# Pulmonary Recruitment Protocol For Organ Donors: A New Strategy to Improve the Rate of Lung Utilization

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ABSTRACT

Because lung transplantation is the only effective therapy for terminal respiratory failure, the demand for donor lungs has increased steadily. However, the number of donors has remained fairly constant over the years, which results in an increasing duration of waiting for lung transplantation. To overcome the lack of organs, various strategies have been developed by transplant centers including use of marginal donors. To increase the lung utilization rate in multiorgan donors, we implemented a simple lung recruitment protocol involving a brief period of controlled sustained inflation. In 2005, the lung utilization rate in the transplant program at our institution was only 20% in multiorgan donors. With the lung recruitment protocol, the rate of lung utilization for transplantation increased to 33%, in 2006, 24% in 2007, and 24% in 2008. Following the lung recruitment protocol, the arterial oxygen tension/fraction of inspired oxygen ratio increased to greater than 15% in more than 40% of donors. We were able to improve gas exchange sufficiently that as many as two-thirds of the lungs were suitable for transplantation. During the protocol, no complications were reported, and no patient became hemodynamically unstable, precluding organ procurement. We believe that optimization of multiorgan donor management with simple interventions may improve oxygenation, reducing the number of inadequate donor lungs and increasing the overall donor pool and organ availability.

LUNG TRANSPLANTATION dates to 1963 when Dr. James D. Hardy performed the first transplantation procedure in a 58-year old patient, who died 18 days postoperatively of renal failure. During the next 2 decades, only 40 lung transplant procedures were performed, with poor results and due to early death organ dysfunction, acute rejection, and anastomotic complications. Outcome, however, has improved progressively as a result of better donor and recipient selection, organ preservation, immunosuppressive drugs, and surgical techniques. The successful transplant outcomes reported by workers at Stanford University and at the University of Toronto in the early 1980 s marked the beginning of the modern era of lung transplantation. With growing experience worldwide, lung transplantation has become a successful established treatment for a variety of end-stage lung diseases.

## BACKGROUND

### Lung Transplantation and Limited Donor Pool

The number of centers reporting lung transplantation had been relatively stable to 1997; however, annual activity has increased by 47% since 1999, with the number of procedures reaching a high of 2169 in 2005.[1] Over the past decade, however, the number of patients on the waiting list has increased progressively and now far exceeds the number of available organs.[1] In the United States, the number of candidates on the lung transplant waiting list increased by 11% from 1997 to 2006.[2] Time on the waiting list for a lung has almost doubled in the United States, and some centers

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in Europe have reported that as many as 50% of patients awaiting transplantation die while on the waiting list.[3,4] With more than 92,000 patients on the waiting list for organ transplantation in the United States in 2005, on average 17 will die each day. Thus, it seems that the low rate of increase in available organs for transplantation cannot close the gap between demand and supply.[5] As therapy for end-stage pulmonary disease, lung transplantation is limited by the supply of suitable donor lungs.[6]

### Optimization and Use of Currently Available Lung Donors

A variety of initiatives in the last several years have been successful in increasing the supply of organs for transplantation. Much of the growth in organ donation has coincided with the establishment of the National Organ Donation Breakthrough Collaborative at the request of the Secretary of the US Department of Health and Human Services. Created in 2003, the Collaborative has made a formal concerted effort to improve the organ donation system by bringing together the donation and transplantation communities.[2,5]

A number of strategies have been advocated to increase the number and access to lung donors. Some centers have developed living related donor programs; others have focused on xenotransplantation to ultimately make up for the insufficient number of donors.[4] To further expand the donor pool, some transplant centers have recently begun to use lungs retrieved from donors after circulatory arrest, so-called donation after cardiac death (DCD) or non–heart beating donors.[7–10] Clinical application of DCD lung transplantation has been under investigation during the last decade, and results from early studies are encouraging. Lungs from DCD donors demonstrate good tolerance to warm ischemia because of their low metabolic requirements when the alveoli are filled with well-saturated blood and oxygen.[7,11,12] Although only a limited number of DCD lung transplantation procedures have been performed worldwide, early survival seems to be similar to or slightly better than those with brain-dead donors.[8]

The persistent organ shortage has led to renewed interest in evaluating the available lung donor pool. The most commonly used selection criteria for lung donors were developed in the early era of lung transplantation, and they generally apply only to ideal donors. These criteria, which are based on personal and group experiences, are largely arbitrary and not based on rigorous scientific evidence.[4] Tremendous efforts have been made to improve donor management and to expand the selection criteria to so-called extended and marginal lung donors. Liberalization of lung donor selection criteria has resulted in substantial expansion of the pool of donor lungs without negatively affecting postoperative morbidity and mortality.[4,13,14] Indeed, short-term and long-term outcomes from such donors are still being evaluated, quantified, and cross-compared. Results with respect to postoperative graft function and survival seem to be acceptable.[6,15] Even though the use of extended donor lungs does not fully resolve the problem of the limited organ supply, it seems that the use of only lung donors who meet standard criteria excludes a considerable number of lungs that are potentially suitable for transplantation without compromising the outcome of the surgery.[13,16] Some groups, however, have cautioned that there may be increased early deaths and primary graft dysfunction with the use of extended criteria donors in lung transplantation.[14,17,18]

### Better Management of Donors for Lung Transplantation

Brain death is associated with numerous events that may complicate and interfere with the management of multiorgan donors, leading to progressive organ deterioration that precludes organ transplantation or resulting in early graft dysfunction.[4] Mechanisms contributing to organ deterioration include fluid overload, hemodynamic instability, endocrine failure, nephrogenic diabetes insipidus, inflammatory response, arrhythmias, hypothermia, coagulopathy, and infection.[4] Proper management of unstable donors is crucial to maintaining good hemodynamics and organ perfusion that helps to optimize organ recovery. The active resuscitation of lungs before retrieval to reverse poor organ function has been extensively described; even ex vivo lung evaluation resuscitation has been advocated.[6,7]

In potential lung donors, endobronchial suctioning should be performed regularly, and bronchoscopy performed to assess the airways and remove any mucus plugs. A pulmonary recruitment maneuver is recommended to prevent atelectasis and to maintain open alveoli to improve gas exchange, especially after the apnea test. Proper management of the ventilator is critical to keep the function of inspired oxygen ($Fio_2$) as low as possible to reduce oxygen toxicity. Partial end-expiratory pressure (PEEP) should be maintained between 5 and 10 cm $H_2O$ to prevent barotrauma and ventilator-induced lung injury. Improved partial arterial oxygen tension ($Pao_2$) from a low baseline value is almost always encouraging, whereas worsening $Pao_2$ in the setting of pulmonary edema or pulmonary infection may preclude lung harvesting.[4]

Our center is the only lung transplantation center in the Province of Quebec. In 2006, we initiated a pulmonary recruitment protocol to improve gas exchange in potential lung donors with low baseline $Pao_2$ to optimize organ utilization. The objective of the present study was to report our early experience with our newly implemented protocol. We believe that better management of potential lung donors with a simple lung recruitment protocol might help to overcome the donor shortage without jeopardizing allocation of other organs from multiorgan donors. We describe herein our current protocol and the results of consecutive lung transplant procedures performed at our institution.

## PULMONARY RECRUITMENT PROTOCOL

Our lung transplantation program was created in 1997. Since then, we have performed more than 300 lung trans-

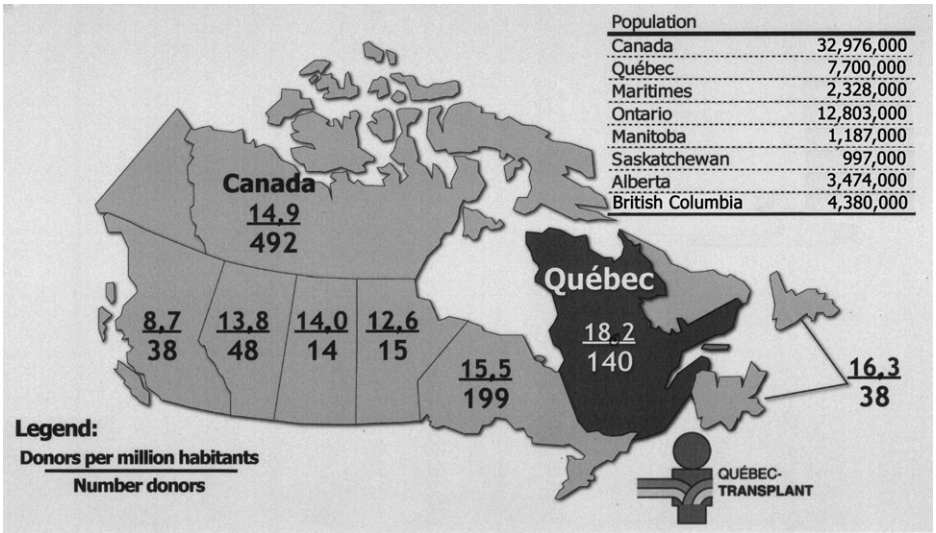


**Fig. 1.** Number of brain-dead donors in each province in Canada per million population and number of multiorgan donors in 2007. The ratio of donors per million population in Quebec was 18.2, for a total of 140 donors, the highest rate for Canada.

plantations. Our lung transplantation center is the only program serving the Province of Quebec, with 8 million inhabitants and a vast territory nearly 3 times the size of France or Texas. Québec-Transplant is the sole provincial organization responsible for coordinating organ donation, allocation, and procurement in Quebec (Fig. 1). Organs are allocated to transplant programs in Quebec but may be shared with other provinces and transplant centers in Canada and the United States.

The management of multiorgan donors is performed in the intensive care unit by a dedicated intensivist. Once an individual has been identified as a potential lung donor, hemodynamics are managed to reduce central venous to a level pressure as low as possible while maintaining adequate tissue perfusion. Our selection criteria for lung donors were reviewed in 2003 (Table 1). Proper pulmonary management is mandatory to preserve oxygenation and integrity of the organ and also to reduce atelectasis and prevent ventilator-induced lung injury. Our lung recruitment protocol relies on increased PEEP for a short time to reduce failure from expansion or closure of lung alveoli. The protocol is applied to al multiorgan donors unless the lungs are not being considered for other reasons, for example, the donor is hemodynamically unstable, the $Pao_2$ >400 mm Hg with $Fio_2$ 100%, or presence of pneumothorax (Table 2).

## RESULTS

Since 2001, the number of multiorgan donors in Quebec has varied from 127 in 2002 to a maximum of 151 in 2008 (Fig. 2). During the same period, the number of patients with end-stage lung disease awaiting transplantation increased from 53 to 82. However, despite the increased demand, the number of available organs and of lung transplantation procedures have not increased sufficiently to meet demand. Although 25 to 30 transplantation procedures were being performed annually, 6 to 16 patients died each year, representing mean mortality of 28% on the waiting list (Fig. 2).

The interval between the indication for lung transplantation and the surgery (i.e., time on the waiting list) varied from a mean of 350 days to 547 days (data not shown). In 2003, we revised our selection criteria to include more marginal or extended-criteria lung donors to improve organ supply. As our use of extended-criteria donor lungs increased, we observed a slight decrease in mean $Pao_2$ over the years (Fig. 3). The age of lung donors did not change ranging from 37 to 44 years (Fig. 3). During the same period, mean (SD) age of multiorgan donors in Quebec was 47.9 (18.9) years (data not shown).

In 2006, the protocol for lung recruitment was initiated. Before implementation of this protocol, only 20% of mul-

**Table 1. Revised Selection Criteria for Lung Donation**

| Variable | 1997–2003 | SCD | Marginal/ECD |
|---|---|---|---|
| Criteria | | | |
| Age, y | <55 | <60 | 60–70 |
| $Pao_2$, mm Hg | >400 | >300 | 200–300 |
| Smoking history, pack-years | <20 | <20 | 20–30 |
| Chest radiographic findings | Normal | Unilateral infiltrate | Bilateral infiltrate, pneumonia, contusion |
| Bronchoscopic findings | Normal | Secretions | Secretions, blood, pus |
| Additional criteria | | No lung disease, no thoracic trauma | Thoracic trauma, extrathoracic sepsis, hepatitis C |

Abbreviations: ECD, extended-criteria donor; $Pao_2$, partial arterial oxygen tension; SCD, standard criteria donor.

**Table 2. Lung Recruitment Protocol**

| |
|---|
| Optimize ventilator settings (tidal volume, rate, pressure) |
| Baseline blood gas obtained with $Fio_2$ 100%; PEEP, 5 cm $H_2O$ |
| Initiate recruitment maneuver |
| 30 seconds of sustained inflation at 30 cm $H_2O$ |
| Hemodynamics closely monitored to prevent hypotension or decreased organ perfusion |
| 2 minutes of normal ventilation |
| 30 seconds of sustained inflation at 30 cm $H_2O$ |
| 1 hour of normal ventilation, $Fio_2$ 40%; PEEP, 10 cm $H_2O$; peak pressure <30 mm Hg |
| Blood gas postrecruitment is obtained with $Fio_2$ 100%; PEEP, 5 cm $H_2O$ for 20 minutes |
| After blood gases are assessed, $Fio_2$ is decreased to <50% |

tiorgan donors ultimately had lungs suitable for transplantation to be shared by our program and other centers. With the lung recruitment protocol, the rate of lung utilization for transplantation increased to 33% in 2006, 24% in 2007, and 24% in 2008 (Table 3). With the lung recruitment protocol, the $Pao_2/Fio_2$ ratio increased to greater than 15% in more than 40% of donors; however, oxygenation deteriorated from 7% to 26% (Table 3). We were able to improve gas exchange sufficiently that as many as two-thirds of the lungs were suitable for transplantation after recruitment. No patient became hemodynamically unstable during the procedure, and no situation precluded organ procurement in the donor.

## DISCUSSION

Over the years, organ donor availability has continued to be a serious problem in Quebec, with a relatively stable pool of potential suitable organs averaging 140 donors for about 8 million population. While the demand for transplantation in patients with end-stage lung disease has increased dramatically, the insufficient supply of donor lungs has resulted in prolonged time on the waiting list, with a substantial number of deaths. The demand for donor lungs clearly exceeds the availability in Quebec, and each year, many of our patients with severe lung disease (28%) awaiting transplantation die before an organ becomes available.

To overcome the donor shortage in Quebec, we initiated a simple, efficient lung recruitment protocol to improve oxygenation, rate of lung procurement, and the number of transplantation procedures. We successfully implemented this lung recruitment protocol, increasing the rate of lung utilization in our multiorgan donors up to 33% in 2006, which surpasses the 20% mean rate reported in the literature.[14,15,17] Blood gases revealed significant improvement in the $Pao_2/Fio_2$ ratio in nearly 50% of patients after lung recruitment, and as many as two-thirds of these donor lungs were used for transplantation.

The lung has always been considered a frail organ, sensitive to damage as part of the disease process or injury that leads to donor death, as a result of resuscitation maneuvers, or as complications of a prolonged intensive care unit stay with endotracheal intubation, nosocomial pneumonia, aspiration, or pulmonary embolism.[6,17] Many potential donor lungs are not harvested because they fail to meet predetermined clinical selection criteria. These criteria help determine the function and viability of the organs while still in the donor; however, there is no absolute evidence that they provide a useful guide as to how the graft will function after implantation.[3] It is

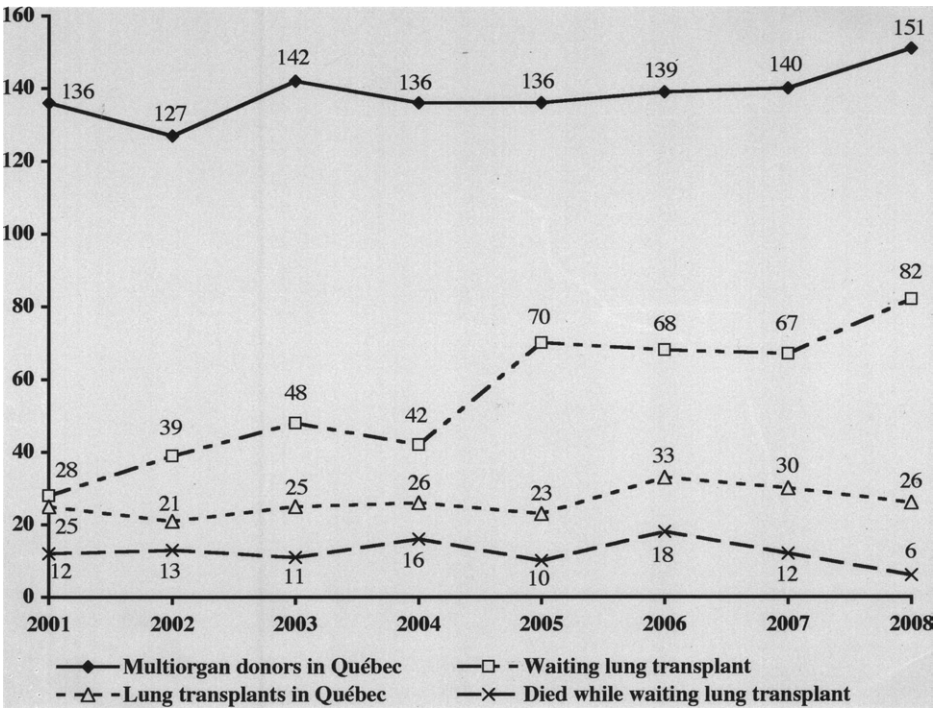


**Fig. 2.** Number of multiorgan donors in Quebec, number of lung transplantations in Quebec, number of lung recipients on waiting list, and number of patients who died while on waiting list.

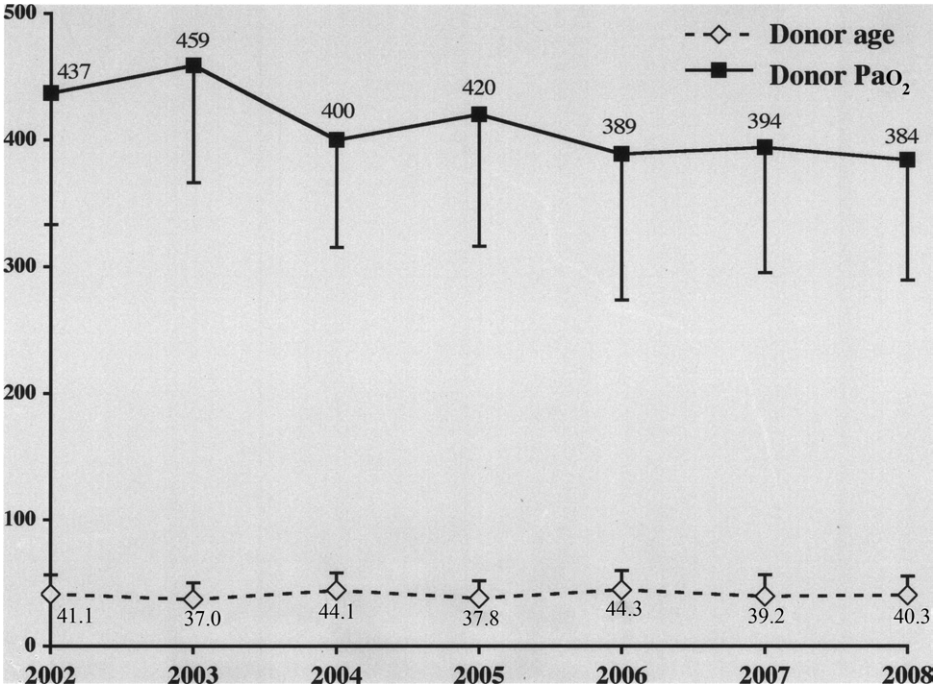


**Fig. 3.** Donor age and $Pao_2$ with $Fio_2$ 100%. Data given as mean (SD).

estimated that 70% to 85% of lungs from multiorgan donors are not suitable for lung transplantation.[7] In the United States in 2006, 2360 of 13,154 lungs (18%) from organ donors were transplanted, compared with 88% of kidney.[2,6,7]

Over the last years, a number of strategies have been described to increase the number of lung donors. With growing experience, lung donor selection criteria have been progressively liberalized, with encouraging results.

A number of events associated with brain death can seriously complicate the management of multiorgan donors and eventually result in organ deterioration. There have been tremendous efforts by several groups to improve pulmonary management in potential donors and to increase the number of suitable lungs for transplantation. The concept of the lung recruitment protocol involves the use of sustained inspiratory inflation for a short period followed by increased PEEP, to open the distal alveoli, reduce atelectasis, and improve oxygenation. We report use of a simple method of lung recruitment with intermittent 30-second periods of sustained inflation at 30 cm $H_2O$. It is crucial to maintain positive pressure ventilation with PEEP of 5 to 10 cm $H_2O$ to prevent further atelectasis. Hemodynamics are closely monitored, the oxygen concentration is kept at a minimum to prevent toxicity, and arterial blood gas values are determined regularly to monitor lung function and adjust ventilator settings.

**Table 3. Lung Recruitment Protocol Performed in Multiorgan Donors Before Transplantation***

| Variable | Year | | |
|---|---|---|---|
| | 2006 | 2007 | 2008 |
| No. of multiorgan donors | 139 | 140 | 151 |
| No. of lung transplantations procedures | 46 | 33 | 36 |
| Rate of lung utilization, % | 33 | 24 | 24 |
| Lung recruitment protocol, no. (%) | 29 | 23 | 17 |
| $Pao_2/Fio_2$ ratio | | | |
| >15% Improvement | 14 (48.3) | 10 (43.5) | 7 (41.2) |
| >15% Deterioration | 2 (6.9) | 6 (26.1) | 3 (17.7) |
| No change | 13 (44.8) | 7 (30.4) | 7 (41.2) |
| Organ transplanted postrecruitment, no. (%) | 19 (65.5) | 9 (39.1) | 7 (41.2) |

*Number of multiorgan donors in Québec province, and number of lung transplantations performed in Québec and other programs combined from Québec lung donors.

In conclusion, we believe the use of better perioperative lung donor evaluation and management improves oxygenation and gas exchange, reducing the number of truly inadequate donor lungs and increasing the overall donor pool. Our simple protocol of lung recruitment with a brief period of controlled sustained inspiratory inflation followed by increased PEEP reduces atelectasis and improves $Pao_2$ with increased odds of accepting lungs for transplantation. This lung recruitment protocol may be repeated as needed. In our experience, it never resulted in significant hemodynamic changes that preventing harvesting of lungs or other organs. We suggest inclusion of this strategy as part of a standard protocol for the management of lung transplantation donors.

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