung capacity; †LT = lung transplantation; ‡MV = mechanical ventilation; §CMV = cytomegalovirus. Data are given as n (%) or mean ± SD.

**Other causes of death include intoxication, meningitis, tumor.

Table 7

Period (months)	Overall	Cystic fibrosis	Pulmonary fibrosis	Pulmonary hypertension
≤ 1	2.35 [1.76; 3.14]	4.87 [2.89; 8.2]	1.72 [1.10; 2.70]	1.06 [0.46; 2.43]
1 - 6	1.17 [0.63; 2.17]	0.86 [0.20; 3.71]	1.20 [0.44; 3.31]	1.78 [0.27; 11.86]
6 - 24	1.54 [0.68; 3.47]	1.07 [0.28; 4.08]	1.97 [0.67; 5.82]	3.58 [0.75; 17.2]
> 24	0.82 [0.39; 1.73]	0.92 [0.26; 3.20]	0.91 [0.29; 2.93]	1.71 [0.10; 30.25]

Legends

Table 1: Donor, recipient, and matching characteristics in patients with COPD/emphysema according to the type of procedure: high emergency and standard lung transplantation. COPD = chronic obstructive pulmonary disease.

Table 2: Hazard Ratio and 95% confidence interval according to 4 postoperative periods in the COPD/emphysema subgroup. COPD = chronic obstructive pulmonary disease.

Table 3: Characteristics of donors, recipients, surgical procedure, and missing data.

Table 4: Comparison of donor, recipient, and matching characteristics, according to the type of procedure: high emergency and standard lung transplantation in the cystic fibrosis subgroup.

Table 5: Comparison of donor, recipient, and matching characteristics according to the type of procedure: high emergency and standard lung transplantation in the pulmonary fibrosis subgroup.

Table 6: Comparison of donor, recipient, and matching characteristics according to the type of procedure: high emergency and standard lung transplantation in the pulmonary hypertension subgroup.

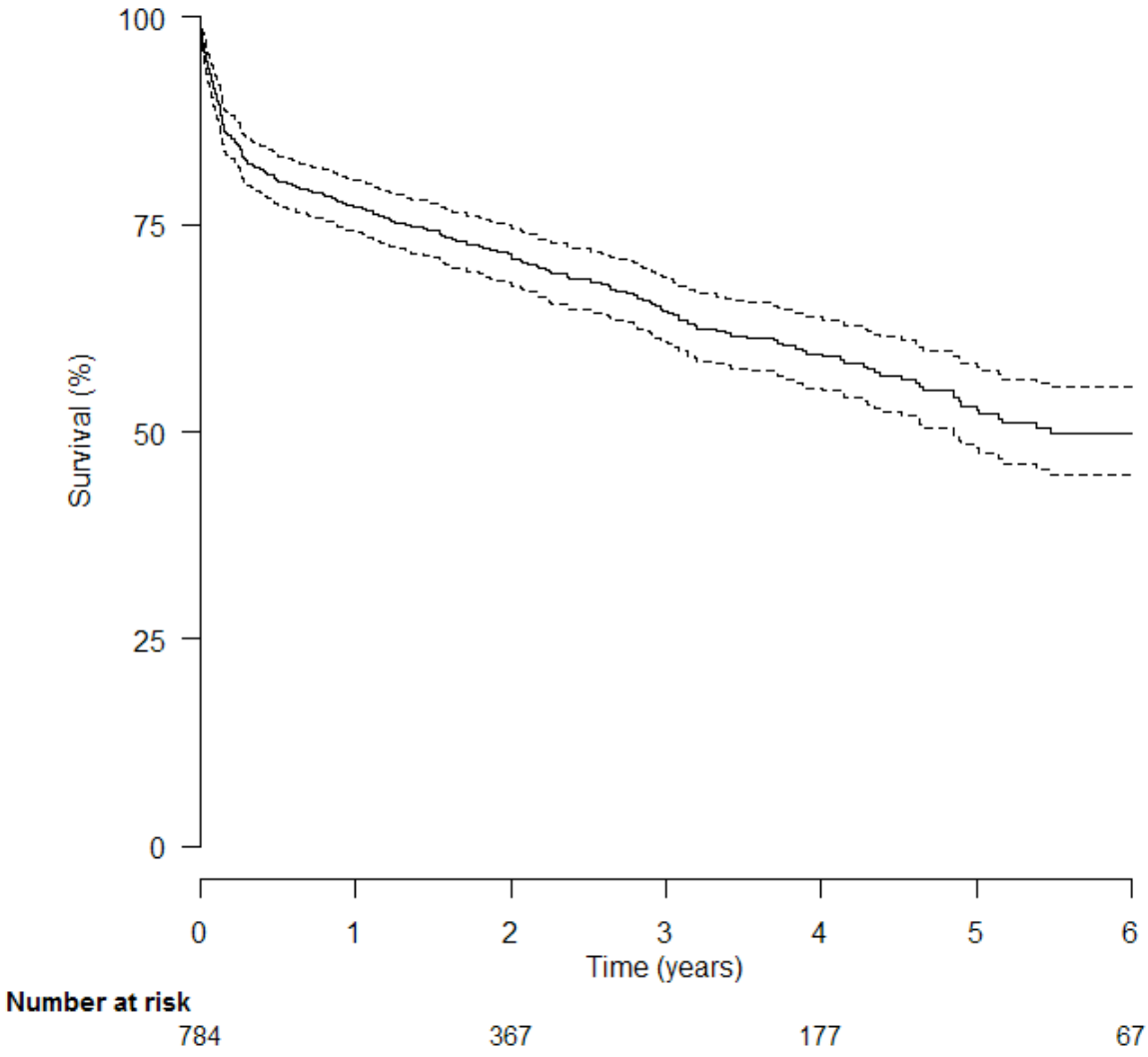
Table 7: Hazard Ratio and 95% confidence interval according to 4 postoperative periods and indications

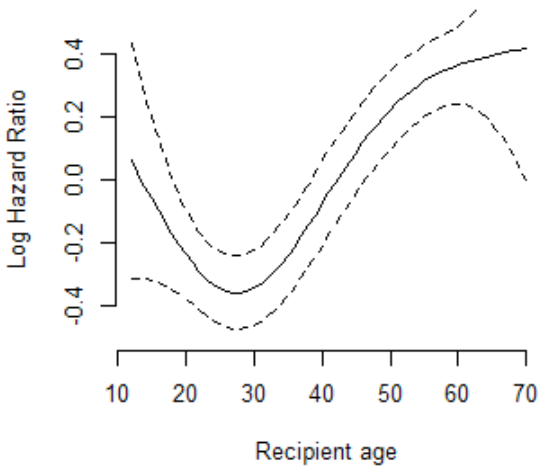
Figure 1: Kaplan-Meier estimates for survival after lung transplantation in the COPD/emphysema subgroup. COPD = chronic obstructive pulmonary disease.

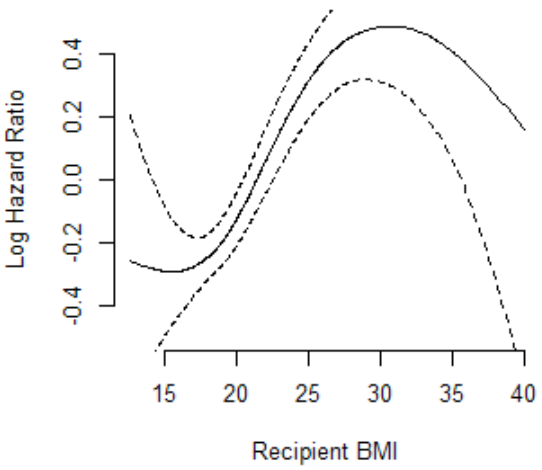
Figure 2: Relationships between continuous recipient characteristics and the relative risk of death estimated by fitting regression splines. BMI = body mass index; TLC = total lung capacity.

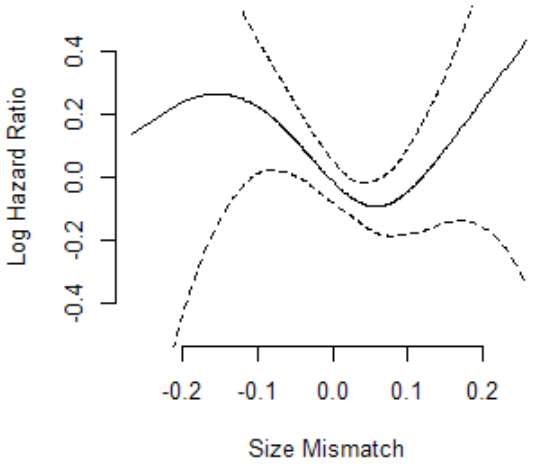
Figure 3: Relationships between continuous donor characteristics and the relative risk of death estimated by fitting regression splines. BMI = body mass index.

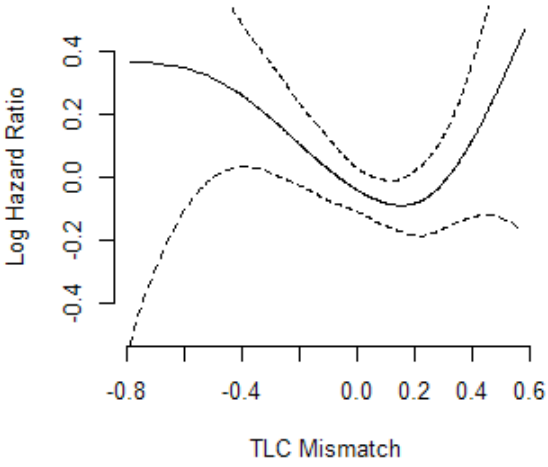
Figures Online Data Supplement

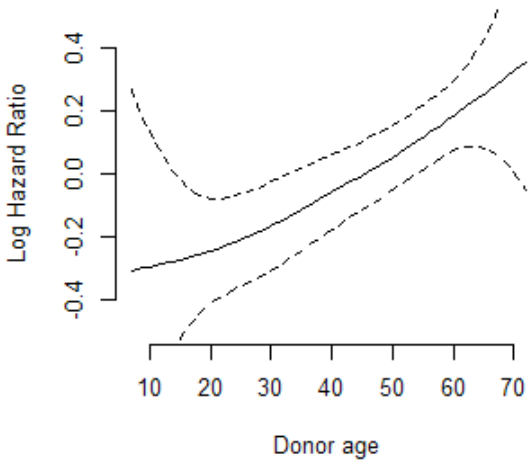


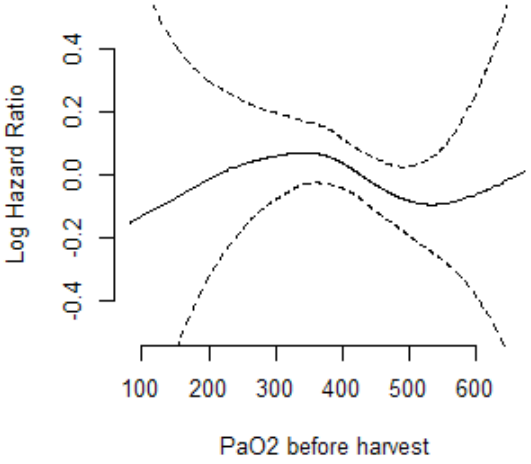

Log Hazard Ratio
-0.4
-0.2
0.0
0.2
0.4
10
20
30
40
50
60
70
Recipient age

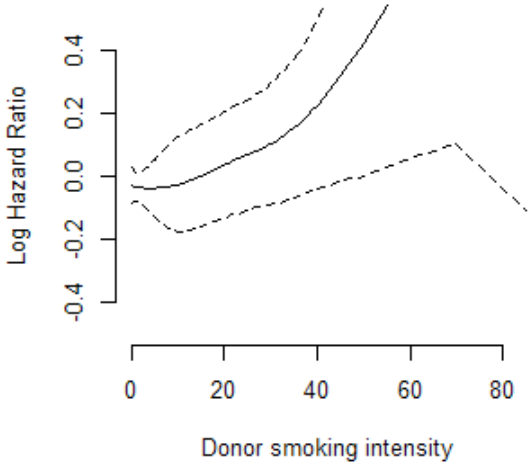

Log Hazard Ratio
-0.4
-0.2
0.0
0.2
0.4
15
20
25
30
35
40
Recipient BMI

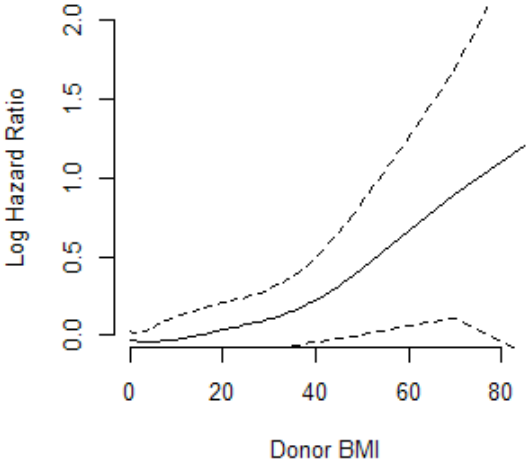

Log Hazard Ratio
-0.4
-0.2
0.0
0.2
0.4
-0.2
-0.1
0.0
0.1
0.2
Size Mismatch


Log Hazard Ratio
-0.4
-0.2
0.0
0.2
0.4
-0.8
-0.4
0.0
0.2
0.4
0.6
TLC Mismatch


Log Hazard Ratio
-0.4
-0.2
0.0
0.2
0.4
10
20
30
40
50
60
70
Donor age


Log Hazard Ratio
-0.4
-0.2
0.0
0.2
0.4
100
200
300
400
500
600
PaO2 before harvest


Log Hazard Ratio
-0.4
-0.2
0.0
0.2
0.4
0
20
40
60
80
Donor smoking intensity


Log Hazard Ratio
0.0
0.5
1.0
1.5
2.0
0
20
40
60
80
Donor BMI