ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

Lung donor treatment protocol in brain dead-donors: A multicenter study

Eduardo Miñambres, MD, PhD,[a] Jose Miguel Pérez-Villares, MD, PhD,[b] Mario Chico-Fernández, MD, PhD,[c] Arturo Zabalegui, MD, PhD,[d] Jose María Dueñas-Jurado, MD,[e] Maite Misis, MD, PhD,[f] Fernando Mosteiro, MD,[g] Gil Rodriguez-Caravaca, MD, PhD,[h] and Elisabeth Coll, MD[i]

From the [a]Service of Intensive Care, University Hospital Marqués de Valdecilla-IDIVAL, Santander; [b]Service of Intensive Care, University Hospital Virgen de las Nieves, Granada; [c]Service of Intensive Care, University Hospital Doce de Octubre, Madrid; [d]Service of Intensive Care, University Hospital de Burgos, Burgos; [e]Service of Intensive Care, University Hospital Reina Sofía, Cordoba; [f]Service of Intensive Care, University Hospital Germans Trias i Pujol, Badalona; [g]Service of Intensive Care, Complexo Hospitalario Universitario A, Coruña, Coruña; [h]Departamento de Medicina Preventiva y Salud Pública, Universidad Rey Juan Carlos, Madrid; and the [i]Organización Nacional de Trasplantes, Madrid, Spain.

KEYWORDS:
brain-dead donor;
lung donor;
protocol;
multicenter study;
donor treatment;
outcome;
primary graft dysfunction

BACKGROUND: The shortage of lung donors for transplantation is the main limitation among patients awaiting this type of surgery. We previously demonstrated that an intensive lung donor-treatment protocol succeeded in increasing the lung procurement rate. We aimed to validate our protocol for centers with or without lung transplant programs.

METHODS: A quasi-experimental study was performed to compare lung donor rate before (historical group, 2010 to 2012) and after (prospective group, 2013) the application of a lung management protocol for donors after brain death (DBDs) in six Spanish hospitals. Lung donor selection criteria remained unchanged in both periods. Outcome measures for lung recipients were early survival and primary graft dysfunction (PGD) rates.

RESULTS: A total of 618 DBDs were included: 453 in the control period and 165 in the protocol period. Donor baseline characteristics were similar in both periods. Lung donation rate in the prospective group was 27.3%, more than twice that of the historical group (13%; $p < 0.001$). The number of lungs retrieved, grafts transplanted, and transplants performed more than doubled over the study period. No differences in early recipients' survival between groups were observed (87.6% vs 84.5%; $p = 0.733$) nor in the rate of PGD.

CONCLUSION: Implementing our intensive lung donor-treatment protocol increases lung procurement rates. This allows more lung transplants to be performed without detriment to either early survival or PGD rate.

J Heart Lung Transplant 2015;34:773–780

The shortage of grafts is a limitation for transplantation, making care of potential organ donors a critical issue. The lack of organ donors is most serious for patients awaiting lung transplantation, because lungs are harvested from only 10% to 20% of organ donors.[1,2]

Reprint requests: Eduardo Miñambres, MD, PhD, Service of Intensive Care Medicine, Hospital Universitario Marqués de Valdecilla, Avenida Marqués de Valdecilla s/n, E-39008 Santander, Spain. Telephone: +34-942-203304. Fax: +34-942-203543.

E-mail address: eminambres@yahoo.es

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2014.09.024

New options such as lungs from donation after cardiac death (DCD) and advances in normothermic ex vivo lung strategies have been proposed to expand the lung donor pool.[3–5] However, most of these strategies require major economic and technological resources and are not available at most centers.

The key to increasing the lung donor pool is to improve multiorgan donor treatment after brain death, and some investigators have put forward proposals for reducing the shortage of lung donors, such as ventilatory strategies, ventilator recruitment maneuvers, hormonal resuscitation and aggressive active medical management of potential lung donors.[6–8] Moreover, the use of invasive hemodynamic monitoring, such as extravascular lung water (EVLW) for monitoring lung edema at the bedside, has recently been proposed as a means of improving lung grafts available for transplantation.[9,10]

There are major differences in lung recovery rates between groups even in the same country, and this depends largely on how donors are managed after brain death.[11] The aim of management strategies should to maintain the overall stability of the donor and maximize the transplantability of as many organs as possible. The management of multiorgan donors after brain death (DBDs) should be approached as a global strategy requiring careful bedside management.[12] Our group recently showed in a single-center study that an intensive lung donor treatment protocol increased lung donation rates with no negative impact on early survival of lung recipients nor on the primary graft dysfunction (PGD) rate after lung transplant.[12]

The aim of this study was to confirm that this lung management protocol, based on a global strategy requiring attentive bedside management in all DBDs, could be easily implemented without the need for specific training. This protocol could increase the lung donation rate in centers with lung transplant programs (LTPs) and in smaller centers lacking an LTP, without impacting early survival and rate of primary graft dysfunction (PGD) in lung transplant recipients.

Methods

Design and study population

A quasi-experimental study was conducted to compare lung donation rates before and after implementation of the lung donor treatment protocol. The required sample size was 159 for each group (before and after protocol implementation), based on a 14% to 25% increase in lung donation rate with 90% confidence level and 80% statistical power. Six Spanish hospitals were selected, 3 with a LTP and 3 without it, on the basis of having >20 DBDs per year and a lung donation rate similar to the national (Spanish) rate.

All DBDs from 2010 to 2012 (historical group) and 2013 (prospective group) were included. In 2013, it was mandatory to follow the protocol in all DBD donors ≤70 years old with no absolute contraindications for lung donation.

Lung donor selection criteria remained unchanged in both periods, no lung donors had radiographically visible infiltrates, and bronchoscopy showed no evidence of copious purulent secretions or aspiration. A relation between arterial oxygen pressure and inspiration oxygen fraction (PaO_2/FIO_2) of <300 mm Hg at the beginning of management did not exclude initiation of the protocol. Low oxygenation discarded lung donation only in theater just before graft recovery.

In both periods, lungs were offered by the Spanish National Transplant Organization (ONT) for procurement to all Spanish lung transplant programs, which made the final decision on the suitability of the lungs.

PGD was defined according to the International Society for Heart and Lung Transplantation.[13]

The ethics committees of all hospitals approved the protocol.

Lung donor treatment

The lung donor treatment protocol (Table 1), which requires no specific prior training, was sent to the centers. Donor fluid balance was clinically assessed and administration of diuretics was recommended, if necessary, to maintain a neutral or negative fluid balance after brain-death was declared. Cardiac output was measured by the arterial pulse curve with a PICCO catheter (Pulsion Medical Systems SE, Munich, Germany), with a target value of EVLW < 10 ml/kg and central venous pressure (CVP) ≤ 8 mm Hg for the lung donors.

Donor management continued until graft recovery and only abandoned if PaO_2/FIO_2 < 300 mm Hg after 3 hours.

Data analysis

A descriptive analysis of the sample was performed, with the results presented as absolute numbers and percentages for categorical variables and as measures of central tendency and dispersion for continuous variables. The main outcome studied was the difference in lung donation rate between the two periods. Number of lungs recovered and implanted, lung transplants performed, and short-term results in lung recipients were also analyzed (30-day survival rate and primary graft dysfunction).

The chi-square test was used for comparisons of categorical variables. For continuous variables, Student's *t*-test, Mann–Whitney *U*-test or median tests were used, according to sample distribution and Kolmogorov–Smirnov normality test. The paired sample *t*-test was used to evaluate protocol parameters over the donation process

Table 1 Lung Donor Management Protocol

1. Apnea test performed with ventilator (continuous positive pressure mode).
2. Mechanical ventilation with PEEP 8–10 cm H_2O and tidal volume 6–8 ml/kg.
3. Recruitment maneuvers once per hour and after any disconnection from the ventilator.
4. Bronchoscopy with bilateral bronchoalveolar lavage immediately after brain death.
5. Hemodynamics closely monitored with PICCO system; goal EVLW <10 ml/kg (with administration of diuretics if necessary) and CVP (objective) <8 mm Hg.
6. Methylprednisolone (15 mg/kg) after brain-death declaration.
7. Alveolar recruitment with controlled ventilation (plateau pressure limit of 35 mm Hg) with PEEP of 18–20 cm H_2O for 1 minute and decreasing by 2 cm H_2O each minute; then increasing 50% tidal volumes for 10 breaths.
8. In those lung donors with PaO_2/FIO_2 <300 mm Hg, semi-lateral decubitus position plus recruitment maneuvers.

CVP, central venous pressure; EVLW, extravascular lung water; PEEP, positive end-expiratory pressure.