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Intensive care readmissions in the first year after lung transplantation:

Incidence, early risk factors and outcome

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Abbreviations:

AKI: acute kidney injury

ARF: acute respiratory failure

BMI: body mass index

COPD: chronic obstructive pulmonary disease

ECMO: extra corporeal membrane oxygenation

HBP: high blood pressure

ICU: intensive care unit

IPF: idiopathic pulmonary fibrosis

LT: lung transplantation

MV: mechanical ventilation

NBA: neuromuscular blocking agents

NIV: non-invasive ventilation

PGD: primary graft dysfunction

PRC: packed red cell

RRT: renal replacement therapy

SAPS II: Simplified Acute Physiology Score II

SOFA: sequential organ failure assessment

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Authors' contribution

EA participated in the study design, acquisition of data, analysis and interpretation of data, performed the statistical analysis and drafted the manuscript. MY participated in the acquisition, analysis and interpretation of data. ATD, SJB, ST, PT, AS, BLJ, LM, AR, YC and HM made substantial contributions to the interpretation of data. CDT and PM were involved in the study design, statistical analysis, interpretation of data and drafted the manuscript. All authors have read and approved the final manuscript.

Ethics and consent to participate

The study was approved by the Paris North Hospitals Institutional Review Board (Paris VII University, AP-HP, IRB No 0006477). According to French law, after information was collected, the absence of refusal was obtained from all patients.

Consent for publication: Not applicable

Competing interests: There are no competing interests related to the publication of this manuscript

ABSTRACT

BACKGROUND

Predictive factors of intensive care readmissions after lung transplantation (LT) have not been established. The main objective of this study was to assess early risk factors for ICU readmission during the first year after LT.

METHODS

This retrospective, observational, single-centre study included all consecutive patients who underwent LT in our institution between January 2016 and November 2019. Patients who died during the initial hospitalisation in the ICU were excluded. Surgical and medical ICU readmissions were collected during the first year. The results are expressed as medians, interquartile ranges, absolute numbers and percentages. Statistical analyses were performed using the chi-square test, Fisher's exact test and Mann-Whitney U test as appropriate ($p < 0.05$ as significance). Multivariate analysis was performed to identify independent risk factors for readmission. The Paris-North-Hospitals Institutional Review Board reviewed and approved the study.

RESULTS

A total of 156 patients were analysed. Eighteen of them (12%) died during the initial ICU hospitalisation. During the first year after LT, ICU readmission was observed for 49/138 (36%) patients. Among these patients, 14/49 (29%) died during the study period. Readmission was

mainly related to respiratory failure (35 (71%) patients), infectious diseases (28 (57%) patients), airway complications (11 (22%) patients), and immunologic complications (4 (8%) patients). In the multivariate analysis, ICU readmission was associated with the use of high doses of catecholamines during surgery, and the increased duration of initial ICU stay.

CONCLUSION

The initial severity of haemodynamic failure and a prolonged postoperative course seem to be key determinants of ICU readmissions after LT.

BACKGROUND

Despite an improved survival rate reported in the most recent cohorts (1), lung transplant recipients are frequently exposed to serious medical complications requiring hospital readmission. Few studies have addressed this issue, most of them are based on a retrospective analysis (2–10). According to previous studies, hospital readmissions after lung transplantation (LT) are mainly related to pulmonary complications (59%), followed by gastrointestinal (18%), cardiac (5%), metabolic (2.5%) and neurologic complications (2.5%) (6,11). Reintubation, male sex, high lung allocation score, bronchopulmonary fistula, and body surface area have been identified as risk factors for hospital readmissions (8).

Studies assessing ICU readmissions after LT are limited, focusing on incidence, reasons for ICU readmission and risk factors for mortality. In these studies, ICU readmissions were first related to sepsis and acute respiratory failure (ARF) (3–5,12). The mortality rate following ICU readmission is high and estimated to be between 25 and 62.5% (3,4,12), with 20 to 40% of these cases related to sepsis. Interestingly, early risk factors for ICU readmission during the first year after LT have not already been assessed.

The main objective of this study was to assess early risk factors for readmission in the ICU during the first year after LT. The secondary aims were to study the incidence, reasons for readmission, characteristics of the second ICU stay and outcomes of these ICU-readmitted patients.

METHODS

Study population

All consecutive patients who underwent LT at Bichat Claude Bernard Hospital, Paris, from January 2016 to November 2019 were prospectively included in this observational, single-centre study and retrospectively analysed. Patients who died during the initial hospitalisation in the ICU after the LT procedure were excluded from the analysis. Before inclusion in the study, the patient's absence of refusal was obtained, according to French law. The Paris-North-Hospitals Institutional Review Board (Paris Diderot University, APHP, IRB No. 0006477) reviewed and approved the study.

Perioperative management

Perioperative care was standardised for all patients (13–15) according to current practices (16). After the surgical procedure, patients were admitted to the surgical ICU.

Data collection

On ICU admission, demographic characteristics, underlying diseases, clinical data, and severity score (SOFA score on admission) were prospectively recorded. Characteristics of the intraoperative period (type of procedure, need for extracorporeal membrane oxygenation (ECMO), catecholamine administration and dose, fluid administration, intraoperative transfusion) were recorded. High doses of catecholamine

were defined as administration of norepinephrine or epinephrine > 0.5 µg/kg/min. Postoperative complications during the initial ICU hospitalisation following LT were recorded (multiple organ dysfunction syndrome defined as development of two or more organ dysfunction, prolonged ECMO support, primary graft dysfunction (PGD) defined according to ISHLT revised definition (17), acute kidney injury (AKI) defined according to KDIGO criteria (18), acute rejection, infectious complications, respiratory status, thoracic reintervention, abdominal surgery). Medical and surgical ICU readmissions, to our institution and others, were collected in the pneumology medical record of all LT recipients during the first year. Reasons for readmission, hospital discharge before ICU readmission, characteristics of the second ICU hospitalisation (organ failure, need for mechanical ventilation (MV), catecholamines, renal replacement therapy (RRT), ECMO), and outcome (death within the first year after LT) were also collected in the medical records of recipients.

Statistical analysis

Qualitative data are expressed as absolute numbers and proportions, and quantitative data are expressed as medians and interquartile ranges. Statistical analysis was performed using the chi-square test or Fisher's exact test for qualitative data and Mann-Whitney or Kruskal-Wallis tests for quantitative data, as appropriate. The level of statistical significance was set at 5%. Multivariate associations were computed with binary logistic regression models. The variables with nominal 2-tailed *p* value less than 0.2 were entered into a backward stepwise selection method. When similar variables were associated with ICU readmission, the variable with the highest clinical relevance was included in

the multivariate analysis. The one-year survival rate was analysed by the Kaplan-Meier test and compared by a log rank test. RCore Team (2013) was used for statistical analysis *(*R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org/*).*

RESULTS

Characteristics of the study population

Between January 2016 and November 2019, 156 patients underwent LT in our institution. Eighteen (12%) of them died during hospitalisation in the ICU after the surgical procedure and were excluded from the analysis. The flow chart of the study is presented in **Figure 1**. Most of the patients were male and underwent bilateral LT, mainly for primary pulmonary fibrosis and COPD, while cystic fibrosis was the indication for LT in one patient. The characteristics of the study population are presented in Table 1. ICU readmission was observed in 49/138 (35%) patients in the first year after LT. Clinical characteristics are presented in **Table 1**, and delay for readmission is presented in **Figure 2**.

Reasons for ICU readmission and characteristics of the second ICU stay

Reasons for ICU readmission and characteristics of the second ICU stay are presented in **Table 2**. Among the ICU-readmitted patients, 19 (39%) had been discharged from the hospital after initial hospitalisation, while 30 (61%) were still hospitalised and readmitted to the ICU. The characteristics and outcomes of ICU-readmitted patients depending on hospital discharge before readmission are presented in **Table 3**.

Outcome of patients with and without readmission in ICU

One-year survival depending on ICU readmission is presented in **Figure 3**. The characteristics of the second ICU stay depending on survival status are presented in **Table 2**. Among the 89 non-readmitted patients, 6 (7%) died in the first year after LT. Among ICU-readmitted patients,

14/49 (29%) died during the first year after LT, 7 of them (50%) died due to *Pseudomonas aeruginosa* pneumonia, 3 of them died because of a bronchopleural fistula, and the others died because of multifactorial aetiologies; 8/14 (57%) patients died after a withdrawing or withholding treatment decision. During the second ICU hospitalisation, the need for ECMO, catecholamine support and MV were significantly associated with death during the first year after LT.

Risk factors for early ICU readmission

Risk factors for early ICU readmission are presented in **Table 1**. None of the preoperative characteristics of LT recipients (demographic data, underlying diseases, comorbidities) were significantly associated with ICU readmission. In the multivariate analysis, the use of high doses of catecholamines during surgery, and an increased duration of ICU stay were independent risk factors for ICU readmission during the first year after LT. The median delay for ICU readmission was not different between the patients receiving high doses of catecholamines during surgery (readmission after 91 [26-155] days) and those without this support (readmission after 134 [36-208] days, $p = 0.094$).

Risk factors for death at one year

The risk factors for death at one year in the multivariate analysis are presented in **Table 4**.

DISCUSSION

In this single-centre retrospective cohort analysing all consecutive patients who underwent LT, one-third of the recipients were readmitted in the ICU in the first year after transplantation. Among them, 61% were still hospitalised at the time of ICU readmission. Readmission was mainly related to respiratory failure, infectious diseases, airway and immunologic complications. The risks factors for ICU readmission in the multivariate analysis were the administration of high doses of catecholamines during surgery, and an increased duration of initial ICU stay. The one-year mortality rate of readmitted patients was 29%.

Despite an improvement in median survival after LT reported in the most recent cohorts (1), which reached 6.7 years, medical and surgical complications requiring hospital readmission frequently occurred during the first year after LT (1,8,19). Although the risk factors for hospital readmission have been identified, risk factors for ICU readmissions have not been as thoroughly explored. Prior studies have focused on reasons for ICU readmissions and risk factors for mortality (3,7,8). To our knowledge, early predictive factors of ICU readmission during the first year after LT have not yet been established.

None of the assessed preoperative characteristics (demographic data, underlying disease and comorbidities) showed an association with ICU readmission during the first year after LT, which is consistent with prior studies (8,11). The diagnosis leading to LT was not identified as a risk

factor for ICU readmission. In our cohort, the characteristics of the initial ICU stay were not significantly different for IPF and COPD patients. In addition, the median number of pneumonias and their duration of ICU stay were not different for these two subgroups of patients.

The only intraoperative risk factor identified on multivariate analysis was the administration of high doses catecholamines during surgery. This association has not yet been identified and could reflect the increased severity of these patients. Clinical severity scores were identified as risk factors for ICU readmissions in general ICU populations (20–22). In univariate analysis, the use of ECMO support during surgery was associated with ICU readmissions during the first year after LT. However, this association was not identified in the multivariate analysis, limiting the value of this observation. Interestingly, the large postoperative use of ECMO was not a discriminative factor. Finally, the prolonged use of this technique was too rare to become a risk factor for readmission.

In the postoperative period, the multivariate analysis identified the duration of the initial ICU stay as an independent risk factor for readmission. In the general population, prolonged ICU stay is a known risk factor for ICU readmission (20,21). We can formulate several hypotheses to explain why this assumption is also valid for ICU readmissions of LT recipients. A longer initial ICU stay reflects higher rates of postoperative complications (duration of haemodynamic failure, number of pneumonia or occurrence of septic shock), with a negative impact on the general condition of the recipients (sarcopenia, ICU-acquired neuromyopathy). ICU-induced deconditioning of LT recipients makes them vulnerable to subsequent complications leading to ICU readmission.

Previous studies identified reintubation, male gender, high lung allocation score, bronchopulmonary fistula, and body surface area as risk factors for hospital readmissions (8). In our cohort, none of the assessed factors (male gender, BMI, reintubation) was identified as risk factor of ICU readmission. The difference in the risk factors for hospital and ICU readmissions can be explained by the low proportion of ICU readmissions among all the hospital readmissions, with different causes of readmissions. The relatively small size of our cohort could also explain the lack of detection of some risk factors.

Previous studies identified sepsis and ARF as the main reasons for ICU readmission after LT (3,4,12). Comparable results were obtained in our study, with a high predominance of ARF (71%), as well as infectious diseases (57%), with a predominance of pneumonia and pleuropneumonia. *Pseudomonas aeruginosa* was responsible for half of all infectious diseases. Airway complications (obstructive ischaemic bronchitis, bronchial stenosis, fistulas) were the third indication for ICU readmission in our study. Airway complications were also a significant risk factor for hospital readmissions in the Mollberg et al. study (6).

In our study, ICU readmission was associated with a high mortality rate. Earlier studies have reported similar mortality rates, estimated between 25 and 62.5% (3,5,12,23), including 20 to 40% that are linked to sepsis (23). These variable results are probably related to differences

in the studied cohorts (pathology leading to LT, immunosuppression protocols, microbiological ecology). In the cohort published by Cohen et al., chronic rejection, sepsis and SOFA score on readmission were associated with mortality (5). Interestingly, in our study, a higher mortality rate was observed in ICU-readmitted patients with airway complications. This variable had not been assessed in previous studies. Other factors linked to mortality were the need for MV or catecholamine support after ICU readmission, which have already been described (5,23). These elements must be considered severity markers rather than the cause of death.

The timing of readmission (during initial hospitalisation *versus* after hospital discharge) showed no difference on admission (severity scores, organ failure) or prognosis at one year in our study. Readmissions for infectious disease were much more frequent after hospital discharge. The very small sample size of each group limits the interpretation of these results.

Our study has several limitations; its monocentric design and the relatively small sample size of the cohort limit the extrapolation of our findings. The major representation of IPF and COPD in our cohort and the low number of LTs for cystic fibrosis (15.4% of the procedures worldwide, a single patient in our study) represent a bias in the analysis of the outcome of our cases. This discrepancy could also explain the high mortality rate at one year observed in our cohort compared to international studies (1). However, we assume that our observations could provide valuable information to the reader and help clinicians identify patients who may be at risk of having a poor prognosis.

CONCLUSION

In this retrospective cohort, ICU readmission during the first year after LT was frequent and associated with a higher risk of mortality. Preoperative and intraoperative factors play only a limited role in early ICU readmissions, except for high operative doses of catecholamines. The initial postoperative course in the ICU is of major relevance in these readmissions during the first year after LT. The deleterious value of increased ICU stay might reflect further postoperative complications with a negative impact on the general condition of the recipients. During the second ICU stay, the need for catecholamine, MV or ECMO support seems to be predictive factors of mortality.

Table 1: Perioperative demographic characteristics of lung transplant recipients and identified risk factors for ICU readmission by multivariate analysis

	All patients N = 138[1]	ICU readmission N = 49 (36)[1]	No ICU readmission	Univariate analysis *P* value[2]	Multivariate analysis OR	95% CI	*P* value
Preoperative variables							
Age, years	49 [35-58]	48 [36-62]	49 [32-56]	0.78	-	-	-
Male sex	89 (64)	35 (71)	54 (61)	0.21	-	-	-
Diagnosis leading to LT							
▪ Pulmonary fibrosis	54 (39)	21 (43)	33 (37)	0.51	-	-	-
▪ COPD	51 (37)	18 (37)	33 (37)	0.97	-	-	-
HBP	29 (21)	10 (20)	19 (21)	0.90	-	-	-
Pulmonary hypertension	70 (52)	22 (47)	48 (55)	0.39	-	-	-
Diabetes mellitus	11 (8)	5 (10)	6 (7)	0.52	-	-	-
Dyslipidaemia	36 (26)	14 (29)	22 (25)	0.62	-	-	-
BMI > 29.9 $kg \cdot m^{-2}$	15 (4)	5 (10)	10 (11)	0.85	-	-	-
MV before surgery	6 (4)	2 (2)	4 (8)	0.19	-	-	-
ECMO before surgery	8 (6)	6 (7)	2 (4)	0.71	-	-	-
Retransplantation	2 (1)	1 (1)	1 (2)	1	-	-	-
High emergency LT	22 (16)	13 (15)	9 (18)	0.56	-	-	-
Intraoperative variables							
Bilateral LT	93 (67)	33 (67)	60 (67)	0.99	-	-	-
Epidural anaesthesia	82 (59)	22 (45)	60 (67)	0.01	-	-	-

Haemodynamic support by ECMO	99 (72)	41 (84)	58 (65)	0.021	2.08		0.82-5.68	0.13
Intraoperative catecholamine administration	132 (96)	48 (98)	84 (94)	0.42	-		-	-
Norepinephrine or epinephrine > 0.5 µg/kg/min	43 (31)	25 (51)	18 (20)	< 0.001	4.07		1.83-9.29	< 0.001
Fluid administration > 30 mL/kg	118 (87)	44 (90)	74 (85)	0.43		-	-	-
Red blood cell transfusion	84 (62)	32 (65)	52 (60)	0.52		-	-	-
Transfusion > 5 PRC	20 (14)	12 (13)	8 (16)	0.65		-	-	-
Fresh frozen plasma transfusion	76 (55)	29 (59)	47 (53)	0.47		-	-	-
Platelet transfusion	30 (22)	10 (20)	20 (22)	0.78		-	-	-
Postoperative variables (ICU stay)								
SOFA on admission in ICU	6 [5-8]	6 [5-7]	6 [5-8]	0.77		-	-	-
SAPS II on admission in ICU	36 [25-47]	37 [25-49]	36 [25-46]	0.37		-	-	-
Lactate on ICU admission > 3 mmol/L	31 (22)	14 (29)	17 (19)	0.20		-	-	-
Multiple organ dysfunction during ICU stay	26 (19)	14 (29)	12 (13)	0.026		-	-	-
Catecholamine administration > 3 days	40 (29)	20 (42)	20 (22)	0.018		-	-	-
Duration of catecholamine administration, days	1 [1-3]	2 [1-3]	1 [1-2]	0.045		-	-	-
Postoperative ECMO support	33 (30)	12 (27)	21 (32)	0.61		-	-	-
Duration of ECMO support > 2 days	7 (6)	3 (7)	4 (6)	1		-	-	-
Atrial fibrillation during ICU hospitalisation	39 (28)	16 (33)	23 (26)	0.35		-	-	-
NBA administration	30 (22)	15 (31)	15 (17)	0.061		-	-	-
Prone positioning	12 (9)	7 (14)	5 (6)	0.11		-	-	-
Duration of MV, days	2 [1-5]	3 [1-6]	2 [1-5]	0.12		-	-	-
Reintubation	17 (12)	6 (12)	11 (12)	1		-	-	-
Tracheostomy for ventilation weaning	22 (16)	13 (27)	9 (10)	0.012		-	-	-
PGD	70 (51)	30 (61)	40 (45)	0.067		-	-	-
Septic shock during ICU stay	22 (16)	12 (24)	10 (11)	0.042		-	-	-
Number of pneumonia cases	1 [1-2]	1 [1-2]	1 [1-1]	0.004		-	-	-
Thoracic reintervention	16 (12)	11 (22)	5 (6)	0.003		-	-	-
Abdominal surgery during ICU stay	11 (8)	5 (10)	6 (7)	0.52		-	-	-
AKI	76 (55)	27 (55)	49 (55)	1		-	-	-
RRT	6 (4)	2 (4)	4 (5)	1		-	-	-
Acute antibody-mediated rejection	36 (26)	16 (33)	20 (22)	0.19		-	-	-

Acute cellular rejection	18 (13)	6 (12)	12 (13)	0.84	-	-	-
Duration of ICU stay, days	14 [9-23]	20 [11-29]	13 [9-20]	0.006	1.03	1.01-1.06	0.007

Continuous variables are expressed as median and interquartile range (IQR) and were compared using the Mann-Whitney U test. Categorical variables are expressed as n (%) and were compared with Fisher's exact test. LT: lung transplantation; COPD: chronic obstructive pulmonary disease; HBP: High blood pressure; ECMO: Extra-Corporeal Membrane Oxygenation; BMI Body mass index; PRC: Packed Red Cell; SOFA: sequential organ failure assessment; SAPS: simplified acute physiology score; MV: mechanical ventilation; PGD: Primary graft dysfunction; NBA: neuromuscular blocking agent; AKI: acute kidney injury; RRT : renal replacement therapy

[1] n (%); Median [IQR]

[2] Wilcoxon rank sum test; Pearson's Chi-square test; Fisher's exact test

Table 2: Characteristics of the second ICU stay

	All patients readmitted N = 49[1]	Survivors N = 35 (71)[1]	Non survivors N = 14 (29)[1]	*p*-value[2]
Reasons for ICU readmission				
Acute respiratory failure	35 (71)	22 (63)	13 (93)	0.042
Infectious disease	28 (57)	21 (60)	7 (50)	0.52
• Pneumonia	22 (45)	15 (43)	7 (50)	0.65
• Pleuropneumonia	3 (6)	3 (9)	0 (0)	0.55
• Bacteraemia	2 (4)	2 (6)	0 (0)	1
• Mediastinitis	1 (2)	1 (3)	0 (0)	1
• *Pseudomonas aeruginosa* infection	14 (29)	10 (29)	4 (29)	1
• *Stenotrophomonas maltophilia* infection	1 (2)	1 (3)	0 (0)	1
Airway complication	11 (22)	5 (14)	6 (43)	0.055
Acute antibody-mediated rejection	4 (8)	4 (11)	0 (0)	0.31
Cardiovascular complication	2 (4)	1 (3)	1 (7)	0.49
• Acute coronary disease	1 (2)	1 (3)	0 (0)	1
• Limb acute ischaemia	1 (2)	0 (0)	1 (7)	0.29
Ketoacidosis	1 (2)	1 (3)	0 (0)	1
Characteristics of ICU stay				
SOFA score on admission	6 4-8	6 [4-8]	7 [4-9]	0.75
• PaO2/FiO2 < 200 on admission	20 (42)	15 (44)	5 (36)	0.59
• Thrombocytopaenia on admission • MAP < 65 mmHg on admission • Glasgow coma scale < 14 on admission	4 (9)	2 (6)	2 (15)	0.30

Delay of ICU readmission, days	17 (35)	12 (35)	5 (36)	1
	13 (29)	8 (25)	5 (38)	0.47
	108 [33-161]	76 [33-160]	136 [50-173]	0.52
Need for catecholamines	20 (41)	7 (20)	13 (93)	< 0.001
NIV	10 (20)	7 (20)	3 (21)	1
High-flow oxygen therapy	6 (12)	5 (14)	1 (7)	0.66
Need for MV	25 (52)	12 (35)	13 (93)	< 0.001
AKI	25 (52)	15 (43)	10 (77)	0.036
Need for RRT	8 (16)	4 (11)	4 (29)	0.20
Need for ECMO	6 (12)	1 (3)	5 (36)	0.005
Decision to withdraw or withhold treatment	8 (16)	3 (9)	5 (36)	0.033

Continuous variables are expressed as median and interquartile range (IQR) and were compared using the Mann-Whitney U test. Categorical variables are expressed as n (%) and were compared with Fisher's exact test. (ICU: intensive care unit; SOFA: sequential organ failure assessment; MAP: mean arterial pressure; NIV: non-invasive ventilation ; MV : mechanical ventilation ; AKI : acute kidney injury; RRT : renal replacement therapy; ECMO : extracorporeal membrane oxygenation)

[1] n (%); Median [IQR]

[2] Fisher's exact test; Pearson's Chi-square test; Wilcoxon rank sum test

Table 3: Characteristics and outcome of readmitted patients depending on hospital discharge after LT *(ICU: intensive care unit; NIV: non-invasive ventilation; MV: mechanical ventilation; AKI: acute kidney injury; RRT: renal replacement therapy; ECMO: extracorporeal membrane oxygenation)*

	ICU readmission after hospital discharge N = 19 (39)[1]	ICU readmission during initial hospitalisation N = 30 (61)[1]	*p*-value[2]
Risks factors for ICU readmission			
High dose of catecholamines	8 (42)	17 (57)	0.39
Duration of ICU stay	15 [9-21]	23 [13-35]	0.035
Reasons for ICU readmission			
Respiratory failure	15 (79)	20 (67)	0.35
Infectious disease	15 (79)	13 (43)	0.014
• Pneumonia	11 (58)	11 (37)	0.15
• Pleuropneumonia	2 (11)	1 (3)	0.55
• Bacteraemia	1 (5)	1 (3)	1
• Mediastinitis	1 (5)	0 (0)	0.39
• *Pseudomonas aeruginosa* infection	8 (42)	6 (20)	0.095
• *Stenotrophomonas maltophilia* infection	1 (5)	0 (0)	0.39
Airway complication	1 (5)	9 (30)	0.066
Acute antibody-mediated rejection	1 (5)	3 (10)	1
Cardiovascular complication	0 (0)	2 (6)	0.52
• Acute coronary disease	0 (0)	1 (3)	1
• Acute limb ischaemia	0 (0)	1 (3)	1
Ketoacidosis	1 (5)	0 (0)	0.39
Characteristics of ICU stay			

Medical ICU	9 (47)	5 (17)	0.020
SOFA score on admission	6 [4-9]	6 [3-8]	0.75
• PaO2/FiO2 < 200 on admission	6 (32)	14 (48)	0.25
• Thrombocytopaenia on admission	2 (11)	2 (7)	0.63
• MAP < 65 mmHg on admission	7 (37)	10 (34)	0.87
• Glasgow coma scale < 14	6 (35)	7 (25)	0.46
Delay of readmission, days	168 [127-242]	42 [23-128]	< 0.001
Need for catecholamines	6 (32)	14 (47)	0.30
NIV	5 (26)	5 (17)	0.48
High-flow oxygen therapy	2 (11)	4 (13)	1
Need for MV	8 (42)	17 (59)	0.26
AKI	11 (58)	14 (48)	0.51
Need for RRT	2(11)	6 (20)	0.46
Need for ECMO	0 (0)	6 (20)	0.069
Decision to withdraw or withhold treatment	3 (16)	5 (17)	1
Outcome			
Death at one year	4 (21)	10 (33)	0.35

Continuous variables are expressed as median and interquartile range (IQR) and were compared using the Mann-Whitney U test. Categorical variables are expressed as n (%) and were compared with Fisher's exact test. (ICU : intensive care unit; SOFA: sequential organ failure assessment; MAP: mean arterial pressure; NIV : non-invasive ventilation ; MV : mechanical ventilation ; AKI : acute kidney injury; RRT : renal replacement therapy; ECMO : extracorporeal membrane oxygenation)

[1] n (%); Median [IQR]

[2] Pearson's Chi-square test; Fisher's exact test; Wilcoxon rank sum test

Table 4: Risk factors for death at one year, multivariate analysis

	OR[1]	95% CI[1]	*p*
Male gender	5.56	1.43-37.2	0.030
ECMO during surgery	1.72	0.47-8.25	0.4
Norepinephrine or epinephrine administration > 0.5 µg/kg/min during surgery	1.45	0.49-4.25	0.5
SAPS II score on ICU admission	1.01	0.97-1.04	0.6
ICU readmission in the first year after LT	4.32	1.50-13.8	0.009

ECMO: Extra Corporeal Membrane Oxygenation, SAPS II: Simplified Acute Physiology Score II, ICU: Intensive Care Unit, LT: Lung Transplantation

[1]OR = Odds Ratio, CI = Confidence Interval

Figure 1: Flow chart of the study

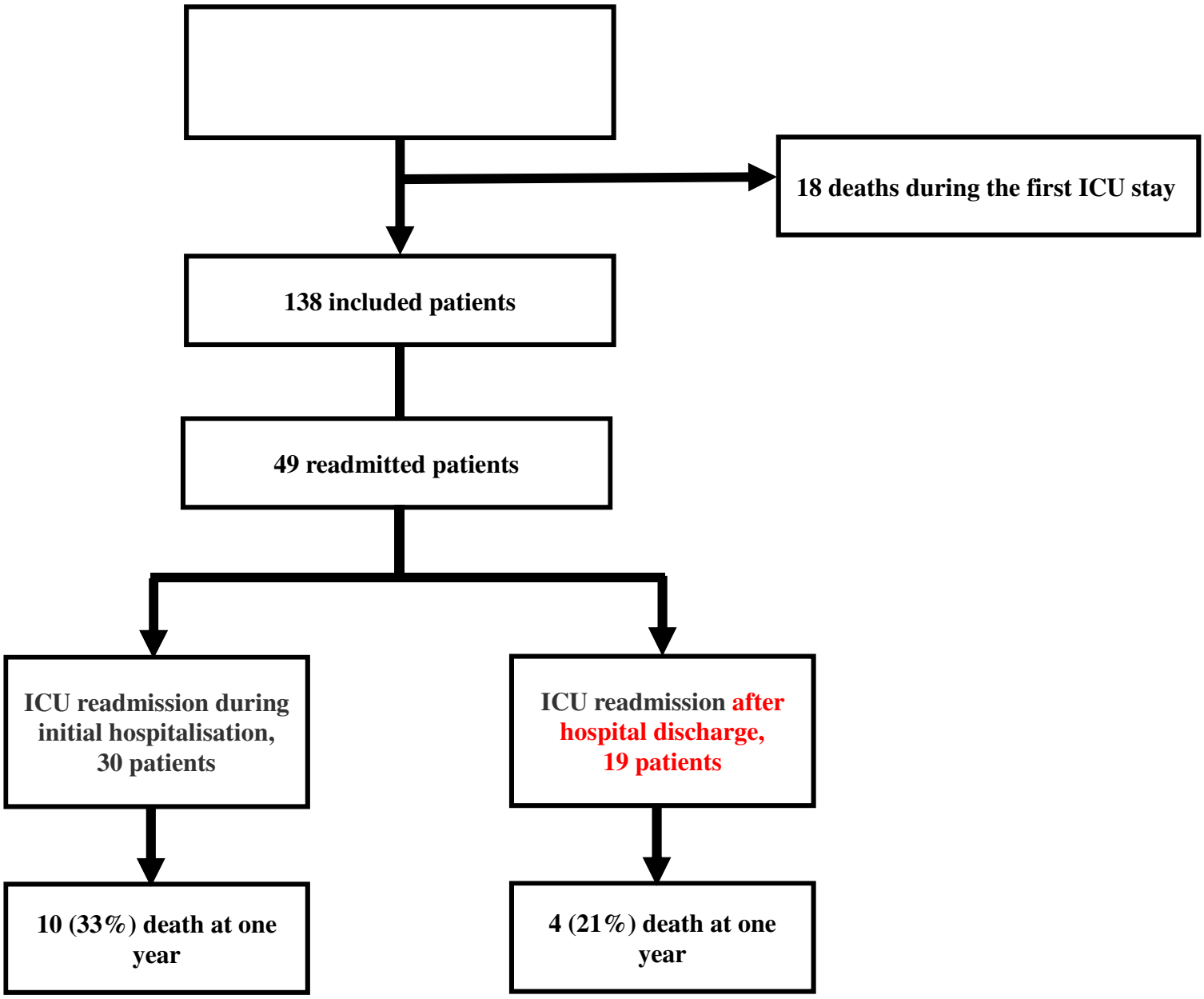


Figure 2: Delay for ICU readmissions during the first year after LT

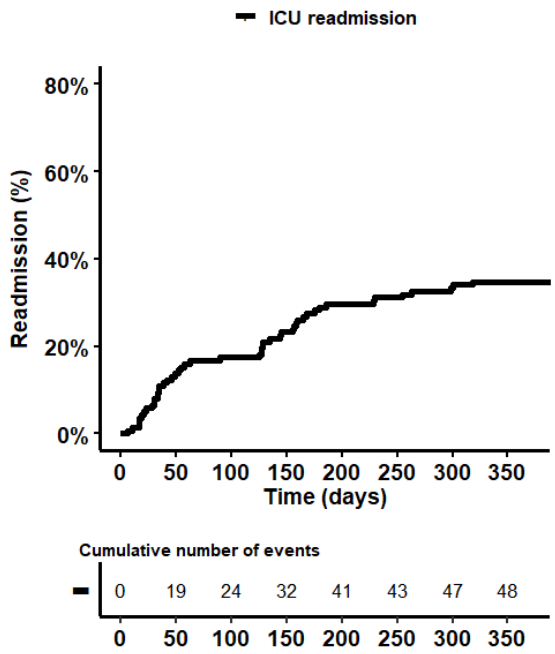
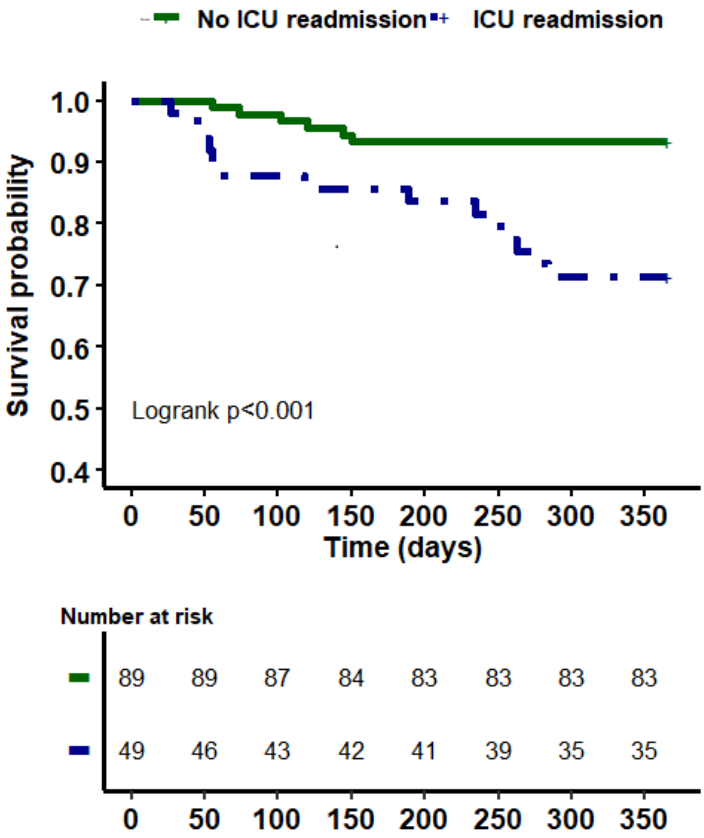


Figure 3: One-year survival depending on ICU readmission during the first year after LT



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