



## Editorial

## Lung Re-Transplantation. The Opposite View Point<sup>☆</sup>

### Retrasplante pulmonar. Visión contraria

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The number of lung transplantations performed in Spain has doubled in the past 10 years.<sup>1</sup> The greatest cause of death after lung transplantation (LTX) is graft dysfunction, also known as chronic lung allograft dysfunction (CLAD), and it is tempting to follow the example of other procedures, such as kidney transplantation, and consider the possibility of lung retransplantation (LRTX).

Data in the literature on retransplantation outcomes are conflicting. This confusion may be due to:

- (1) The very term “retransplantation”. LRTX can be defined as either a new contralateral graft after failure of a single lung transplant (in our group, we call this procedure “second transplantation”), or replacement of the initially implanted organ(s). While contralateral transplantation can simplify the procedure and improve initial survival, preserving the dysfunctional organ can impair the immunological system and increase the risk of infection.
- (2) Indication and time of retransplantation. Survival after early LRTX, either due to primary graft dysfunction or airway complications, is significantly worse than after late LRTX.<sup>2</sup> Two clear CLAD phenotypes have been identified: obstructive, generally known as bronchiolitis obliterans syndrome (BOS); and restrictive, known as restrictive allograft syndrome (RAS) or rCLAD.<sup>3</sup> In LRTX, survival and the CLAD-free period are shorter than after the initial LTX, and even shorter in patients with the rCLAD phenotype than those with BOS.<sup>4,5</sup>

LRTX is specifically discussed in the 2015 consensus document on the selection of LTX candidates.<sup>6</sup> In brief, these guidelines state that while survival after LRTX has improved in recent years, it is still clearly lower than after the initial LTX.

LT teams need to select their patients carefully to optimize such a scarce resource as donor lungs, and offer the procedure only to patients who will obtain a real benefit, bearing in mind the intrinsic morbidity and mortality and elevated healthcare costs.

The international consensus guidelines<sup>6</sup> recommend that an LTX candidate should be a patient with terminal chronic respiratory disease who meets all the following requirements: (a) >50% risk of death within 2 years if LTX is not performed, and (b) >80% probability of survival during the first 90 days and, assuming adequate graft function, during the 5 years post-LTX.

Patient registries are the best source of LTX data. Spanish LTX outcomes are published annually in the National Transplant Organization report,<sup>1</sup> and the International Society of Heart and Lung Transplantation (ISHLT) provides data on procedures performed worldwide.<sup>7</sup> It is clear from both sources that the relative burden of LRTX has fallen in recent years. In 2017 in Spain, only 6 LRTX were performed, representing 1.6% of all LTX procedures. According to the ISHLT registry, LRTX accounts for 4% of the total procedures, and is performed more frequently in the US than in European countries.

LRTX outcomes are less than promising, and do not achieve the goals set in the clinical guidelines for the selection of candidates. According to ISHLT data, median survival after the first LTX in the period 2009–2015 was 6 years, while after LRTX it was 2.9 years.<sup>7</sup> LRTX survival is significantly lower than survival among patients transplanted for idiopathic pulmonary fibrosis, the disease with worst prognosis after the initial LTX (4.9 years). This might suggest that mortality in LRTX is mainly limited to the initial post-procedure period due to early graft dysfunction associated with a more complex technique, but this is not the only cause. Graft dysfunction in LRTX develops earlier and faster: graft dysfunction occurs one year after the initial LTX in 8.6% of patients, and at 5 years in 50%; in LRTX, meanwhile, these figures rise to 15.2% in the first year, and to 50% at 3 years.<sup>7</sup> Moreover, with regard to survival, Hall et al. studied a series from a single American center,<sup>5</sup> and found that LRTX survival at 1, 3, and 5 years was 64%, 34%, and 21%, while LTX survival was 84%, 71%, and 61%, respectively. If we analyze long-term survival, defined as survival beyond the first year post-procedure (not including initial mortality), LRTX outcomes in 2009–2015 are worse than in the previous years,<sup>7</sup> possibly due to faster development of graft dysfunction and retransplantation being made available to patients with more comorbidities. Such comorbidities include severe renal dysfunction, defined as patients requiring dialysis or kidney transplantation. A heavy comorbidity burden is much more common after LRTX,<sup>7</sup> and is a predictor of mortality.

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Therefore, an LRTX recipient is *per se* a high-risk patient, with a consequently poorer prognosis than a first LTX recipient. This situation could potentially be aggravated by the use of suboptimal donor organs due to expanded criteria or non-standardized risk criteria, circumstances that are not unusual in the current profile of lung donors.<sup>1,8</sup>

Last, but not least, we must consider the ethical conflicts.<sup>9,10</sup> Does LRTX violate the principles of equal opportunities and fairness in access to the first transplantation? We must not overlook the fact that, on the hierarchy of principles, justice ranks higher than beneficence. And another point: are the current clinical outcomes of LRTX acceptable and do they justify these procedures? Not at the present time, we feel, but a more careful selection of candidates and future advances in techniques may make us change our mind.

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