

# Airway Pressure Release Ventilation and Successful Lung Donation

Kenny Hanna, MD; Christopher W. Seder, MD; Jeffrey B. Weinberger, MD; Patty A. Sills, RN; Michael Hagan, MD; Randy J. Janczyk, MD

**Hypothesis:** Donor management with airway pressure release ventilation (APRV) improves oxygenation and increases lung donation while maintaining equivalent graft survival.

**Design:** Retrospective case series.

**Setting:** Private, tertiary care, level I trauma center.

**Patients:** Forty-five consecutive organ donors.

**Interventions:** Management with assist/control ventilation (ACV) or APRV.

**Main Outcome Measures:** Demographic characteristics, medical history, mode of brain death, and partial pressure of arterial oxygen (PaO<sub>2</sub>)/fraction of inspired oxygen (FiO<sub>2</sub>) ratios on admission and after 100% oxygen challenge, percentage of lungs transplanted, and graft survival.

**Results:** Twenty potential donors were managed with ACV and 25 were managed with APRV during the study

period. The APRV patients were younger than the ACV patients (mean [SD] age, 34 [11] vs 41 [12] years, respectively;  $P = .05$ ). Otherwise, there was no difference between the ACV and APRV groups with respect to demographic characteristics, medical history, or mode of brain death. Although the ACV and APRV groups had similar PaO<sub>2</sub>/FiO<sub>2</sub> ratios on admission and the mean time on the ventilator was the same, the APRV group had a higher PaO<sub>2</sub>/FiO<sub>2</sub> ratio than the ACV group (mean [SD], 498 [43] vs 334 [104] mm Hg, respectively;  $P < .001$ ) after 100% oxygen challenge. The ACV group ultimately donated 7 of 40 potential lungs (18%) compared with 42 of 50 potential lungs (84%) in the APRV group ( $P < .001$ ). There was no difference in the number of other organs per donor procured from the 2 groups. Survival of grafts managed with both APRV and ACV compared favorably with national averages.

**Conclusion:** The use of APRV prior to procurement may increase the rate of successful lung donation.

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**A**PPROXIMATELY 2000 patients are currently on the lung transplantation waiting list in the United States. The median time spent on the waiting list prior to transplantation is almost 3 years. In 2005, only 16.9% of potential organ donors donated lungs. That year, more than 400 patients on the waiting list died without a transplant or became too sick to withstand an operation.<sup>1</sup>

Consistent with the national trend, our institution historically had a low rate of lung donation. No lungs were accepted for donation in 2003. Furthermore, of the 40 potential pulmonary allografts in 2004 and 2005, fewer than 20% were accepted. Most of the lungs were rejected owing to a low partial pressure of arterial oxygen (PaO<sub>2</sub>) after 100% fraction of inspired oxygen (FiO<sub>2</sub>) challenge. During this period, assist/control ventilation (ACV) was routinely

used to manage potential organ donors. The low rate of lung donation at our institution as a result of low PaO<sub>2</sub> prompted us to evaluate an alternative mode of ventilation for the management of potential organ donors.

Airway pressure release ventilation (APRV) was first used by Stock et al<sup>2</sup> in 1987 as continuous positive airway pressure with an intermittent pressure release phase. It is a pressure-limited, time-cycled, volume-variable mode of ventilation. Continuous airway pressure is applied to maintain adequate lung volume and improve alveolar recruitment. The addition of a time-cycled release phase allows for carbon dioxide removal.<sup>3</sup> Alveoli remain inflated at the inspiratory pressure for most of the respiratory cycle, which allows for a higher mean airway pressure at lower peak airway pressures. Airway pressure release ventilation produces similar or improved oxygenation

**Author Affiliations:** Division of Trauma and Critical Care, Department of Surgery, William Beaumont Hospitals, Royal Oak (Drs Hanna, Seder, Weinberger, and Janczyk and Ms Sills), and Gift of Life Michigan, Ann Arbor (Dr Hagan), Michigan.

**Table. Demographic Characteristics of Potential Lung Donors Between 2003 and 2008**

Characteristic	APRV (n=25)	ACV (n=20)	P Value
Male, No. (%)	12 (48)	9 (45)	.77
Age, mean (SD), y	34 (11)	41 (12)	.05
Trauma, No. (%)	18 (71)	7 (35)	.54
EBD, No. (%)	19 (76)	15 (75)	.43
Smoker, No. (%)	11 (43)	11 (55)	.75
Smoking history, mean (SD), pack-years	12 (18)	6 (12)	.30
PaO <sub>2</sub> /Fio <sub>2</sub> ratio at admission, mean (SD), mm Hg	272 (127)	334 (128)	.12
Ventilator time, mean (SD), h	34 (11)	41 (12)	.86

Abbreviations: ACV, assist/control ventilation; APRV, airway pressure release ventilation; EBD, explosive brain death; Fio<sub>2</sub>, fraction of inspired oxygen; PaO<sub>2</sub>, partial pressure of arterial oxygen.

with lower peak airway pressures with no significant hemodynamic effects compared with alternative modes of ventilation in neonatal, pediatric, and adult populations.<sup>4-10</sup> Based on these studies and our institution's low rate of lung donation, we changed our ventilatory strategy for potential organ donors from ACV to APRV. In this study, we retrospectively reviewed and stratified potential lung donors according to ventilatory mode. We hypothesized that the use of APRV in potential organ donors would improve PaO<sub>2</sub>/Fio<sub>2</sub> ratios and thus increase our rate of lung donation without compromising graft survival.

## METHODS

After approval by the William Beaumont Hospitals Institutional Review Board, data were retrospectively collected on all potential organ donors between January 1, 2003, and December 31, 2008, at a private, tertiary care, 1061-bed, level I trauma center. In 2004, we transitioned from strictly using ACV to the intermittent use of APRV for potential organ donors. The mode of ventilation used was determined by the surgical intensivist caring for the individual donor. All patients were managed using 840 ventilators (Mallinckrodt, Inc, Hazelwood, Missouri). Patients managed with ACV were placed on initial ventilator settings of 10 to 12 breaths/min, with a tidal volume of 5 to 10 mL/kg, Fio<sub>2</sub> of 0.4, positive end-expiratory pressure of 5 cm H<sub>2</sub>O, and pressure support of 4 cm H<sub>2</sub>O. Those managed with APRV were initially placed on a release rate of 6 to 10 breaths/min, an inspiratory pressure of 20 to 25 cm H<sub>2</sub>O, and an Fio<sub>2</sub> of 0.4. The ventilators were adjusted as deemed appropriate by the intensivist caring for the patient. Apart from the incorporation of APRV, no other changes in the overall management strategy for potential organ donors were made during the study period.

The medical records of all organ donors during the study period were abstracted and stratified by mechanical ventilatory mode. Exclusion criteria included not meeting standard lung donor criteria: being younger than 55 years, ABO blood group compatibility, clear chest radiograph, less than a 20-pack-year tobacco history, PaO<sub>2</sub> greater than 300 mm Hg on an Fio<sub>2</sub> of 1.0 and positive end-expiratory pressure of 5 cm H<sub>2</sub>O, absence of chest trauma, aspiration, or sepsis, and lack of bacteria, fungus, or leukocytes in sputum. Demographic variables examined included age, sex, smoking history, admission diagnosis of trauma, and mode of brain death (explosive vs nonexplosive brain death). Explosive brain

death was defined as traumatic brain death that resulted from a gunshot wound to the head, head trauma, or an intracranial bleed that rapidly progressed to brain death. Potential donors managed with ACV were compared with those managed with APRV with respect to PaO<sub>2</sub>/Fio<sub>2</sub> ratios at intensive care unit admission and following 100% oxygen challenge, time on ventilator prior to organ procurement, number of organs procured, and graft survival. The 100% oxygen challenges were carried out by obtaining an arterial blood gas sample after 45 minutes on an Fio<sub>2</sub> of 100%. The decision to procure individual organs was made by the intended recipient's transplantation team. These teams always came from another institution because our hospital is not a transplant center for lungs. All graft survival data were obtained from Gift of Life Michigan and are current through September 1, 2009. Graft survival was defined as recipient survival without retransplantation.

The ACV and APRV groups were compared using *t* tests and  $\chi^2$  tests as appropriate. *P* < .05 was considered statistically significant. We used SAS version 9.1.3 statistical software (SAS Institute, Inc, Cary, North Carolina) for all analyses.

## RESULTS

During the study period, 20 potential donors were managed with ACV and 25 were managed with APRV. The APRV patients were younger than the ACV patients (mean [SD] age, 34 [11] vs 41 [12] years, respectively; *P* = .05); however, there was no difference between the groups with regard to sex, percentage admitted for trauma, mode of brain death, or smoking history prior to organ donation (**Table**). The ACV and APRV groups had similar PaO<sub>2</sub>/Fio<sub>2</sub> ratios on admission to the surgical intensive care unit (mean [SD], 334 [128] vs 272 [127] mm Hg, respectively; *P* = .12). Although time spent on the ventilator prior to donation was similar between groups (mean [SD], 41 [12] hours for the ACV group vs 34 [11] hours for the APRV group; *P* = .86), APRV patients had a higher PaO<sub>2</sub>/Fio<sub>2</sub> ratio following 100% oxygen challenge than ACV patients (mean [SD], 498 [43] vs 334 [104], respectively; *P* < .001) (**Figure 1**). The ACV group donated 7 of 40 potential lungs (18%) and the APRV group donated 42 of 50 potential lungs (84%) (*P* < .001). Twenty of the 33 unacceptable lungs in the ACV group were rejected for low PaO<sub>2</sub>/Fio<sub>2</sub> ratio, 4 for hemodynamic instability, 2 for positive sputum cultures, 2 for pulmonary infiltrates, 2 for aspiration, 2 secondary to intraoperative time constraints by the heart team, and 1 for poor vascular flush. In the APRV group, 8 lungs were not accepted for donation. Five were rejected for low intraoperative PaO<sub>2</sub>, 1 for aspiration, and 2 secondary to time constraints by the cardiac procurement team. There were means of 3.8 extrapulmonary organs donated per patient in the ACV group and 3.5 in the APRV group (*P* = .91).

During the study period, 49 lungs from our institution were successfully transplanted. Five of 7 grafts (71%) managed with ACV were alive at a mean follow-up of 42 months. Ten of 11 grafts (91%) managed with APRV and transplanted between January 1, 2003, and December 31, 2005, were alive at a mean follow-up of 36 months. Our graft survival compares favorably to the Organ Procurement and Transplantation Network (OPTN) 36-month survival data for lung recipients aged 12 years or older (91% for APRV grafts and 71% for ACV grafts vs 64% for OPTN; *P* = .13) (**Figure 2**). Among recipients of APRV

lungs donated between January 1, 2006, and December 31, 2008, 29 of 31 grafts (94%) were alive at a mean follow-up of 12 months. These rates also compare favorably with the OPTN 12-month survival statistics (94% for APRV grafts vs 82% for OPTN;  $P = .19$ ).<sup>1</sup> One recipient of an APRV lung died 3 months after transplantation, of complications of a second lung transplant. The cause of the initial graft failure is unknown. The other 2 APRV patients died of cardiac complications unrelated to lung transplantation.

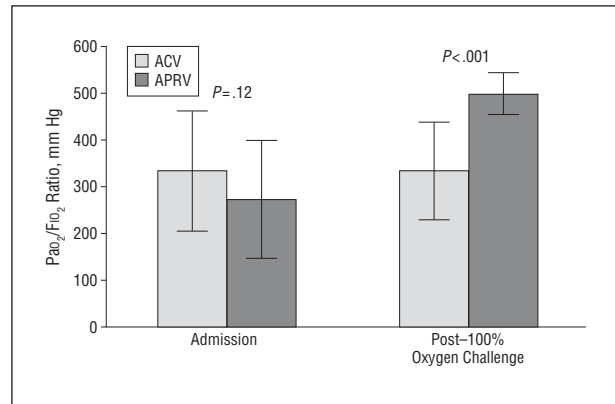
## COMMENT

The utilization rate for donated lungs continues to be low, with only about 15% of all potential lungs accepted for transplantation.<sup>11</sup> The reasons for this are multifactorial. Lungs are exceedingly sensitive to the rigors of procurement and transplantation. In an effort to maintain kidney viability, aggressive fluid resuscitation can lead to pulmonary edema and inability to transplant the lungs. Furthermore, aspiration pneumonitis, pulmonary contusions, or a substantial smoking history may result in poor pulmonary function that precludes donation.<sup>12,13</sup> In addition, atelectasis and surfactant loss must be minimized, which often proves to be a difficult task.<sup>14</sup> Ventilatory mode, a variable under the control of the medical team, may also be a factor in successful lung donation.<sup>15</sup>

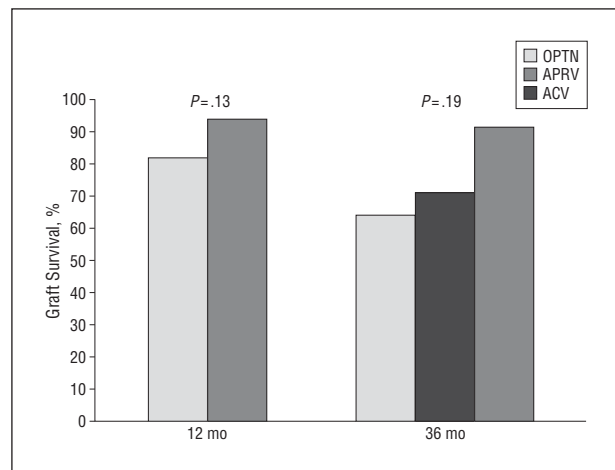
Airway pressure release ventilation is a technique of open lung ventilation that has been successfully used in a variety of patient populations. It has demonstrated effectiveness in the management of routine ventilated patients as well as those with severe acute lung injury and respiratory distress syndrome.<sup>16</sup> In our study, APRV increased the  $\text{PaO}_2/\text{FIO}_2$  ratio to a greater degree than ACV in lung donors meeting standard criteria. The dramatic improvement in oxygenation in the APRV group is likely a result of improved alveolar recruitment and resolution of pulmonary atelectasis. By maintaining a high mean airway pressure, APRV overcomes the critical opening pressure of the quiescent alveoli without the shear stress and barotrauma associated with ACV. The use of APRV maximized the donors'  $\text{PaO}_2/\text{FIO}_2$  ratio and seemingly revealed their lungs' true potential for gas exchange.

In our study, both donors and nondonors met the  $\text{PaO}_2/\text{FIO}_2$  standard criteria for lung donation on admission and after 100% oxygen challenge. However, studies have demonstrated a significant increase in the relative risk of death when the donor  $\text{PaO}_2/\text{FIO}_2$  ratio falls below 350 mm Hg.<sup>17</sup> In addition, it has been our experience that transplant centers prefer a  $\text{PaO}_2/\text{FIO}_2$  ratio greater than that required by the standard lung donor criteria when evaluating organs for transplantation. This bias may explain why 20 of our potential donors were rejected for a low  $\text{PaO}_2/\text{FIO}_2$  ratio despite meeting the standard lung donation criteria.

Our data suggest that the transition from ACV to APRV may have led to an improvement in  $\text{PaO}_2/\text{FIO}_2$  ratios at our institution. We attribute the concurrent rise in the rate of lung donation to this increase in oxygenation. In addition, grafts donated from APRV and ACV patients have demonstrated posttransplant survivals that compare favorably with national averages. This suggests that



**Figure 1.** Partial pressure of arterial oxygen ( $\text{PaO}_2$ )/fraction of inspired oxygen ( $\text{FIO}_2$ ) ratios on admission to the intensive care unit and following 100% oxygen challenge. ACV indicates assist/control ventilation; APRV, airway pressure release ventilation; and error bars, standard deviation.



**Figure 2.** Survival of grafts managed with airway pressure release ventilation (APRV) at 12 months and 36 months and assist/control ventilation (ACV) at 36 months compared with national data from the Organ Procurement and Transplantation Network (OPTN).

APRV does not falsely elevate oxygenation levels, but instead it demonstrates the lungs' true potential for gas exchange. Perhaps a more aggressive ventilatory approach to potential donors by transplant centers would increase the number of successful lung transplantations. While APRV was the vehicle used in this study, other methods of increasing lung donation have been used with success. Serial bronchoscopy, the use of naloxone hydrochloride, and recruitment maneuvers in potential donors have also led to improvements in  $\text{PaO}_2/\text{FIO}_2$  ratios and lung donation.<sup>18-20</sup>

Of the 90 potential donor lungs (40 from the ACV group, 50 from the APRV group), 2 ACV lungs and 1 APRV lung were rejected secondary to aspiration (3 of 90 lungs [3%]). These 3 lungs came from 2 patients, both of whom had severe head trauma and aspirated prior to arrival in our surgical intensive care unit. One of the patients sustained a transoral gunshot wound with massive oropharyngeal tissue destruction, making aspiration nearly unavoidable prior to intubation. Maintaining high endotracheal cuff pressures and performing frequent bronchoscopies can be useful in minimizing aspi-

ration and its sequelae. This loss of donor lungs highlights the importance of obtaining and maintaining a secure airway in trauma patients, especially in those with neurologic injury or those who lack a cough reflex.

In our study, 4 lungs were not procured owing to intraoperative time constraints by the heart team. As our institution does not perform cardiac or lung transplantation, the maximal allocation of organs is dependent on the coordination of the intended recipients' procurement teams. This often includes multiple teams traveling from different centers. In 2 instances (4 lungs), the visiting cardiac transplantation team deemed the urgent need for cardiac procurement sufficient to proceed prior to the arrival of the pulmonary procurement team. Clearly, the efficient allocation of organs is dependent on the coordination of the intended recipients' transplantation teams and every attempt should be made to coordinate efforts.

Our study has potential limitations. Like all retrospective series, these data are subject to selection bias. Early in the study period, we noticed that the intermittent use of APRV was well tolerated and seemed to improve oxygenation and donation. It is possible that when the increase in lung donation during the transition from ACV to APRV was recognized, more attention was given to recruitment maneuvers and pulmonary optimization. However, our subjective impression is that this was not the case. In addition, although we demonstrated highly significant differences in lung donation rate and post-100% oxygen challenge PaO<sub>2</sub>/FIO<sub>2</sub> ratios, some of our negative results may be due to insufficient statistical power given the sample size.

In summary, our data suggest that the use of APRV leads to a significant improvement in PaO<sub>2</sub>/FIO<sub>2</sub> ratios and rate of lung donation in organ donors meeting standard criteria. In addition, graft survival of donors managed with APRV and ACV compare favorably with national averages. Perhaps by using alternative ventilator strategies such as APRV, donor pulmonary function can be maximized and lungs previously deemed unacceptable can be transplanted.

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**Correspondence:** Randy J. Janczyk, MD, Division of Trauma and Critical Care, Department of Surgery, William Beaumont Hospitals, 3601 W 13 Mile Rd, Royal Oak, MI 48073 (rjanczyk@beaumont.edu).

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