



## UPDATE IN INTENSIVE CARE: TRANSPLANTS

### The impact of lung transplantation on ICU personnel

### El impacto del trasplante pulmonar sobre el personal de la UCI

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During recent months, a series of up-dating articles about lung transplant published by members of PLUTO Network (Postoperative Lung Transplant Network) and Grupo de Trasplantes de SEMICYUC, have appeared in *Medicina Intensiva*.

Even though lung transplant (LT) results have been improving over the last thirty years, and it is accepted as a real therapeutic option for patients in end-stage disease, some issues are still open. Dr. Rello's article lays down a challenge in terms of developing strategies to increase lung retrieval rates.<sup>1</sup>

Generally speaking, efficiency in lung retrieval is very poor, due to the physiological changes deriving from brain death (BD) and difficulties in the management of potential donors. Efficiency in lung harvesting is usually under 16% of all potential donors.<sup>2</sup> This is due to the fact that lung dysfunction is frequent in patients with severe brain damage; between 15 and 20% develop ALI/SDRA.<sup>3</sup> This, together with changes related to BD such as neurogenic oedema or related to base pathologies including pneumonia or bronchoaspiration, explain the deterioration in oxygen exchange.

Different authors agree that having a specialized team for managing potential donors will result in more organs for transplant.<sup>4–6</sup> Although there is no unique treatment model when talking about donor management, there are different strategies called "protective strategies" related to the mechanical ventilation parameters which are widely

accepted.<sup>7</sup> Some authors propose "aggressive" procurement such as the use of systematic bronchoscopy or recruitment manoeuvres with high or very high PEEP.<sup>4,8</sup>

Scarcity of grafts for transplant is partially due to poor efficiency and the fact that there is no evidence supporting the ultra-strict accepted criteria. Present expanded criteria includes: age > 55, smoking antecedents, abnormal chest X-ray (unilateral: for aspiration or trauma), or even known positive sputum culture and the use of organs with PaO<sub>2</sub> < 300 mmHg through recruitment manoeuvres or ex vivo perfusion.<sup>9</sup> Perhaps the moment has arrived to extend current criteria even further.<sup>10</sup>

Another proposed strategy to increase the organ pool is the use of lungs from NHBD (non heart-beating donors): Maastricht type II (uncontrolled donors) and type III (controlled), although these represent a small percentage of transplanted lungs. Results with organs proceeding from NHBD type II are acceptable related to mortality and survival rates.<sup>9</sup>

Yet some other strategies are far removed from our desired intention, for example, the risky procedure of living lung donation.

Dr. Masclans et al., state in their special article<sup>11</sup> that whilst training for resident doctors in terms of organ donation is of good quality, as courses are performed all over the country, there is little or no emphasis at the level of immediate transplant post-operative care, management of immunosuppressant treatment and complications, specifically linked to rejection and infection. Bearing in mind that the current training plan dates back to 1996, some degree of modernization should be considered.

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Dr. Masclans et al. suggest that training in these increasingly complex areas could be useful for both resident doctors and indeed any doctors coming into contact with this type of patients. To be familiar with the process will make dealing with this kind of patients easier.

Moving on to the main issues within the post-operative period we find three related articles: primary graft dysfunction (PGD), antibiotic prophylaxis/infectious disease and advances in immunosuppression.

PGD is a common postoperative complication; between 15 and 20% of patients will present some degree of dysfunction. The Consensus Document of ISHLT in 2005<sup>12</sup> defines as a non cardiogenic pulmonary oedema less than 72 h of reperfusion and at the same time alterations of lung parenchyma. The degree of PGD (1-3) correlated to the outcome and survival rates.<sup>13</sup> Treatment, as referred to by Dr. Suárez López et al.<sup>14</sup> should be underpinned from two perspectives: (1) that of excellent donor management (attempting to minimize the inflammatory response due to BD) and avoidance of further complications, where the awareness and dedication of intensive care doctors is indispensable. (2) Managing the post-operative period so as to anticipate the following kinds of problems: hemodynamic stabilization, antibiotic prophylactic treatment, individualization of immunosuppression, taking into account the physiological condition of this type of patient.

Graft rejection is the next challenge to solve in LT. An acceptable balance between immunosuppression and side effects is the sought-after end-point.

We now know the different mechanisms involved in rejection. Up till now we have only paid attention to the cellular rejection (mediated by T cells). Nowadays we also know that humoral rejection (mediated by antibody-anti HLA) influences the immediate and long term LT outcome.

One of the difficulties in this field is the current impossibility of performing the cross-match before surgery in order to not only select the ideal match, but also the amount of antigens carried by the transplanted graft.

An excellent revision is performed by Dr. J.M. Borro regarding the evolution of immune response mechanisms and the different therapeutic regimes currently in place,<sup>15</sup> although the immunosuppressive regime in LT is far from being a uniform practice. Induction treatment has increased in the last 8 years (with polyclonal antilymphocyte globulins at the beginning, converting to interleukin-2 receptor antagonists and alemtuzumab today). Induction with IL-2R is correlated with better long term outcomes, with a lower number of acute rejection episodes and delayed kidney lesions.<sup>16</sup> However, in 2010, only 50% of patients had some type of induction representing a clear drop in this practice (ISHLT 2012).<sup>14</sup> The majority of immunosuppressive treatments include three drugs: a calcineurin inhibitor, an anti-proliferative drug and steroids. In the long term immunosuppressive regime, trends are more prone to maintain tacrolimus plus mycophenolic acid although there are other possibilities such as cyclosporine or azatioprine.<sup>15,17</sup> Ideally, the immunosuppressive regime should be tailored to each patient.

Whilst infection is relatively common in the post-operative period, there is no consensus regarding the antibiotic prophylaxis. The use of double or triple antibiotic therapy immediately after the surgery is common, followed

by the introduction of antifungals<sup>18</sup> and any cytomegalovirus (CMV) prophylaxis. So far the length of treatment after LT has not been agreed upon.

Dr. J. Sacanell states, as a result of a survey fulfilled for the seven active LT programs in Spain, that the most frequent prophylactic antifungal used is inhaled amphotericin B, which changes with the appearance of bronchospasms to a second line antifungal. In that sense, anidulafungin is used as a preferred second line treatment, even though micafungin has provided greater efficiency against *Aspergillus* sp. and *Candida* sp.<sup>19</sup>

Finally, a different approach is offered by Dr. R. Vicente et al.<sup>20</sup> who considered the use of mechanical devices like extracorporeal membrane oxygenation (ECMO) which have created some expectation. ECMO could be used (and the results are acceptable) as a bridge to transplant (BTT)<sup>21</sup> in extremely ill patients who would otherwise die while awaiting a graft, or even in conscious patients who are on waiting list.<sup>22</sup> It is also used for management of primary graft dysfunction within the postoperative period, allowing physicians to sustain treatment and offer the possibility of survival to some patients while the graft is recovering.

It is important not to forget that LT is a relatively new field of transplant and consequently all technological and other advances are currently at the experimental stage. Much work and effort is still required by all the professionals involved.

## Conflict of interest

The authors have no conflict of interest to declare.

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