

# Novel method of delivery of continuous positive airway pressure for apnea testing during brain death evaluation

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Received 13 September 2016

Revised 22 November 2016

Accepted 25 November 2016

## ABSTRACT

**Background** There are several methods for apnea testing for the evaluation of neurological death, including oxygen via T-piece, oxygen cannula inserted into the endotracheal tube, and continuous positive airway pressure (CPAP). Lung suitability for transplantation is determined in part by the partial pressure of arterial oxygen (PaO<sub>2</sub>) to fraction of inspired oxygen (FiO<sub>2</sub>; P:F) ratio. We hypothesized that delivery of CPAP during apnea testing using a novel method would improve post-test P:F ratios.

**Methods** A retrospective review was performed at a level I trauma center for all patients undergoing apnea testing from 2010 to 2016. The CPAP system used a flow-inflating bag and was made available in 2012. It was used at the discretion of the clinician. Patients were classified as having an apnea test by CPAP or by non-CPAP method (T-piece, oxygen cannula in endotracheal tube, etc). The two groups were compared for baseline characteristics and the primary outcome of postapnea test P:F ratio.

**Results** During the study period, 145 patients underwent apnea testing; 67 patients by the CPAP method and 78 by non-CPAP method. There were no significant differences in demographics, mechanism of brain injury, pneumonia rate, smoking status, or antibiotic usage between the two groups. The pretest P:F ratio was similar between groups, but the CPAP group had significantly higher post-test P:F ratio (304 vs 250,  $p=0.02$ ). There were no reported complications arising from CPAP use.

**Conclusions** We describe a novel method of delivering CPAP by a flow-inflating bag during examination for brain death. This method led to improved oxygenation, P:F ratios, and may decrease barotrauma. The flow-inflating bag was inexpensive, easily implemented, and without adverse effects. Multicentered, prospective trials are needed to elicit significant benefit in lung donation and transplantation.

**Level of evidence** Level IV, diagnostic tests.

## BACKGROUND

Organ shortages continue to grow in the USA. As of August, 2016, there were over 77 000 people on the active waiting list for organ transplantation.<sup>1</sup> This great need for organs demands that as many organs as possible are procured from potential donors.<sup>2</sup> One of the organs with the lowest rate of recovery is lungs. In 2015, there were 9079 deceased donors. Of these, only 3791 lungs (left and right counted separately) were recovered, compared with 16 408 kidneys and 7416 livers.<sup>3</sup> Essentially all lung transplants come from deceased

donors;<sup>1</sup> therefore, management of deceased donors may greatly influence the quality of these organs.

Apnea testing is an essential component of declaration of death by neurological criteria,<sup>4–6</sup> the prerequisite for donation by deceased donors. In their most recent guidelines, the American Academy of Neurology recommends that the apnea testing component of declaration of death by neurological criteria be performed by inserting an oxygen cannula into the trachea or using a T-piece for the maintenance of oxygenation.<sup>6</sup> Unfortunately, disconnecting the ventilator and using an oxygen cannula or T-piece leads to atelectasis. For those patients who go on to become organ donors, atelectasis and higher pressures necessary to recruit the collapsed alveoli induced by apnea testing can cause significant injury and potentially decrease lung recovery rates.<sup>7</sup> The objective measure of lung quality used by most transplant surgeons is the P:F ratio, the ratio of the partial pressure of arterial oxygen (PaO<sub>2</sub>) to fraction of inspired oxygen (FiO<sub>2</sub>). The P:F ratio has been found to be significantly associated with organ recipient prognosis<sup>8</sup> and most transplant surgeons require a P:F ratio of >300 on a positive end expiratory pressure (PEEP) of 5 for eligibility.<sup>9</sup>

Continuous positive airway pressure (CPAP) delivers a constant pressure in the airways, either by invasive or non-invasive routes. CPAP has been shown to decrease atelectasis, increase P:F ratio, and decrease dyspnea in patients with respiratory compromise.<sup>10</sup> The potential benefit of decreased atelectasis with CPAP can also be used during apnea testing. CPAP was shown to improve oxygenation in a small trial where three methods (CPAP, oxygen cannula in trachea, and T-piece) were used in each patient,<sup>11</sup> and in a separate case report.<sup>12</sup> For the current study, we hypothesized that apnea testing with the use of CPAP would improve post-test P:F ratios and potentially lung transplantation rates.

## METHODS

Prior to 2012, there was no protocol for apnea testing at Community Regional Medical Center, a 650-bed, American College of Surgeons (ACS)-verified level 1 trauma center in Fresno, California. The medical and surgical intensivists variously used a T-piece with high flow oxygen, with the high flow oxygen cannula placed within the endotracheal tube, or CPAP via the ventilator at the discretion of the attending physician. The use of CPAP was anecdotally noted to cause less physiological disruption to the patient, but was

**To cite:** Hubbard JL, Dirks RC, Veneman WL, et al. *Trauma Surg Acute Care Open* Published Online First: [please include Day Month Year] doi:10.1136/tsaco-2016-000046

complicated by the automatic ventilator's safety feature giving breaths after prolonged periods of apnea (60 s). In conjunction with our respiratory care practitioners (RCPs), we developed a novel method of delivering CPAP via a flow inflating bag (figure 1). The flow inflating bag, also called an anesthesia bag, only inflates when connected to a gas source. CPAP is accomplished by an adjustable flow control valve and the opening must be sealed to sustain CPAP, that is, connected to the endotracheal tube. The gas used in this case was 100% oxygen. Most clinicians are more familiar with this device being used for neonates and children, but it can also be applied in the adult population. This method was made widely available throughout our multi-specialty intensive care units in 2012.

Subsequently, a retrospective review was performed for all patients undergoing apnea testing from January, 2010 to March, 2016. The study was approved by the regional organ procurement organization (OPO) Institutional Review Board (IRB) and deemed exempt by the University of California San Francisco Fresno IRB. The CPAP protocol, made available in 2012, was used at the discretion of the clinician, although encouraged by department leaders. Patients were classified as having an apnea test by CPAP or by non-CPAP method (T-piece, oxygen cannula in endotracheal tube, etc). The two groups were compared for baseline characteristics including demographics, mechanism of brain injury, torso trauma, pneumonia rate, smoking status, antibiotic usage, and ventilator mode. The primary outcomes were postapnea test P:F ratio and lung transplantation rates. Categorical data were analyzed by Fisher's exact or  $\chi^2$  tests and continuous variables analyzed by Mann-Whitney U tests with significance attributed to a p value  $\leq 0.05$ . Data were collected from the hospital's electronic medical records as well as records supplied by our regional OPO.

## RESULTS

During the study period, 145 patients underwent apnea testing; 67 patients by the CPAP method and 78 by non-CPAP method. There were no significant differences in demographics, mechanism of brain injury, smoking status, pneumonia rate, torso trauma, or antibiotic usage between the two groups (table 1). There was also no difference in the incidence of pneumonia, (community-acquired



**Figure 1** Flow inflating bag with adjustable pressure dial.

**Table 1** Baseline characteristics

	CPAP (n=67)	T-piece/O <sub>2</sub> cannula (n=78)	p Value
Age (mean±SD)	41±15	41±18	0.81
Male gender	49 (73%)	53 (68%)	0.50
Mechanism			
Penetrating trauma	13 (19%)	16 (21%)	0.87
Blunt trauma	25 (37%)	22 (28%)	0.24
Stroke	21 (31%)	32 (41%)	0.23
Anoxia	6 (9%)	8 (10%)	0.79
Other	2 (3%)	0	0.21
Smoking history			
Yes	7 (10%)	6 (8%)	0.92
No	20 (30%)	16 (20%)	(for known history)
Unknown	40 (60%)	56 (72%)	0.022
Pulmonary contusion	14 (21%)	6 (8%)	0.30
Rib fractures	6 (9%)	3 (4%)	0.25
Clinical pneumonia	8 (12%)	5 (6%)	
Respiratory cultures			
Negative	26 (39%)	28 (36%)	0.72
Community-acquired*	20 (30%)	21 (27%)	0.70
Hospital-acquired†	10 (15%)	10 (13%)	0.71
Not done	11 (16%)	19 (24%)	0.24
Antibiotics			
None	50 (75%)	55 (71%)	0.58
Narrow spectrum	5 (7%)	4 (5%)	0.73
Broad spectrum	12 (18%)	19 (24%)	0.35
Clinical performing test			
Surgical	35 (52%)	41 (53%)	0.97
Medical	30 (45%)	34 (44%)	0.89
Neurosurgical	2 (3%)	3 (4%)	0.78
Days postadmit (mean)	2.9±2.8	2.7±2.5	0.47
Donor management with APRV (% of authorized donors)	11 (23%)	3 (5%)	0.009

\*Organisms susceptible to narrow-spectrum antibiotics and usually acquired outside of a healthcare facility.

†Organisms resistant to narrow-spectrum antibiotics and usually acquired in a healthcare facility.

APRV, airway pressure release ventilation; CPAP, continuous positive airway pressure.

organisms or healthcare facility-acquired organisms) or admission service (medical vs surgical). There was a higher rate of pulmonary contusions in the CPAP group (21% vs 8%,  $p=0.022$ ).

Table 2 demonstrates the outcomes measured between the two groups. Pretest ventilator modes, oxygenation, and P:F ratios were similar between groups. The CPAP group versus non-CPAP group had significantly higher post-test P:F ratio (304 vs 250,  $p=0.02$ ). The CPAP group had longer length of tests that approached statistical significance (11.1 vs 10.4 min,  $p=0.052$ ). Additionally, the percentage of lung donors was higher in the CPAP group, although the power was not sufficient to obtain statistical significance. There were no reported complications arising from CPAP use.

## DISCUSSION

Organ shortages throughout the USA continue to be problematic. One way to increase the number of organs available is to maximize the number and quality of organs from each donor. This requires meticulous care of the donor while they are still a living patient, through the process of declaration of death by neurological criteria, and after declaration of death, when the

**Table 2** Outcomes

	CPAP (n=67)	T-piece/O <sub>2</sub> cannula (n=78)	p Value
Pretest vent mode APRV	1 (1%)	4 (5%)	0.37
Pretest PaO <sub>2</sub>	128±63	130±67	0.93
Pretest P:F	316±97	331±120	0.65
End-of-test P:F	304±135	250±143	0.02
Post-test compliance (mL/cm H <sub>2</sub> O)	41±17	40±11	0.77
Length of test (min)	11.1±2.2	10.4±2.4	0.052
Post-test vent mode APRV	2 (3%)	2 (3%)	1.00
Next day P:F	296±117	297±122	0.87
Authorization for organ donation	47 (70%)	57 (73%)	0.70
Lungs transplanted (% of authorized donors)	15 (32%)	13 (23%)	0.30

APRV, airway pressure release ventilation; CPAP, continuous positive airway pressure; FiO<sub>2</sub>, fraction of inspired oxygen; P:F, ratio of PaO<sub>2</sub> to FiO<sub>2</sub>; PaO<sub>2</sub>, partial pressure of arterial oxygen.

OPO takes over care of the patient. Our organization routinely uses lung-protective strategies with low tidal volumes (5–8 mL/kg) as this was shown to improve lung transplantation rates in a prior randomized trial.<sup>13</sup> However, our lung retrieval and transplantation rates were still suboptimal. In this study, we describe a technique which minimizes atelectasis by using CPAP for apnea testing for declaration of death by neurological criteria in order to prevent further injury to the lungs.

When an apneic patient is disconnected from the ventilator circuit for even brief periods of time, atelectasis, or collapse of the alveoli occurs. Once atelectasis occurs, greater pressure is required to reopen the airway than to maintain expansion of an already open airway.<sup>14</sup> Therefore, maintaining expansion of the alveoli during a prolonged period of apnea should lead to decreased pressure needed to re-expand the airway and less barotrauma to the airways. When we first took on this quality improvement initiative, it seemed easiest to use the ventilator in a CPAP mode. However, ventilators have a safety over-ride that initiates a breath after prolonged periods of apnea. The clinicians could determine that it was not a patient-initiated breath, but it confounds the overall validity of the test, as well as causing further confusion to family members who were present for the test. Using a flow inflating bag eliminated the possibility of an over-ride mechanism, yet remained inexpensive and simple to use.

Implementation of the CPAP protocol in our hospital was straightforward. The training for the RCPs took place as part of their monthly mandatory training sessions. The overall use of the device is simple and was easily implemented. When a physician notified the RCP that they were going to perform an apnea test, the RCP suggested use of the flow-inflating bag method. Over time, more physicians have adopted this method as its use has demonstrated good results and improved oxygenation. The flow inflating bag is equipment that is already available in most acute care hospitals, particularly in the emergency department, operating room, or in areas caring for children and neonates. The overall cost of the apparatus is \$10–\$20, limiting additional cost to the patient and hospital. The technique is now used by all clinicians in our institution. It has become our standard of care. Since the system is quite simple and effective, no changes have been made since it was instituted.

Although there was no statistical difference noted in most of the outcomes, the experience of the clinicians using this method was uniformly positive. Anecdotally, we were able to perform apnea tests for longer periods of time with little or no oxygen

desaturation. Saturations during the apnea test are not recorded in the medical record and the length of the test is documented inconsistently, so we were unable to statistically analyze these variables. We also anecdotally noted that we were able to complete apnea tests on patients with worse pulmonary function using the CPAP method, as was similarly noted in a prior case report.<sup>12</sup>

Interestingly, as noted in table 2, the end-of-test P:F ratio was significantly higher in the CPAP group. Furthermore, several patients actually had higher PaO<sub>2</sub> at the end of the test than they did at the beginning of the test. Feedback from the OPO was that the lung quality was significantly better in patients undergoing apnea testing with the CPAP method. The following day P:F ratios returned to essentially equivalent values, likely reflecting the ability of the lung to overcome the atelectasis. The amount of barotrauma re-expansion causes is unknown, but may play a role in the overall quality of the lungs. Unfortunately, this did not translate into a significant increase in the number of lungs transplanted during the study period. While we cannot ascertain the exact cause, it is likely a combination of factors such as an underpowered study in combination with clinical factors used in consideration of suitability for transplantation. A larger, randomized study might be able to assess these factors fully.

There are limitations to our study. The sample size is small and outcomes such as lung recovery rate are affected by a myriad of factors beyond a single procedure. As with any retrospective study, the possibility of selection bias exists. Prior to institution of the CPAP method, the method of apnea testing was always left to the treating physician. This continued to be the case after the method was instituted, though the RCPs and department leaders encouraged the switch. This was confirmed in reviewing the patient records. It appears that the selection of test method was based more on physician preference and not patient characteristics. This is reinforced by the similarity of the baseline characteristics between groups. A further confounding factor is the increased use of airway pressure release ventilation (APRV) in the CPAP group. In small series, APRV has been shown to improve lung retrieval rates.<sup>15</sup> After further investigation, we found that the vast majority of patients who had use of APRV were on it for <6 hours. The increased use of APRV in the CPAP group also likely reflects a shift in management strategies over time. The CPAP method was employed more frequently in the later time periods. This coincided with a shift in OPO management that included the use of APRV for short periods of time for selected patients. Further studies are needed to delineate the optimum protocols for management of donors prior to declaration of death by neurological criteria and OPO management after declaration.

In conclusion, apnea testing using CPAP has only been reported in a case report and a small series in the literature and has never been reported using a flow-inflating bag method. In this novel pilot study, we found that use of CPAP for apnea testing improved P:F ratios. This method was inexpensive, easily implemented, and without adverse effects. Further investigations with multicentered, prospective trials are warranted to elicit a true benefit in outcomes.

**Acknowledgements** Significant portions of data were provided by Donor Network West. The authors sincerely appreciate their help and support with this project. National statistics and data was supported in part by Health Resources and Services Administration contract 234-2005-37011C.

**Contributors** JLH and WLV designed the protocol and the study and did the data collection. RCD performed the statistical analysis. All authors participated in data interpretation. JLH wrote the manuscript, which all authors critically revised.

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**Competing interests** None declared.

**Patient consent** Obtained.

**Ethics approval** Local ethics committee in each of the participating centers.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** The only unpublished data are various clinical findings immediately before, during, and after apnea testing. Only the authors have access to the data.

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