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Urgent lung transplant programme in Italy: analysis of the first 14 months†

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Abstract

OBJECTIVES: Lung transplantation (LTx) is the only effective treatment for end-stage lung disease. In rapidly deteriorating patients awaiting transplant, supportive strategies for lung function allow only a short period of support and lung transplantation remains the definitive therapy. An urgent transplant programme may reduce the waiting time, allowing lung transplantation in these patients.

METHODS: Since November 2010 a nation-wide urgent lung transplant programme has been established in Italy and patients on the waiting list dependent on mechanical ventilation and/or extracorporeal lung support (ECLS) can be transplanted on an emergency basis with the first available graft in the country. Results of the first 14 months of this programme are analysed here.

RESULTS: From November 2010 to December 2011, 28 patients (14 males, mean age 33.6 ± 14.4 years) were considered for urgent LTx. Rapidly deteriorating lung function was supported with mechanical ventilation alone in 4 patients (14.3%), ECLS in 13 patients (46.4%) and mechanical ventilation plus ECLS in the remaining 11 patients (39.3%). Three patients (10.7%) were excluded because of worsening conditions, 3 patients (10.7%) while on the urgent listed and 22 patients (78.6%) underwent transplantation after 9.8 ± 6.2 days of being on the urgent list. The 30-day mortality rate after LTx was 18%, and the 1-year survival rate was 71.4%.

CONCLUSIONS: The urgent lung transplant programme allowed transplantation in a significant percentage of prioritized patients with acceptable 30-day and 1-year mortality rates. An accurate selection of recipients may further improve the clinical impact of this programme, reducing the ethical concerns about transplantation in high-risk patients.

Keywords: Lung transplantation • Urgent lung transplantation • Extracorporeal membrane • Oxygenation • Extracorporeal lung support • Mechanical ventilation

INTRODUCTION

Lung transplantation (LTx) is the only effective treatment for end-stage lung disease in selected patients [1]. Owing to a low graft suitability rate, patients awaiting LTx suffer from a longer period and a higher mortality rate while on the list, when compared with data from other solid organ transplants. Furthermore, in contrast to end-stage heart and kidney disease, long-term supportive strategies are not available as a bridge to lung transplant for rapidly deteriorating patients. Only short-term devices [such as mechanical ventilation (MV) and extracorporeal lung support (ECLS)] can be used and LTx remains the definitive therapy after a relatively brief period of assistance.

Several strategies (the use of marginal grafts, the reconditioning of grafts with poor function and from donation-after-cardiac-death (DCD) donors, and living lobar transplant) have been developed to increase the number of transplants. These techniques

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may reduce but not eliminate the percentage of deteriorated patients and urgent lung transplant remains the only effective solution.

The aim of this study was to evaluate the first 14-month results of the Italian Urgent Lung Transplant programme (IULTp).

MATERIALS AND METHODS

In October 2010, under the supervision of Centro Nazionale Trapianti (CNT), all Italian lung transplant centres created and agreed on a common protocol to identify patients requiring lung transplant priority. From November 2010, the IULTp has been started. Strict inclusion and exclusion criteria were adopted to minimize the percentage of graft waste. Inclusion and exclusion criteria are reported in Table 1. IULTp is reserved for young listed patients requiring MV and/or ECLS with extracorporeal membrane oxygenator (ECMO) or Novalung. Retransplantation is not considered an exclusion criteria. Priority can last just 1 week and can be renewed a maximum of twice. Therefore, the longest period allowed to benefit from the IULTp is 3 weeks. All available lungs in the country must be considered for urgent transplant first and violations of inclusion/exclusion criteria can be considered in selected cases upon CNT approval only.

Statistical analysis

Descriptive statistics are presented as means, standard deviations, medians and ranges for continuous variables. Comparison between groups were performed using χ^2 and unequal variance *t*-test as appropriate. Kaplan–Meier analysis was used to evaluate long-term survival. Statistical analysis was performed using IBM® SPSS Statistic®, Version 21.

RESULTS

From November 2010 till December 2011, 28 patients [14 males; mean age 33.6 ± 14.4 years; body mass index (BMI) 17.6 ± 6.2] entered IULTp. Indications for LTx were: cystic fibrosis (14 patients—50%), idiopathic pulmonary fibrosis (9 patients—32%), Eisenmenger syndrome (2 patients—7%), histiocytosis × (1 patient—4%) and graft failure (2 patients—7%). Rapidly deteriorating lung function was supported with MV alone in 4 patients (14%), ECLS in 13 patients (47%) and MV plus ECLS in the remaining 11 patients (39%) (Table 2). ECLS was accomplished through veno-venous ECMO in 22 patients and veno-arterial ECMO in 1 patient, respectively. Among those, 3 patients (11%) died while on the urgent waiting list and 3 patients (11%) were excluded because of worsening conditions. After 9.8 ± 6.2 days (range: 2–23 days) on the urgent list, 22 patients (79%) underwent transplantation. Most patients (91%) were on ECLS; MV was required on 12 patients (54.5%) (Table 3). Donor characteristics are summarized in Table 3. Notably, optimal grafts without reconditioned lungs were used. Twenty patients (90%) received a double lung transplant (DLTx) and only two patients received a single right graft (SLTx). Only three procedures were performed off-pump, the remaining 19 were conducted on extracorporeal support (14 standard cardiopulmonary by-pass and 5 veno-venous ECMO). Median duration of post-transplant MV and intensive care unit (ICU) stay were 120 h and 30 days, respectively. Twelve patients (54.5%) needed ECMO after transplant for a median duration of support of 2 days (Table 3). One patient died on ECMO on postoperative day (POD) 18 and the remaining 11 patients recovered an acceptable pulmonary function, allowing ECMO weaning after 4.9 ± 6.2 days (median 2 days). Overall 30-day mortality was 18% (4 patients). The causes of death were: cerebral haemorrhage 1 patient (POD 17), sepsis 1 patient (POD 18), and multiorgan failure 2 patients (both on POD 2). All patients who died were on ECLS pretransplant with three of them also requiring pretransplant MV. The comparison between the subgroup of patients dying (DCD) and surviving (no DCD) showed a longer ECMO support after transplant in the DCD cohort (10.5 ± 9.8 vs 3.7 ± 4.3 days, $P = 0.04$). Although not statistically significant, post-transplant ECMO was required in 100% of DCD patients versus 44% of those surviving. Donor characteristics were similar for the two subgroups (Table 4) even if DCD patients received grafts from slightly older donors (Table 5). Thirty-day, 6-month and 1-year survival rates are 81.8, 76.2 and 71.4%, respectively (Fig. 1A). Figure 1B shows survival curves according to the presence or absence of pretransplant MV.

Table 6 shows the impact of pretransplant MV on clinical outcomes. No differences were found in post-transplant ECMO incidence, duration of MV, ICU stay and 30-day mortality. However, the duration of post-transplant ECMO support was longer in ventilated patients ($P = 0.012$). The negative influence of MV was also evident in the cohort of patients requiring pretransplant ECLS. In fact, among preoperative ECLS patients, those who also needed MV experienced a longer period of post-transplant ECMO support and a tendency towards a higher 30-day mortality (3 patients out of 10, 30% vs 1 out of 10, 10%, $P = 0.33$) (Table 7).

Table 1: Inclusion and exclusion criteria for Italian Urgent Lung Transplantation programme

Inclusion criteria	Exclusion criteria
Age ≤50 y/o	BMI < 18 or >30
MV and/or ECLS (except for DECAP®)	Sepsis
Previous LTx waiting list	Multiorgan failure
	Haemorrhagic shock
	Neurological damage
	ECLS and/or MV >14 days

MV: mechanical ventilation, ECLS: extracorporeal lung support, BMI: body mass index; LTx: lung transplantation.

Table 2: Pretransplant characteristics of patients enrolled in Italian Urgent Lung Transplantation programme (*n* = 28)

Male	14 (50%)
Age (years)	33.6 ± 14.4, median 35
Body mass index	17.6 ± 6.2, median 18.4
Diagnosis	
Cystic fibrosis	14 (50%) patients
Idiopathic pulmonary fibrosis	9 (32%) patients
Eisenmenger	2 (7%) patients
Histiocytosis X	1 (4%) patient
Graft failure	2 (7%) patients
Waiting list time (days)	202.9 ± 316, median 30
Infection	14 (50%)
Mechanical ventilation (MV)	4 (14.3%)
Extracorporeal lung support (ECLS)	13 (46.4%)
MV + ECLS	11 (39.3%)

Table 3: Transplanted patients' characteristics (n = 22)

Pretransplant	
Male	11 (50%)
Age (years)	38.4 ± 11.2, median 40.5
Body mass index	17.8 ± 6.7, median 18.5
Diagnosis	
Cystic fibrosis	11 (50%)
Idiopathic pulmonary fibrosis	8 (36%)
Histiocytosis X	1 (5%)
Graft failure	2 (9%)
Mechanical ventilation (MV) alone	2 (9%)
Extracorporeal lung support (ECLS) alone	10 (45.5%)
MV + ECLS	10 (45.5%)
Urgent WL time (days)	9.8 ± 6.2, median 5.5
Lung transplantation	
DLTx	20 (90.9%)
SLTX (r)	2 (9.1%)
Post-transplant	
ECMO	12 (54.5%)
ECMO duration (days)	6 ± 7.03, median 2
MV (h)	292.9 ± 326.8, median 120
Intensive care unit stay (days)	32 ± 24.9, median 30
Death	
4 patients (18%)	CVA: 1 patient (25%) Sepsis: 1 patient (25%) MOF: 2 patients (50%)

ECMO: extracorporeal membrane oxygenation; CVA: cerebro-vascular accident; MOF: multiorgan failure; DLTx: double lung transplant; SLTx (r): right lung transplant.

Table 4: Donors' characteristics (n = 22)

Male	15 (68%)
Age (years)	43.5 ± 10.9, median 45
Body mass index	23.6 ± 3.3, median 23.7
History of smoke	9 (45%)
Mechanical ventilation (h)	75.4 ± 91.8, median 48
Intensive care unit stay (days)	3.9 ± 3.4, median 2
P/F (FiO_2 100%)*	467.1 ± 72.5, median 460

*P/F (FiO_2 100%): arterial oxygen concentration at 100% of inspired oxygen.

DISCUSSION

When compared with other solid organ transplants, LTx is characterized by a smaller number of procedures performed worldwide [1]. This is intimately related to the low rate of graft suitability [2]. Therefore, lung grafts are scarce and very precious resources. Transplantation of severely critically ill patients may have a significant impact on results and it may jeopardize short- and long-term results. Ethical concerns arise when lungs are used on an urgent basis because it implies that elective patients would suffer from a longer wait on the list. This leads to a double consequence. First, a more favourable risk/benefit ratio is lost, proportionately to the severity status of the urgent recipient. Second, elective patients are exposed to a longer waiting time and they may become urgent cases because of the progression of their lung disease with an increased risk at the time of transplantation. By contrast, the absence of an urgent programme condemns critically ill recipients to a fatal outcome. For all these reasons, careful evaluation and strict selection of recipients are crucial.

These preliminary results of activation of the IULTp are encouraging. The interim analysis shows a good performance of fulfilment (~80%) of a national-based request. Despite initial concerns, early and medium-term results are also acceptable, owing to thoughtful and strict identification of those patients who may obtain a survival benefit from transplant, despite the severity of their pretransplant illness. Very recently, two papers described the results of urgent LTx in Italy [3, 4]. However, in both these articles, the study population was represented by patients with lung transplantation on an urgent basis from 2009 to 2011. IULTp was activated on 1 November 2010 and, before this urgent recipients could not receive the graft automatically according to a well-defined protocol. Thus, results reported by Pretagostini *et al.* suffer from this bias. Moreover, the results are mainly focused on request fulfilment and on the impact on on-list mortality. Our analysis considers patients who effectively entered IULTp and our data analyses clinical results in terms of donor characteristics, hospital mortality, impact of pretransplant MV and ECMO, and medium-term survival.

According to the protocol, urgent transplants are reserved for patients on MV and/or extracorporeal oxygenation. It is well known that MV is associated with a higher risk of infection [3, 5], diaphragmatic weakness [4, 6] and muscle wasting [5, 7], and that they all may have a negative impact on the postoperative outcome.

According to the International Registry [8], MV is a recognized risk factor for 1-year mortality with a relative risk of 1.53. Singer *et al.* [9] demonstrated that MV is associated with a significant reduction of overall survival after LTx, increasing twice the risk of death in the first 6 months. However, conditional survival to 6 months is not influenced by the presence/absence of MV. Furthermore, MV seems to have a different impact even on early post-transplant survival, depending on the underlying disease, being the highest for cystic fibrosis or fibrotic lung disease patients, and null for chronic obstructive pulmonary disease patients. Data from United Network for Organ sharing [10] showed that ventilated patients have both an adjusted and an unadjusted worse survival in comparison with unsupported patients. In our series, ventilated patients showed the same incidence of post-transplant ECMO implant when compared with those not requiring pretransplant MV. However, the duration of post-transplant circulatory support was significantly longer in MV patients. This result is difficult to explain. It could be speculated that the multiorgan detrimental effects of MV on those patients may contribute to a general impairment requiring a longer period of extracorporeal support. MV also seems to have an impact on hospital mortality and its effect is even more evident when ECMO is required. The negative prognostic effect of MV is maintained in the medium term, although these differences do not reach statistical significance probably due to the small cohort of patients enrolled in the study.

As for MV, the role of ECMO before LTx is still debated, with a reported 1-year post-transplant survival rate between 50 and 92% [10–13]. Historically, ECMO support has been considered a contraindication in many lung transplant centres [14]. More recently, extracorporeal support has become increasingly accepted and it now has an important role in bridging critically ill patients to LTx [15]. Lang *et al.* analysed data on 38 patients awaiting lung transplant supported with ECMO. They showed that ECMO support is a feasible bridging strategy, with acceptable clinical results [16].

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Table 5: Comparison between DCD (*n* = 4) and no DCD patients (*n* = 18)

	DCD (*n* = 4)	No DCD (*n* = 18)	*P*-value
Pre-LTx			
Age (years)	41.3 ± 10.6, median 41.5	37.7 ± 11.5, median 37.5	0.57
MV alone	0 patient (0%)	2 patients (11%)	0.66
ECLS alone	1 patient (25%)	9 patients (50%)	0.44
MV + ECLS	3 patients (75%)	7 patients (39%)	0.25
IULTp waiting time (days)	7.75 ± 7.5, median 4	8.1 ± 6.5, median 6	0.93
Colonization	1 patient (25%)	9 patients (50%)	0.44
Post-LTx			
MV (h)	494.3 ± 225.7, median 504	255.2 ± 34.3, median 96	0.19
ICU stay (days)	25.8 ± 5.7, median 27.5	33.5 ± 27.6, median 32	0.59
ECMO	4 patients (100%)	8 patients (44%)	0.07
ECMO duration (days)	10.5 ± 9.8, median 10	3.7 ± 4.3, median 2	0.04
CPB	4 patients (100%)	15 patients (83%)	0.53
Donors			
Age (years)	52.5 ± 9.9, median 55	41.6 ± 10.3, median 43.5	0.07
BMI	26.3 ± 5.5, median 26.3	23 ± 2.5, median 23.2	0.07
History of smoke	1 patient (25%)	9 patients (50%)	0.44
Cause of death	CVA 2 patients (50%) other 2 patients (50%)	CVA 7 patients (39%) trauma 7 patients (39%) other 4 patients (22%)	
ICU stay (days)	1.75 ± 0.5, median 2	4.3 ± 3.6, median 3	0.18
MV (h)	42.5 ± 12.4, median 48	88.5 ± 107, median 48	0.41
P/F (FiO_2 100%)*	461 ± 22.6, median 467	468.7 ± 82, median 453	0.86

MV: mechanical ventilation; ECLS: extracorporeal lung support; IULTp: Italian Urgent Lung Transplantation programme; ICU: intensive care unit; ECMO: extracorporeal membrane oxygenation; BMI: body mass index; CPB: cardiopulmonary bypass.
*P/F (FiO_2 100%): arterial oxygen concentration at 100% of inspired oxygen.

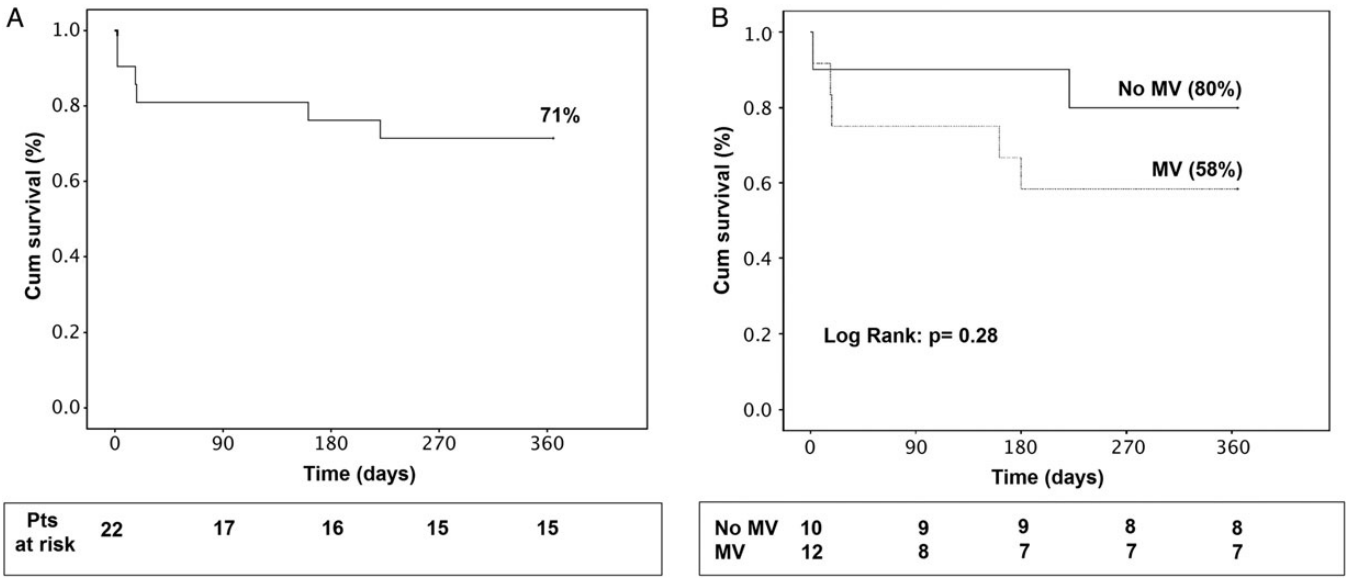

Figure 1: (**A**) Kaplan–Meier survival curve of IULTp patients; (**B**) Kaplan–Meier survival curve of ventilated (MV) and not ventilated (no MV) patients before LTx. IULTp: Italian Urgent Lung Transplant Programme; MV: mechanical ventilation; LTx: lung transplantation.

However, due to a limited number of reports and single-centre series [17–18], further clinical experience on a larger population is required to prove its safety and efficacy. A wider application of ECLS techniques is the result of recent improvements in the available devices, including polymethylpentene oxygenators [19], heparin-coated circuits, double-lumen cannulas [13], pumpless technologies [20] and new-generation centrifugal pumps. Technological amelioration has made ECMO devices more reliable and the application of ECMO to reduce the need of MV has been advocated, expanding its use in the clinical arena [21]. However, although anecdotal cases of prolonged ECMO support before LTx [22] have been reported, ECLS should be still considered a short-term bridge. In a recently published series [9], each day on ECMO increased the risk of death (mortality hazard ratio of 1.06) and a support longer than 14 days identified a high-mortality subgroup of patients. This demonstrates that patients should be transplanted as soon as possible while on ECMO to reduce post-transplant mortality and morbidity. In this context, an

Table 6: Comparison between ventilated ($n = 12$) and not ventilated patients ($n = 10$)

	MV ($n = 12$)	No MV ($n = 10$)	*P*-value
Urgent WL time (days)	9.2 ± 7.8, median 6	6.6 ± 4.6, median 5	0.22
ECMO post-LTx	6 patients (50%)	6 patients (60%)	0.67
ECMO duration (days)	9.8 ± 8.4, median 8.5	2.2 ± 1.5, median 2	0.012
MV post-LTx (h)	288.3 ± 346.7, median 96	297.1 ± 326.8, median 120	0.95
ICU stay (days)	32.1 ± 15.3, median 30	31 ± 33.5, median 25	0.93
DCD	3 patients (25%)	1 patients (10%)	0.43

MV: mechanical ventilation; ICU: intensive care unit; ECMO: extracorporeal membrane oxygenation; LTx: lung transplantation.

Table 7: Comparison between extracorporeal lung support (ECLS) patients ($n = 10$) and mechanical ventilation + ECLS patients ($n = 10$)

	ECLS ($n = 10$)	MV + ECLS ($n = 10$)	*P*-value
Urgent WL time (days)	6.6 ± 4.6, median 5	7.8 ± 7.1, median 5	0.7
ECMO post-LTx	6 patients (60%)	5 patients (50%)	0.68
ECMO duration (days)	2.16 ± 1.47, median 2	11.4 ± 8.4, median 14	0.002
MV post-LTx (h)	297.1 ± 326.8, median 120	240.3 ± 337.2, median 72	0.7
ICU stay (days)	31 ± 33.5, median 25	35.9 ± 15.3, median 32	0.7
DCD	1 patient (10%)	3 patients (30%)	0.33

MV: mechanical ventilation; ICU: intensive care unit; ECMO: extracorporeal membrane oxygenation; LTx: lung transplantation.

urgent lung transplant programme becomes crucial. In our experience, only 1 out of 10 unventilated ECMO-supported patients died after lung transplant, suggesting that ECMO may be effective and safe even in case of critically ill patients, if MV can be avoided. Our results could have been influenced by several factors: the type of ECMO used (veno venous configuration in all patients except one), the most recent available technologies used with polymethylpentene oxygenators in all cases and a limited duration of support (maximal duration 23 days).

Reports of urgent LTx results are scarce. Román *et al*. [23] described the urgent LTx programme in Spain with dismal survival rates of 47.9, 40.8 and 37.1% at 1, 3 and 5 years, respectively. These results may be explained by the fact that this experience refers to an older era characterized by a learning curve in the application of new technologies. The indication for urgent listing in this protocol was also different, including only patients on MV or with life-threatening primary pulmonary hypertension without mention on the use of ECMO. Better results were reported by Saeressig *et al*. [24] on a single-centre cystic fibrosis population, in France. Comparison between urgent and elective transplants did not show any difference in terms of ICU length of stay, severity of primary graft dysfunction, 1- and 2.5-year survival rates. However, according to their protocol, MV and or ECMO were not essential requirements for priority, and the percentage of ventilated or circulatory assisted patients is not reported in the two groups. More recently, Boussaud *et al*. [25] reported results of the French high-emergency LTx (HELTx) programme from July 2007 to June 2008. In this analysis, a poorer survival of HELTx has been shown, if compared with outcomes of non-urgent transplants.

Further investigations including a larger group of lung recipients and encompassing a longer period of time may better confirm the positive preliminary results of our study. The limited sample size does not allow meaningful statistical comparisons. We acknowledge that the results are merely descriptive and a comparison with 'elective' lung transplant procedures during the same period would have been useful to better demonstrate the safety and efficacy of the IULTp.

In conclusion, the nation-wide Italian Urgent Lung Transplant Programme allowed transplantation in a significant percentage of patients with acceptable clinical results. An accurate selection of recipients may further improve the clinical impact of this programme, reducing the ethical concerns about transplantation in high-risk patients.

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REFERENCES

[1] Boffini M, Ranieri VM, Rinaldi M. Lung transplantation: is it still an experimental procedure? Curr Opin Crit Care 2010;16:53–61.
[2] Punch JD, Hayes DH, LaPorte FB, McBride V, Seely MS. Organ donation and utilization in the United States, 1996–2005. Am J Transpl 2007;7:1327–38.
[3] Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165:867–903.
[4] Pretagostini R, Rizzato L, Ricci A, Puoti F, Peritore D, Nanni Costa A. Urgent liver, heart, and lung transplantation programs in Italy: activities and evaluation of outcomes. Transplant Proc 2013;45:2616–8.
[5] Pretagostini R, Peritore D, Rizzato L, Stabile D, D'Alessandro F, Michelangeli G *et al*. Urgent lung transplantation national program: the Italian experience. Transplant Proc 2013;45:2607–9.
[6] Vassilakopoulos T, Petrof BJ. Ventilator-induced diaphragmatic dysfunction. Am J Respir Crit Care Med 2004;169:336–41.
[7] Gruther W, Benesch T, Zorn C, Paternostro-Sluga T, Quittan M, Fialka-Moser V *et al*. Muscle wasting in intensive care patients: ultrasound observation of the M. quadriceps femoris muscle layer. J Rehabil Med 2008;40:185–9.
[8] Christie JD, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Dobbels F *et al*. The Registry of the International Society for Heart and Lung Transplantation: 29th adult lung and heart-lung transplant report-2012. J Heart Lung Transplant 2012;31:1073–86.
[9] Singer JP, Blanc PD, Hoopes C, Golden JA, Koff JL, Leard LE *et al*. The impact of pretransplant mechanical ventilation on short- and long-term survival after lung transplantation. Am J Transplant 2011;11:2197–204.
[10] Mason DP, Thuita L, Nowicki ER, Murthy SC, Pettersson GB, Blackstone EH. Should lung transplantation be performed for patients in mechanical respiratory support? The US experience. J Thorac Cardiovasc Surg 2010; 139:765–73.
[11] Crotti S, Iotti GA, Lissoni A, Bollato M, Zanierato M, Chierichetti M *et al*. The organ allocation waiting time during extracorporeal bridge to lung transplantation affects outcomes. Chest 2013;144:1018–25.
[12] Hammainen P, Schersten H, Lemstrom K, Riise GC, Kukkonen S, Sward K *et al*. Usefulness of extracorporeal membrane oxygenation as a bridge to lung transplantation: a descriptive study. J Heart Lung Transplant 2011;30:103–7.
[13] Bermudez CA, Rocha RV, Sappington PL, Toyoda J, Murray HN, Boujoukos AJ. Initial experience with single cannulation for venovenous extracorporeal oxygenation in adults. Ann Thorac Surg 2010;90:991–5.
[14] Orens JB, Estenne M, Arcasoy S, Conte JV, Corris P, Egan JJ *et al*. International guidelines for the selection of lung transplant candidates: 2006 update—a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant 2006;25:745–55.
[15] Del Sorbo L, Boffini M, Rinaldi M, Ranieri VM. Bridging to lung transplantation by extracorporeal support. Minerva Anestesiol 2012;78:243–50.
[16] Lang G, Taghavi S, Aigner C, Rényi-Vámos F, Jaksch P, Augustin V *et al*. Primary lung transplantation after bridge with extracorporeal membrane oxygenation: a plea for a shift in our paradigms for indications. Transplantation 2012;93:729–36.
[17] Jurmann MJ, Haverich A, Demertzis S, Schaefers HJ, Wagner TO, Borst HG. Extracorporeal membrane oxygenator as a bridge to lung transplant. Eur J Cardiothorac Surg 1991;5:94–7.
[18] Jackson A, Cropper J, Pye R, Junius F, Malouf M, Glanville A. Use of extracorporeal membrane oxygenator as a bridge to primary lung transplant: 3 consecutive, successful cases and a review of the literature. J Heart Lung Transplant 2008;27:348–52.
[19] Hartwig MG, Walczak R, Lin SS, Davis RD. Improved survival but marginal allograft function in patients treated with extracorporeal membrane oxygenation after lung transplantation. Ann Thorac Surg 2012;93:366–71.
[20] Ricci D, Boffini M, Del Sorbo L, El Qarra S, Comoglio C, Ribezzo M *et al*. The use of CO2 removal devices in patients awaiting lung transplantation: an initial experience. Transplant Proc 2010;42:1255–8.
[21] Nosotti M, Rosso L, Tosi D, Palleschi A, Mendogni P, Nataloni IF *et al*. Extracorporeal membrane oxygenation with spontaneous breathing as a bridge to lung transplantation. Interact CardioVasc Thorac Surg 2013;16: 55–9.
[22] Iacono A, Groves S, Garcia J, Griffith B. Lung transplantation following 107 days of extracorporeal membrane oxygenation. Eur J Cardiothorac Surg 2010;37:969–71.
[23] Román A, Calvo V, Ussetti P, Borro JM, Lama R, Zurbano F *et al*. Urgent lung transplantation in Spain. Transplant Proc 2005;37:3987–90.
[24] Saeressig MG, Pellau S, Sermet I, Souilamas R. Urgent lung transplantation in cystic fibrosis patients: experience of a French center. Eur J Cardiothorac Surg 2011;40:e101–6.
[25] Boussaud V, Mal H, Trinquart L, Thabut G, Danner-Boucher I, Dromer C *et al*. One-year experience with high-emergency lung transplantation in France. Transplantation 2012;93:1058–63.

APPENDIX. CONFERENCE DISCUSSION

Dr J. Bekkers *(Rotterdam, Netherlands)*: Waiting list mortality is, of course, a serious problem in lung transplantation. The ultimate goal for an effective programme is to provide end-stage lung failure patients with well-functioning donor organs at the right time. For that purpose, many countries have systems that prioritize patients who are in a deteriorating condition, such as the lung allocation score used in the United States and more recently also adopted in most European transplant countries.

In your presentation you describe the introduction of an urgent lung transplant programme in Italy in 2010. And in the abstract, the objective for this programme is to reduce the waiting list mortality for this kind of patient. But in your results I don't find an analysis of waiting list mortality. So my first question is: what was the policy in Italy before 2010 for patients deteriorating on a waiting list? Was there any urgency system then for those patients? And did you indeed analyse whether the introduction of this system led to reduction of this waiting list mortality?

Dr Boffini: In Italy the organization was quite complex because we have three areas for organ allocation. Before November 2010, you could indicate that you had an urgent patient, but every single centre could decide to keep the donor and to go for transplant or to offer you the graft. So it wasn't a system that worked well, and we had the feeling that things should be changed. These are very preliminary results and they are coming from a national database, so they are not completed. We are looking into the issue that you raise, but I haven't got the answer at the moment.

Dr Bekkers: Then a second question is that in your programme only patients on mechanical ventilation or on ECMO are accepted as urgent patients, whereas other systems do have less strict criteria and also accept patients with higher urgency who are deteriorating even as an outpatient or not yet on ventilation or ECMO. And because mechanical ventilation and ECMO are both complex treatment options with increasing risk for patients, wouldn't it be advisable then to have a system to have patients get a priority status before they end up on ventilation or ECMO? What's your opinion about that?

Dr Boffini: The aim of the group was to be quite strict in the identification of patients who may enter the programme, because in Italy we are suffering from a severe decrease of donations, especially for thoracic organs. And the purpose of this programme was to define the most critically ill patients, with an acceptable risk/benefit ratio, trying not to impair the results. And for this reason we excluded, for example, decapneization, and we included only ECMO and the Novalung.

Dr Bekkers: So there is no priority given to patients not yet on ECMO or ventilation?

Dr Boffini: No.

Dr W. Klepetko *(Vienna, Austria)*: In the interests of time we have to move forward, but I would like to add that you really can be congratulated for delivering such exciting good results for multicentre cooperation work.