Impact of High-Priority Allocation on Lung and Heart-Lung Transplantation for Pulmonary Hypertension

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Background. **Since 2006 and 2007, patients in France with severe pulmonary hypertension (PH) who are at imminent risk of death, despite optimal treatment in the intensive care unit, are placed on a high-priority list (HPL) for heart-lung transplantation (HLT) or double-lung transplantation (DLT). We assessed the effect of this approach on the waiting list and outcomes after transplantation.**

Methods. **We conducted a single-center, retrospective, before-and-after study of consecutive patients with severe group 1, 1′, or 4 PH listed for DLT or HLT between 2000 and 2013 (ie, 6 years before and 6 years after HPL implementation).**

Results. **We included 234 patients. HPL implementation resulted in a significant decrease of the cumulative incidence of death on the waiting list at 1 and 2 years ($p < 0.0001$). The cumulative incidence of transplantation increased significantly from 48% to 76% after 2 years ($p < 0.0001$). Overall survival after transplantation was not significantly different between the pre-HPL and post-HPL era. In the HPL period, patients on the regular list who received a transplant had a nonsignificant trend toward improved overall survival compared with those on the HPL who received a transplant (at 1, 2, 3, and 5 years: 85%, 77%, 72%, and 72% vs 67%, 61%, 58%, and 50%; $p = 0.053$). Finally, survival after listing improved significantly after HPL implementation (at 1, 2, 3, and 5 years: 69%, 62%, 58%, and 54% vs 54%, 45%, 34%, and 26% before the HPL; $p < 0.001$).**

Conclusions. **HPL implementation was followed by higher survival of PH patients after registration on the DLT or HLT waiting list and by a higher cumulative incidence of transplantation among waiting-list patients.**

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Despite the introduction of new medications, pulmonary arterial hypertension (PAH) remains a progressive fatal disease [1–5]. Double-lung transplantation (DLT) and heart-lung transplantation (HLT) are well-established options for patients with end-stage PAH unresponsive to optimal pharmacotherapy [6, 7]. However, the International Society for Heart and Lung Transplantation (ISHLT) registry shows that compared with patients with other conditions, those with PAH have lower 3- and 12-month posttransplantation survival as a result of higher early complication rates [8]. Furthermore, patients with PAH who are on DLT or HLT waiting lists

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Abbreviations and Acronyms

6MWD	= 6-minute walking distance
BMI	= body mass index
CLAD	= chronic lung allograft dysfunction
CO	= cardiac output
CTEPH	= chronic thromboembolic pulmonary hypertension
DLT	= double-lung transplantation
ECLS	= extracorporeal life support
ECMO	= extracorporeal membrane oxygenation
F_{IO_2}	= fraction of inspired oxygen
HLT	= heart-lung transplantation
HPAP	= high priority allocation program
HPL	= high-priority list
ISHLT	= International Society for Heart and Lung Transplantation
mPAP	= mean pulmonary arterial pressure
MV	= mechanical ventilation
NYHA FC	= New York Heart Association Functional Class
PAH	= pulmonary arterial hypertension
P_{aO_2}	= partial pressure of arterial oxygen
PAP	= pulmonary artery pressure
PCWP	= pulmonary capillary wedge pressure
PH	= pulmonary hypertension
PVOD	= pulmonary veno-occlusive disease
PVR	= pulmonary vascular resistance
RAP	= right atrial pressure

are at high risk for death due to acute right heart failure, whose short-term prognosis is extremely poor [9–11].

To decrease waiting list deaths, most countries have revised transplant allocation rules during the past decade. In the United States, implementation in May 2005 of an algorithm based on a lung allocation score determined at list registration [12] was followed by improved outcomes in patients with idiopathic PAH [13], who remained, however, at higher risk for death compared with other transplantation waiting list patients [14].

In France, since September 2006 for HLT and July 2007 for DLT, waiting list patients with cystic fibrosis, interstitial lung disease, or pulmonary hypertension (PH) who experience an event that remains immediately life threatening, despite optimal treatment in the intensive care unit, are placed on a high-priority list (HPL) providing nationwide emergency access to transplants. A patient can be on the HPL for 8 days, renewable once [15]. The aim of our study was to look for changes in waiting list deaths, overall survival after listing, and postoperative outcomes in patients with PH after HPL implementation.

Patients and Methods

Study Population

The HPL was implemented in France for PH in September 2006 for HLT and July 2007 for DLT. We performed a before-and-after study of consecutive patients with PAH, pulmonary veno-occlusive disease (PVOD), or chronic thromboembolic pulmonary hypertension (CTEPH)—group 1, 1′, or 4 disease in the international classification of PH [3, 16]—who were listed for DLT or HLT between January 2000 and December 2013 (6 years before and 6 years after HPL implementation) at the Marie Lannelongue Hospital. All study data were collected prospectively.

According to French legislation, ethics committee agreement and provision of informed consent are not required for retrospective analysis of data corresponding to current practice. However, the database was compiled anonymously within the restrictive requirements of the "Commission National Informatique et Libertés," the organization dedicated to privacy, information technology, and civil rights in France.

All patients who met PH criteria underwent extensive investigations for additional causes or risk factors. The study excluded patients with associated left-sided heart disease or pulmonary disease and those with PH with unclear or multifactorial causes.

The patients were divided into two groups by time of listing or transplantation, or both, relative to time of HPL implementation. Patients listed after, or listed before but who received the transplant after HPL implementation, were included in the HPL group. All other patients were in the pre-HPL group. Patients in the HPL group who received a transplant were divided into two subgroups by whether their transplant was obtained through the HPL or the regular list.

In the HPL period, registration on the HPL was considered for each patient who developed a life-threatening complication and had none of the contraindications to transplantation defined in international recommendations [6]. Eligibility criteria for HPL was defined by the French national transplantation agency as severe PH not improving after more than 72 hours of maximum medical treatment in an intensive care unit, including continuous administration of inotropes and combination therapy for PH. All requests of high emergency graft allocation were reviewed and approved by 2 independent experts mandated by the French national transplantation agency. HPL is approved in all cases for a period of 8 days, renewable once [15].

Data Collection

The data listed in the Supplemental Material were collected prospectively.

Statistical Analysis

All data are described as mean ± SD or median and interquartile range, as appropriate. To evaluate the effect of HPL on waiting list deaths, we first computed the cumulative incidence of death on the waiting list or removal from the list because of clinical worsening leading to DLT/HLT contraindication. Second, the cumulative incidence of transplantation among waiting list patients was compared between the pre-HPL and HPL periods. We compared these two periods regarding patient characteristics at transplantation and the proportion of patients